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Chuyên luyện thi IELTS/SAT → AP / IB / A-levels

8020 ENGLISH

AP Biology

Giáo trình luyện thi chuyên sâu

Song ngữ Anh–Việt

8020 ENGLISH

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Lời mở đầu · Foreword

Cuốn sách này thuộc bộ giáo trình luyện thi chương trình quốc tế của **8020 English (8020 Education)** — trung tâm luyện thi trọng điểm **IELTS · SAT · AP · IB · A-level · IGCSE** và săn học bổng du học. Toàn bộ nội dung được biên soạn bởi đội ngũ **Giáo sư · Tiến sĩ · Thạc sĩ** tốt nghiệp các trường top đầu thế giới, bám sát khung chương trình chính thức, trình bày đầy đủ lý thuyết, ví dụ mẫu, hình minh hoạ và hệ thống bài tập có lời giải chi tiết.

This book is part of the 8020 English international exam-prep series: complete English theory with Vietnamese explanations, worked examples, illustrations and fully-solved practice, aligned to the official framework.

Thành tích 8020 English

9.0 IELTS cao nhất	**1570** SAT cao nhất
5/5 AP — điểm tuyệt đối	**90/100** IB Diploma
100% GV $\geq$ 8.0 IELTS / 1500 SAT	**CMU** Tiến sĩ ĐH #1 Hoa Kỳ về CS

Đội ngũ tiêu biểu: Thầy Châu Cát Tường (Academic Head, ThS Western Sydney, top 1% IELTS 8.5) · TS Nguyễn Anh Huy (Carnegie Mellon, cựu kỹ sư Amazon) · TS Nguyễn Phước Trường (Toán, ĐH Klagenfurt) · cùng đội ngũ giảng viên SAT 1500–1600, IELTS 8.0–8.5.

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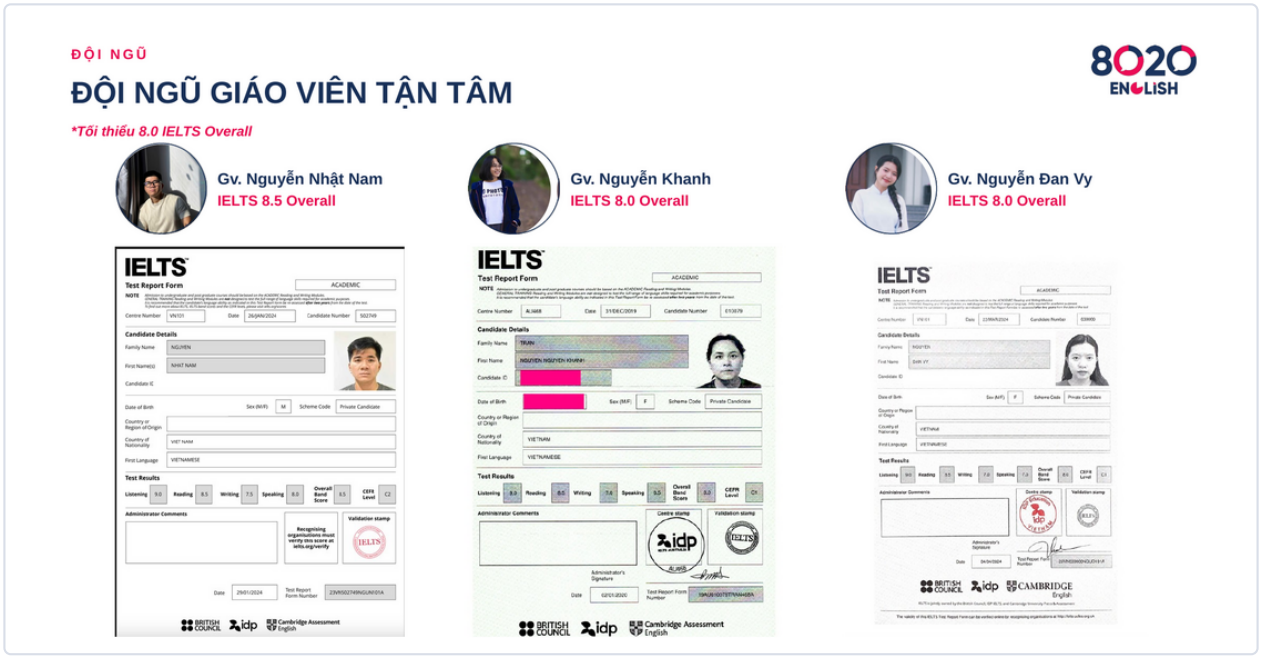
"Cuối cùng đã đậu vào trường top như mong muốn." — Phan Thị Thanh Hằng, IELTS Overall 8.5.

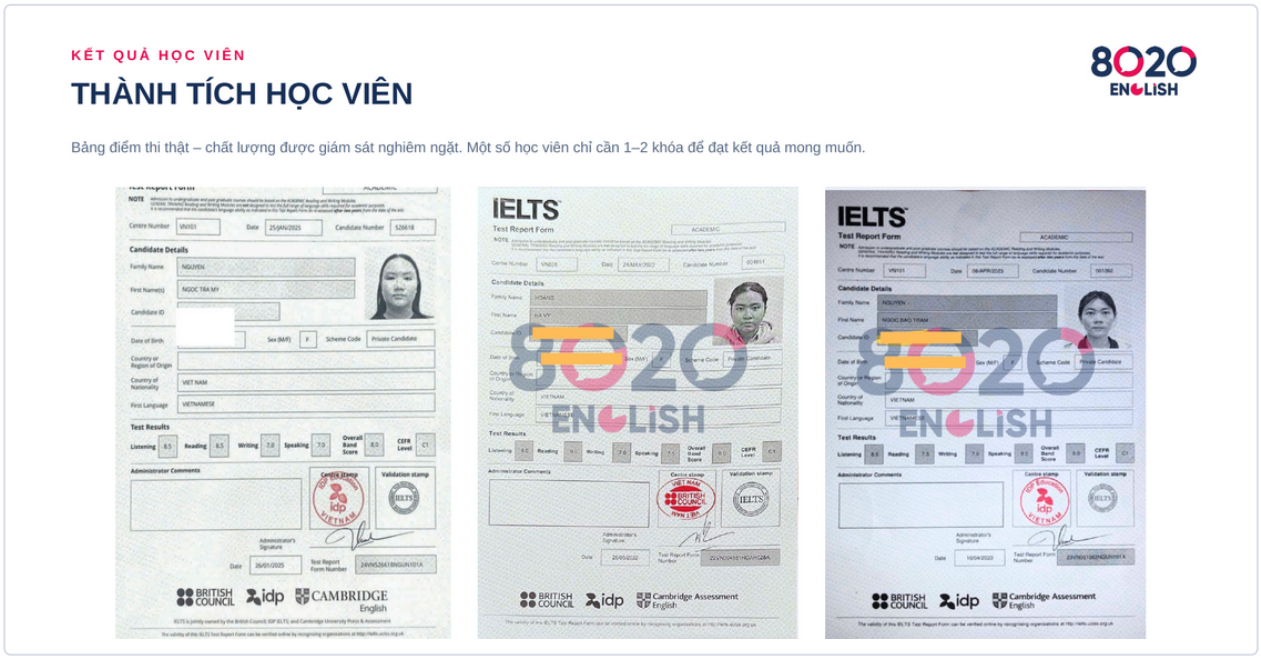
Cách dùng sách hiệu quả: mỗi Unit gồm (1) **Lý thuyết trọng tâm** tiếng Anh kèm **giải thích tiếng Việt**; (2) **Ví dụ mẫu** có lời giải; (3) **Hệ thống bài tập** kèm **lời giải chi tiết**. Hãy tự làm bài trước khi xem lời giải để đạt hiệu quả tối đa.

THÀNH TÍCH THỰC TẾ · 8020 ENGLISH

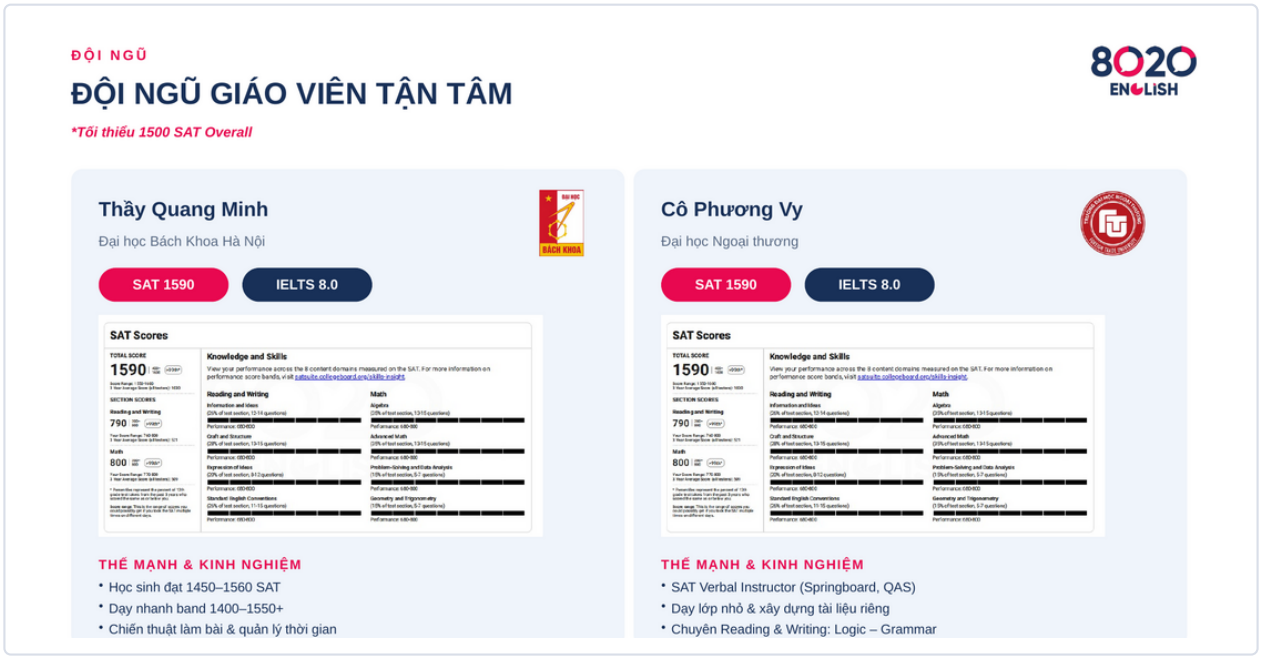
Điểm thi thật · Bằng & bảng điểm thật của giảng viên và học viên 8020 English — **Điểm thật · Thầy thật · Kết quả thật**



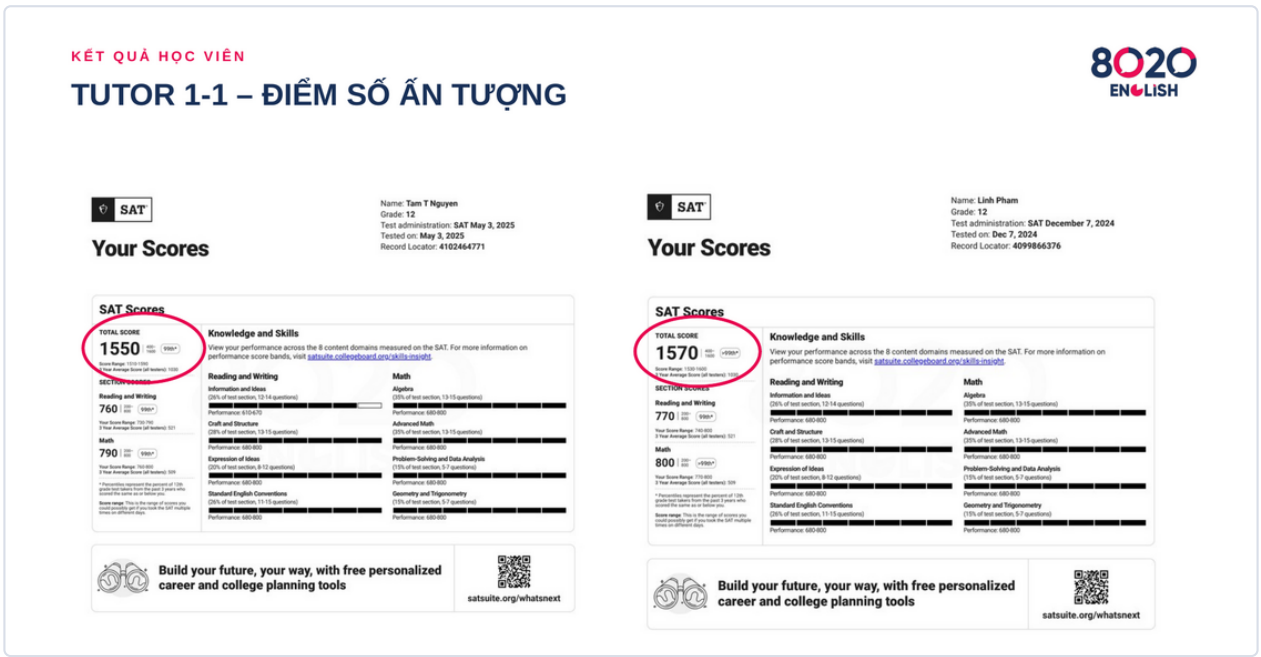
Giảng viên 8020 — IELTS 8.5 & 8.0 Overall (British Council · IDP · Cambridge)



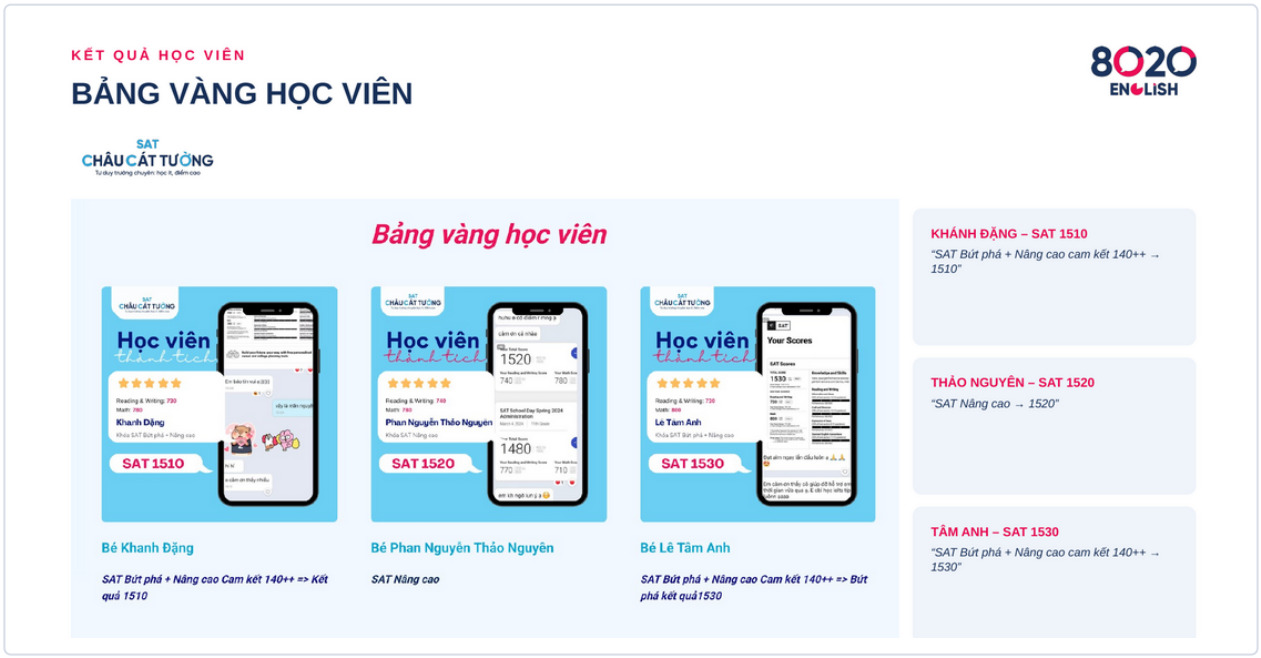
Học viên 8020 — IELTS 8.0 Overall (bảng điểm thật)



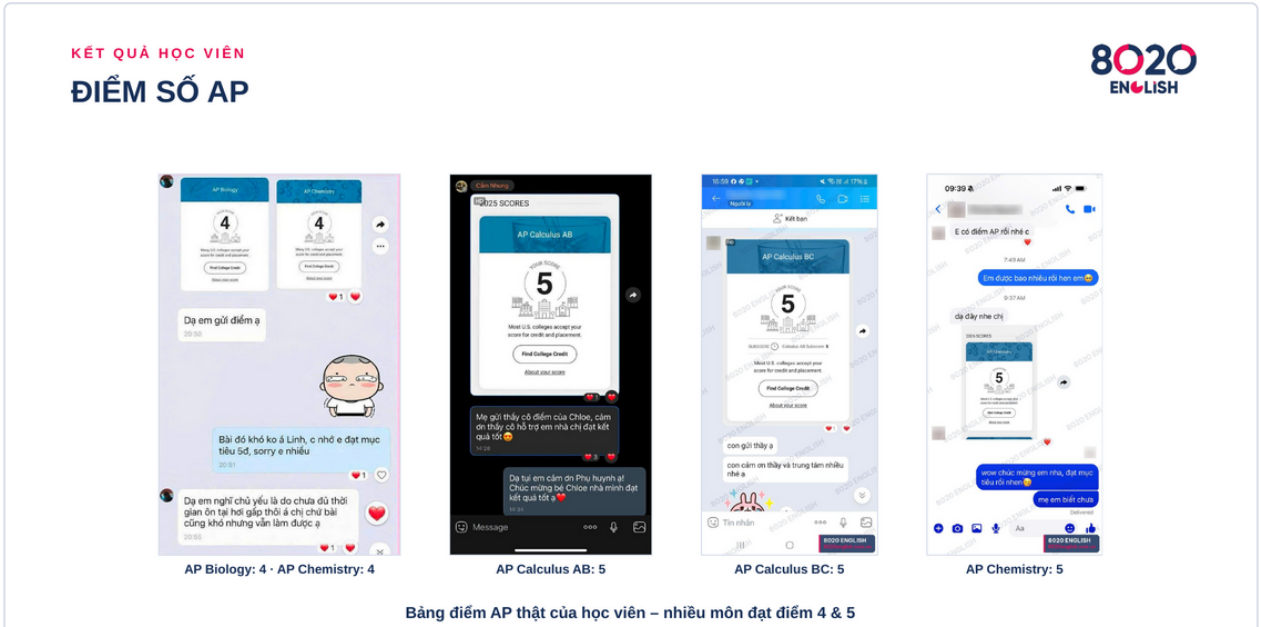
Giảng viên 8020 — SAT 1590 (ĐH Bách Khoa Hà Nội & ĐH Ngoại thương)



Học viên 8020 — SAT 1550 & 1570 (College Board)



Bảng vàng SAT — Học viên đạt 1510 · 1520 · 1530



Điểm AP thật — Calculus AB/BC 5/5 · Biology & Chemistry 4–5 (College Board)

Mục lục · Contents

Chemistry of Life

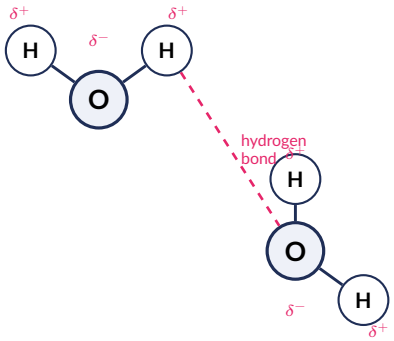
Mục tiêu Unit: Tính phân cực và liên kết hydro của nước cùng các tính chất đặc biệt (sức căng bề mặt, mao dẫn, nhiệt dung riêng cao, băng nổi, dung môi vạn năng); thang pH, acid–base và hệ đệm sinh học; các nguyên tố cấu tạo sự sống (CHNOPS) và nhóm chức hữu cơ; nguyên tắc chung tổng hợp – thuỷ phân đại phân tử; và cấu trúc – chức năng của bốn nhóm đại phân tử sinh học: carbohydrate, lipid, protein, và acid nucleic.

1.1 Water: Structure and Emergent Properties

1.1.1 Polarity and hydrogen bonding

A water molecule (H_2O) consists of one oxygen atom covalently bonded to two hydrogen atoms, bent at an angle of about $104.5°$. Because oxygen is far more electronegative than hydrogen, the shared electrons in each O–H bond sit closer to the oxygen nucleus. This produces a **polar covalent molecule**: the oxygen carries a partial negative charge (δ^-) and each hydrogen carries a partial positive charge (δ^+). The bent geometry means these partial charges do not cancel, so the whole molecule has a permanent dipole.

Because neighboring water molecules carry opposite partial charges on their O and H atoms, the δ^+ hydrogen of one molecule is weakly attracted to the δ^- oxygen of an adjacent molecule. This attraction is a **hydrogen bond**: a weak, non-covalent interaction (roughly 5–10% the strength of a covalent bond) that forms whenever a hydrogen atom is covalently bonded to a highly electronegative atom (O, N, or F) and is attracted to another electronegative atom nearby. Each water molecule can donate two hydrogen bonds (through its two H atoms) and accept two more (through the two lone electron pairs on O), so on average each molecule in liquid water hydrogen-bonds to about four neighbors at any instant. Individually weak, collectively these bonds are constantly breaking and re-forming, and their sheer number gives liquid water an extensive, dynamic three-dimensional network responsible for nearly every distinctive property of water discussed below.



Two water molecules: the bent shape and unequal sharing of electrons give each molecule partial charges (δ^+ on H, δ^- on O). The dashed line shows one hydrogen bond linking a δ^+ hydrogen of one molecule to the δ^- oxygen of a neighbor.

VN **GIẢI THÍCH TIẾNG VIỆT**

Phân tử nước có hình chữ V (góc liên kết $\approx 104.5°$) do oxy có độ âm điện lớn hơn hydro nên electron dùng chung bị kéo lệch về phía oxy, tạo ra **điện tích một phần**: oxy mang δ^-, mỗi

hydro mang δ^+. Vì phân tử không đối xứng nên các điện tích này không triệt tiêu nhau — nước là phân tử **phân cực**. **Liên kết hydro** hình thành giữa nguyên tử H mang δ^+ của phân tử này với nguyên tử O mang δ^- của phân tử bên cạnh; đây là liên kết yếu nhưng do số lượng rất lớn nên tạo ra mạng lưới liên kết hydro đặc trưng của nước lỏng — chính mạng lưới này là nguồn gốc của mọi tính chất đặc biệt của nước trình bày ở phần sau.

1.1.2 Emergent properties of water

The hydrogen-bonded network gives liquid water a set of **emergent properties** — properties not predictable just from the individual H_2O molecule — that make life as we know it possible.

Emergent properties of water

- **Cohesion:** hydrogen bonds hold water molecules to one another, giving liquid water unusually high internal attraction (responsible for the long, unbroken columns of water pulled up through plant xylem).
- **Adhesion:** water also hydrogen-bonds to other polar surfaces (e.g., the cellulose walls of xylem vessels).
- **Capillary action:** the combined effect of cohesion and adhesion, allowing water to rise against gravity in narrow tubes.
- **Surface tension:** cohesive hydrogen bonding at the air–water interface creates an elastic "skin," resisting an object breaking the surface (allows insects such as water striders to walk on water).
- **High specific heat:** large amounts of thermal energy must be absorbed to break hydrogen bonds and raise water's temperature (and released when it cools), so water resists rapid temperature change and buffers the temperature of cells, organisms, and aquatic environments. A related property, high **heat of vaporization**, is why evaporating sweat cools the skin so effectively.
- **Lower density of ice than liquid water:** in ice, each molecule forms four fixed hydrogen bonds in an open hexagonal lattice that holds molecules farther apart than in the more randomly packed liquid; ice is therefore about 9% less dense and floats, insulating the liquid water below and allowing aquatic life to survive winters.
- **Versatile ("universal") solvent:** water's polarity lets it surround and dissolve other polar and ionic substances, forming hydration shells around ions (e.g., Na^+, Cl^-) and polar molecules (e.g., sugars), which is essential for the aqueous chemistry of the cell.

Ví dụ mẫu · Water's high specific heat and thermoregulation

During moderate exercise, a 70 kg person generates 2.1×10^5 J of excess metabolic heat over 30 minutes. Water makes up about 60% of body mass. Assuming (for simplicity) that this heat is absorbed only by the body's water content, with no heat lost to the surroundings, estimate the resulting rise in body temperature. Use $c_{\text{water}} = 4.184$ J/(g $\cdot^\circ$ C).

Mass of water: $70\,000$ g $\times\, 0.60 = 42\,000$ g.

Apply $q = mc\Delta T \Rightarrow \Delta T = \dfrac{q}{mc}$:

$$\Delta T = \frac{2.1 \times 10^5 \text{ J}}{(42\,000 \text{ g})(4.184 \text{ J/(g}\cdot^\circ\text{C)})} = \frac{2.1 \times 10^5}{1.757 \times 10^5} \approx 1.2^\circ\text{C}.$$

Despite generating a large amount of heat, the body's high water content limits the temperature rise to only about $1.2°$C — but this residual heat is exactly why additional cooling mechanisms (sweating and evaporative heat loss) are still needed during sustained exercise.

VN **GIẢI THÍCH TIẾNG VIỆT**

Nhiệt dung riêng của nước rất cao (4.184 J/(g $\cdot\,^\circ$ C)) vì phần lớn nhiệt năng đưa vào bị dùng để **bẻ gãy liên kết hydro** thay vì làm tăng động năng (nhiệt độ) của phân tử. Nhờ vậy, nước trong cơ thể và trong các hệ sinh thái dưới nước đóng vai trò như một "bộ đệm nhiệt" — hấp thụ hoặc giải phóng một lượng nhiệt lớn mà nhiệt độ chỉ thay đổi rất ít, giúp ổn định môi trường sống cho sinh vật.

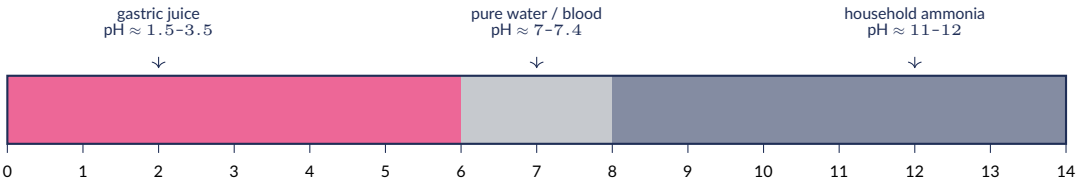
(!) Lỗi thường gặp: "Chất rắn luôn đặc hơn chất lỏng cùng loại" — sai đối với nước. Trong nước đá, mỗi phân tử bị khoá cố định trong **4** liên kết hydro tạo mạng tinh thể lục giác cồng kềnh, khiến các phân tử cách xa nhau hơn so với nước lỏng (nơi liên kết hydro liên tục đứt và tái tạo, các phân tử có thể xếp gần nhau hơn). Do đó băng *nổi* trên nước lỏng — một tính chất bất thường nhưng quan trọng, giúp cách nhiệt cho lớp nước bên dưới vào mùa đông.

1.1.3 pH, acids, bases, and buffers

Water molecules occasionally dissociate into a hydrogen ion (H^+, essentially a bare proton) and a hydroxide ion (OH^-). The **pH scale** quantifies the hydrogen ion concentration of an aqueous solution:

$$\text{pH} = -\log_{10}[H^+]$$

The scale runs from 0 to 14. Pure water at $25°$C has $[H^+] = 10^{-7}$ M, so pH $= 7$ (**neutral**). An **acid** donates H^+ and lowers pH (pH < 7); a **base** accepts H^+ (or donates OH^-) and raises pH (pH > 7). Because the scale is logarithmic, each single-unit drop in pH represents a **tenfold** increase in $[H^+]$.



The pH scale: 0 (strongly acidic) to 14 (strongly basic); pH 7 is neutral. Each whole-number step is a tenfold change in $[H^+]$.

Living systems must keep internal pH within a very narrow range, because the ionization state of functional groups on proteins and nucleic acids (and therefore their shape and activity) is pH-sensitive. A **buffer** is a solution that resists pH change by reversibly absorbing or releasing H^+, typically using a weak acid and its conjugate base in equilibrium.

Ví dụ mẫu · The bicarbonate buffer system

During intense exercise, muscle cells release lactic acid, adding H^+ to the bloodstream. Explain how the bicarbonate buffer system keeps blood pH close to its normal range of 7.35–7.45, given the equilibrium:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

Reasoning: added H^+ shifts the equilibrium to the *left* (Le Chatelier's principle) — excess H^+ combines with bicarbonate (HCO_3^-) to form carbonic acid (H_2CO_3), which decomposes to CO_2 and H_2O. This consumes the free H^+ before it can substantially lower blood pH. The CO_2 produced then diffuses into the lungs and is exhaled, removing it from the equilibrium entirely and allowing the buffering capacity to continue. (Conversely, hyperventilating — exhaling CO_2 faster than it is produced — also pulls the equilibrium to the *left* to replace the lost CO_2, drawing H^+ and HCO_3^- back toward H_2CO_3; this consumes H^+ and raises blood pH.)

VN **GIẢI THÍCH TIẾNG VIỆT**

Hệ đệm bicarbonate trong máu hoạt động theo cân bằng $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$. Khi có thêm H^+ (ví dụ do acid lactic sinh ra khi vận động mạnh), cân bằng dịch chuyển sang trái để "hấp thụ" bớt H^+, giữ pH máu ổn định trong khoảng hẹp 7.35–7.45; khí CO_2 dư sau đó được thải ra qua phổi. Đây là ví dụ điển hình cho thấy hệ đệm không "triệt tiêu" acid/base mà chỉ làm chậm và giảm thiểu sự thay đổi pH.

1.2 The Building Blocks of Life

1.2.1 CHNOPS and trace elements

Roughly 96% of the mass of a living cell is built from just four elements — **C**arbon, **H**ydrogen, **N**itrogen, and **O**xygen — with **P**hosphorus and **S**ulfur close behind, together giving the mnemonic **CHNOPS**. These six elements form the backbones and functional groups of the four major biological macromolecules covered later in this unit. A handful of additional elements are required only in tiny amounts — **trace elements** — yet are just as essential: for example, **iron (Fe)** is a component of hemoglobin and the cytochromes of the electron transport chain; **iodine (I)** is required to build thyroid hormones; **calcium (Ca)** is used in bone, shell, and intracellular signaling; **magnesium (Mg)** sits at the center of the chlorophyll molecule and acts as a cofactor for many enzymes; and **sodium and potassium (Na, K)** generate the electrochemical gradients that drive nerve impulses.

VN **GIẢI THÍCH TIẾNG VIỆT**

CHNOPS (Carbon, Hydrogen, Nitrogen, Oxygen, Phosphorus, Sulfur) chiếm phần lớn khối lượng cơ thể sống và là thành phần chính của bốn nhóm đại phân tử sinh học. Bên cạnh đó, các **nguyên tố vi lượng** (trace elements) chỉ cần với lượng rất nhỏ nhưng không thể thiếu: Fe trong hemoglobin, I trong hormone tuyến giáp, Ca trong xương và tín hiệu tế bào, Mg trong diệp lục. "Vi lượng" không có nghĩa là "không quan trọng" — thiếu i-ốt hay sắt vẫn gây bệnh lý nghiêm trọng dù chỉ cần một lượng rất nhỏ mỗi ngày.

1.2.2 Carbon's tetravalency and molecular diversity

Carbon is the structural backbone of essentially every biological molecule. With four valence electrons, a carbon atom forms exactly **four covalent bonds**, which can be single, double, or triple, and can be made to other carbons or to H, N, O, P, or S. This tetravalency lets carbon atoms link into long chains, branched trees, and closed rings, and to do so while still leaving bonding positions free for the functional groups that give each molecule its chemical personality. The combination of near-unlimited skeletal variety (chain length, branching, ring formation, double-bond placement) and attachable functional groups is what allows a small set of elements to generate the immense structural diversity of carbohydrates, lipids, proteins, and nucleic acids.

Why carbon?

Carbon's four bonds, combined with strong, kinetically stable carbon–carbon and carbon–hydrogen bonds across the range of temperatures compatible with life, allow it to form the long chains, branches, and rings that no other common element matches — the chemical basis of organic (carbon-based) molecular diversity.

VN **GIẢI THÍCH TIẾNG VIỆT**

Carbon có 4 electron hoá trị nên luôn tạo đúng 4 liên kết cộng hoá trị (đơn, đôi, hoặc ba), cho phép nó liên kết thành mạch thẳng, mạch nhánh, hoặc vòng kín, đồng thời vẫn còn vị trí để gắn thêm các nhóm chức khác nhau. Chính khả năng "khung xương" linh hoạt này — kết hợp với các nhóm chức — tạo ra sự đa dạng gần như vô hạn của các phân tử hữu cơ, là nền tảng hoá học của toàn bộ sự sống.

1.2.3 Functional groups

A **functional group** is a small cluster of atoms, attached to a carbon skeleton, that behaves consistently and predictably wherever it appears — it determines how a molecule interacts with water and with other molecules. Seven functional groups recur constantly in biological macromolecules:

Group	Structure	Polarity / charge	Where it matters
Hydroxyl	$-OH$	polar; H-bond donor/acceptor	alcohols, sugars — raises solubility
Carbonyl	$-C{=}O$	polar	terminal = *aldehyde*; internal = *ketone* (e.g., sugars)
Carboxyl	$-COOH$	acidic; ionizes to $-COO^-$	amino acids, fatty acids
Amino	$-NH_2$	basic; ionizes to $-NH_3^+$	amino acids — forms peptide bonds
Phosphate	$-OPO_3^{2-}$	acidic; strongly polar, negatively charged	nucleotides (DNA/RNA, ATP), phospholipid heads
Sulfhydryl	$-SH$	polar	cysteine — forms disulfide bridges ($-S{-}S-$)
Methyl	$-CH_3$	nonpolar; hydrophobic	affects shape/hydrophobicity; DNA methylation regulates genes

Ví dụ mẫu · Identifying functional groups

Serine, an amino acid, has the structure $H_2N{-}CH(CH_2OH){-}COOH$. Identify its functional groups and predict its behavior in water.

Scanning the structure: an **amino group** ($-NH_2$, basic) on the central carbon, a **carboxyl group** ($-COOH$, acidic) also on the central carbon, and a **hydroxyl group** ($-OH$) on the side chain. All three groups are polar/ionizable, so serine is highly water-soluble; the amino and carboxyl groups can each ionize (to $-NH_3^+$ and $-COO^-$), which is why free amino acids in solution near neutral pH exist mostly as **zwitterions** (carrying both a positive and a negative charge simultaneously).

VN **GIẢI THÍCH TIẾNG VIỆT**

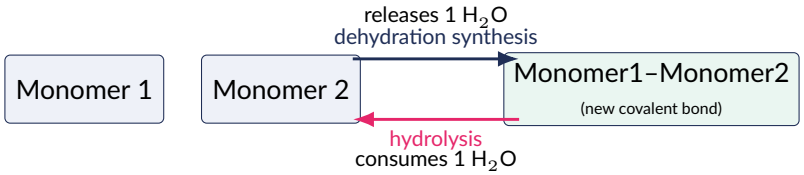
Nhóm chức quyết định tính chất hoá học của một phân tử hữu cơ, bất kể phân tử đó lớn hay nhỏ. Nhóm **hydroxyl, carbonyl** phân cực nhưng trung hoà điện; nhóm **carboxyl** và **phosphate** có tính acid (dễ mất H^+ để tích điện âm); nhóm **amino** có tính base (dễ nhận thêm H^+ để tích điện dương); nhóm **sulfhydryl** đặc biệt vì hai nhóm $-SH$ có thể liên kết với nhau tạo cầu nối

disulfide, rất quan trọng trong việc giữ ổn định cấu trúc protein; còn nhóm **methyl** không phân cực, làm tăng tính kỵ nước và còn đóng vai trò điều hoà biểu hiện gene (methyl hoá DNA).

1.3 Macromolecules: Assembly and Breakdown

1.3.1 Monomers, polymers, dehydration synthesis, and hydrolysis

Three of the four classes of biological macromolecules — carbohydrates, proteins, and nucleic acids — are built as **polymers**: long chains assembled from repeating smaller subunits called **monomers**. Monomers are joined by a reaction called **dehydration synthesis** (or condensation): a hydroxyl group (—OH) is removed from one monomer and a hydrogen atom (—H) is removed from the other, forming a new covalent bond between them and releasing one molecule of water. Because this reaction requires an input of energy and specific enzymes to proceed, cells build polymers only where and when it is metabolically favorable to do so. The reverse reaction, **hydrolysis** ("water-splitting"), adds a water molecule across a covalent bond, using the —H and —OH from that water to break the bond and separate the two monomers again; hydrolysis is how digestive enzymes disassemble food polymers into absorbable monomers.



Dehydration synthesis joins two monomers by removing —H from one and —OH from the other, releasing one H_2O per new bond. Hydrolysis is the reverse: one H_2O molecule is consumed to break the bond and regenerate the two monomers.

Macromolecule	Monomer	Linking bond	Example polymers
Carbohydrates	Monosaccharide	Glycosidic bond	Starch, glycogen, cellulose, chitin
Proteins	Amino acid	Peptide bond	Enzymes, antibodies, keratin, collagen
Nucleic acids	Nucleotide	Phosphodiester bond	DNA, RNA
Lipids	(not a true repeating polymer)	Ester bond	Triglycerides, phospholipids

VN **GIẢI THÍCH TIẾNG VIỆT**

Tổng hợp khử nước / trùng ngưng (dehydration synthesis) nối hai monomer lại với nhau, *giải phóng* một phân tử H_2O cho mỗi liên kết mới; **thuỷ phân** (hydrolysis) là phản ứng ngược lại, *sử dụng* một phân tử H_2O để cắt đứt liên kết. Ba trong bốn nhóm đại phân tử (carbohydrate, protein, acid nucleic) là các **polymer** thật sự — chuỗi lặp lại của monomer; riêng **lipid** (ví dụ triglyceride) được hình thành bằng cùng cơ chế tổng hợp khử nước nhưng không phải là polymer theo đúng nghĩa (glycerol không phải là đơn vị lặp lại).

(!) Lỗi thường gặp: Đừng nhầm chiều của hai phản ứng. **Tổng hợp khử nước (dehydration synthesis)**: 2 monomer → 1 polymer + H_2O (giải phóng nước, "xây dựng"). **Thuỷ phân (hydrolysis)**: 1 polymer + H_2O → 2 monomer (tiêu thụ nước, "phá vỡ"). Ghi nhớ: chữ "hydro" trong hydrolysis nghĩa là nước tham gia vào phản ứng như một *chất phản ứng* (bị tiêu thụ), không phải sản phẩm.

1.4 Carbohydrates

1.4.1 Monosaccharides and disaccharides

Monosaccharides are the simplest carbohydrates: single-sugar molecules with the general formula $(CH_2O)_n$, typically containing one carbonyl group and multiple hydroxyl groups. The most important six-carbon (hexose) sugar is **glucose** ($C_6H_{12}O_6$), the primary fuel of cellular respiration; its structural isomers **fructose** (fruit sugar) and **galactose** share the same molecular formula but differ in atom arrangement, giving each a distinct shape and taste. Five-carbon (pentose) sugars — **ribose** and **deoxyribose** — form the sugar component of RNA and DNA nucleotides, respectively (Section 1.7).

Two monosaccharides join by dehydration synthesis to form a **disaccharide**, linked by a **glycosidic bond**. **Maltose** (glucose + glucose) forms during starch digestion; **sucrose** (glucose + fructose) is common table sugar, transported through plant phloem; **lactose** (galactose + glucose) is the sugar of milk.

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Monosaccharide là đường đơn (glucose, fructose, galactose — cùng công thức $C_6H_{12}O_6$ nhưng khác cấu trúc không gian nên là đồng phân cấu trúc của nhau). Hai monosaccharide liên kết bằng **liên kết glycosidic** (qua phản ứng tổng hợp khử nước) tạo thành **disaccharide**: maltose (glucose–glucose), sucrose (glucose–fructose, đường ăn hàng ngày), lactose (galactose–glucose, đường trong sữa).

1.4.2 Polysaccharides and glycosidic linkages

Polysaccharides are long polymers of hundreds to thousands of monosaccharides. The geometry of the glycosidic bond matters enormously for structure and function. Glucose can close into a ring in two slightly different orientations: in **α-glucose** the hydroxyl on carbon 1 points below the ring plane; in **β-glucose** it points above. Polymers built from α-glucose form helical, easily-hydrolyzed chains (storage molecules); polymers built from β-glucose form straight, tightly hydrogen-bonded, mechanically tough chains (structural molecules) — and critically, most animals' digestive enzymes can hydrolyze α but not β glycosidic bonds.

Polysaccharide	Monomer linkage	Branching	Found in	Role
Starch (amylose/amylopectin)	α-1,4 (amylopectin also α-1,6)	unbranched / moderately branched	plants (seeds, tubers)	energy storage
Glycogen	α-1,4 and α-1,6	highly branched	animals (liver, muscle)	energy storage
Cellulose	β-1,4	unbranched	plant cell walls	structural
Chitin	β-1,4 (of N-acetylglucosamine)	unbranched	arthropod exoskeletons, fungal cell walls	structural

Starch and glycogen are both storage polysaccharides built from α-glucose, but glycogen is far more heavily branched, exposing many more free ends from which glucose can be rapidly added or removed to meet an animal's fluctuating energy demands. Cellulose, built from β-glucose, forms straight chains that pack side-by-side into hydrogen-bonded microfibrils of great tensile strength — the main structural component of plant cell walls. Chitin is chemically similar to cellulose but its glucose monomer is modified into **N-acetylglucosamine** (a nitrogen-containing derivative); it forms the exoskeletons of arthropods and the cell walls of fungi.

Ví dụ mẫu · Counting bonds in polysaccharide hydrolysis

A cellulose fragment is a linear chain of $n = 1000$ glucose monomers joined end-to-end by β-1,4 glycosidic bonds. If the fragment is completely hydrolyzed: (a) how many glycosidic bonds are broken? (b) how many water molecules are consumed? (c) how many free glucose

monomers result?

For a linear chain of n monomers, there are always $n-1$ bonds linking them. Here $n-1 = 1000-1 = 999$ glycosidic bonds. **(a)** 999 bonds broken. **(b)** Each hydrolysis reaction consumes exactly one H_2O per bond broken, so 999 water molecules are consumed. **(c)** All 1000 glucose monomers are released as free monosaccharides.

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Sự khác biệt duy nhất giữa tinh bột (starch) và cellulose — về mặt hoá học — là hướng của liên kết glycosidic: α-1,4 (starch) so với β-1,4 (cellulose). Enzyme amylase của người chỉ nhận diện và cắt được liên kết α, nên ta tiêu hoá được tinh bột nhưng không tiêu hoá được cellulose (chất xơ) — dù cả hai đều chỉ là chuỗi glucose. Glycogen là dạng dự trữ năng lượng ở động vật (gan, cơ), phân nhánh nhiều hơn tinh bột thực vật để huy động glucose nhanh hơn khi cần.

1.5 Lipids

1.5.1 Triglycerides: saturated and unsaturated fatty acids

Lipids are a chemically diverse group unified by one property: they are **hydrophobic** (nonpolar, poorly soluble in water) because they consist mostly of long hydrocarbon chains. A **triglyceride** (fat/oil) forms when one **glycerol** molecule (a three-carbon alcohol with three hydroxyl groups) undergoes dehydration synthesis with three **fatty acids** (long hydrocarbon chains ending in a carboxyl group), forming three **ester bonds**. Triglycerides store roughly twice the energy per gram of carbohydrates because their carbon skeleton is more reduced (more C–H bonds, fewer oxygen atoms already present to "waste" further oxidation on).

A fatty acid is **saturated** if it has no carbon–carbon double bonds — every carbon is "saturated" with the maximum number of hydrogens, giving a straight chain. A fatty acid is **unsaturated** if it contains one (monounsaturated) or more (polyunsaturated) C=C double bonds, which typically introduce a rigid $\approx 30^\circ$ kink (in the common *cis* configuration).

Ví dụ mẫu · Saturation and melting point

Compare stearic acid ($18{:}0$, fully saturated) and oleic acid ($18{:}1$, one *cis* double bond) at room temperature (≈ 20–25°C). Which is solid, which is liquid, and why?

Stearic acid's straight, saturated chain allows neighboring fatty acid tails to pack closely together, maximizing van der Waals contact between chains; this gives it a high melting point ($\approx 69^\circ$C), so it is **solid** at room temperature. Oleic acid's *cis* double bond puts a fixed kink in the chain, preventing tight packing and weakening van der Waals interactions between neighboring molecules; its melting point drops to $\approx 13^\circ$C, so it is **liquid** at room temperature. This is the general rule: more double bonds $\Rightarrow$ more kinks $\Rightarrow$ looser packing $\Rightarrow$ lower melting point — which is why animal fats (mostly saturated) are typically solid and plant oils (mostly unsaturated) are typically liquid.

Ví dụ mẫu · Counting waters released in triglyceride formation

One triglyceride forms from one glycerol and three fatty acids through three separate dehydration reactions. How many water molecules are released in total, and what kind of bond links each fatty acid to glycerol?

Each of the three ester bonds forms by removing an $-$OH from glycerol and an $-$H from a fatty acid's carboxyl group, releasing one H_2O per bond. Total released: $3 \times H_2O = 3$ water

molecules. Each fatty acid is attached to glycerol by an **ester bond** (the condensation product of a hydroxyl and a carboxyl group).

VN **GIẢI THÍCH TIẾNG VIỆT**

Triglyceride = 1 glycerol $+ 3$ acid béo, liên kết bằng 3 liên kết ester (giải phóng 3 phân tử nước). Acid béo **bão hoà** (saturated — không có liên kết đôi C=C) có mạch thẳng, xếp khít nhau, thường ở thể **rắn** ở nhiệt độ phòng (mỡ động vật). Acid béo **không bão hoà** (unsaturated — có ≥ 1 liên kết đôi) bị "gãy khúc" tại vị trí liên kết đôi, xếp lỏng lẻo hơn, thường ở thể **lỏng** ở nhiệt độ phòng (dầu thực vật).

(!) Lỗi thường gặp: "Chất béo bão hoà (saturated) $=$ không tốt cho sức khoẻ, chất béo không bão hoà $=$ tốt cho sức khoẻ" là một sự đơn giản hoá quá mức. Về mặt *cấu trúc hoá học*, sự khác biệt chỉ là có hay không có liên kết đôi C=C — cả hai loại đều được tế bào sử dụng làm nguồn dự trữ năng lượng và (với phospholipid) thành phần màng tế bào. Ngoại lệ đáng chú ý: **chất béo chuyển hoá (trans fat)**, tạo ra khi hydro hoá một phần dầu thực vật, là chất béo không bão hoà nhưng có cấu hình *trans* khiến mạch thẳng như chất béo bão hoà — kết hợp tính chất "dễ đóng rắn" của bão hoà lẫn nguồn gốc "không bão hoà".

1.5.2 Phospholipids and membrane formation

A **phospholipid** resembles a triglyceride, but one of the three fatty acids is replaced by a phosphate-containing group (often further modified, e.g., with choline). This gives the molecule two very different ends: a hydrophilic ("water-loving") **polar head** built around the charged phosphate group, and two hydrophobic ("water-fearing") nonpolar **fatty acid tails**. A molecule with both hydrophilic and hydrophobic regions is called **amphipathic**. When phospholipids are placed in water, they spontaneously self-assemble so that hydrophobic tails cluster away from water while polar heads face outward into the surrounding water on both sides — forming a **phospholipid bilayer**, the basic architecture of every cell membrane.

VN **GIẢI THÍCH TIẾNG VIỆT**

Phospholipid có cấu trúc **lưỡng tính (amphipathic)**: đầu phosphate ưa nước (hydrophilic) và hai đuôi acid béo kỵ nước (hydrophobic). Trong môi trường nước, các phân tử này tự sắp xếp sao cho đuôi kỵ nước "trốn" vào bên trong, đầu ưa nước quay ra ngoài tiếp xúc với nước ở cả hai phía — tạo thành **lớp kép phospholipid (bilayer)**, cấu trúc nền tảng của mọi màng sinh chất.

1.5.3 Steroids and waxes

Steroids are lipids built around a distinctive carbon skeleton of four fused rings — three six-membered and one five-membered. **Cholesterol**, the best-known steroid, is a component of animal cell membranes (where it modulates membrane fluidity) and is the metabolic precursor of steroid hormones such as testosterone, estrogen, and cortisol. **Waxes** are esters of a long-chain fatty acid with a long-chain alcohol; extremely hydrophobic, they form protective, waterproof coatings such as the cuticle of plant leaves, bird feather coatings, and the exoskeleton surface of insects.

VN **GIẢI THÍCH TIẾNG VIỆT**

Steroid có khung sườn đặc trưng gồm 4 vòng carbon gắn liền nhau (3 vòng 6 cạnh $+ 1$ vòng 5 cạnh). **Cholesterol** vừa là thành phần màng tế bào động vật (điều hoà độ linh động của màng) vừa là tiền chất để tổng hợp các hormone steroid (testosterone, estrogen, cortisol). **Sáp (wax)** là ester của acid béo mạch dài với rượu mạch dài, rất kỵ nước, dùng để chống thấm nước (lớp

cutin lá cây, lông vũ chim, vỏ côn trùng).

1.6 Proteins

1.6.1 Amino acid structure and polarity

Proteins are polymers of **amino acids**. Every one of the 20 standard amino acids shares the same core structure: a central (α) carbon bonded to (1) an amino group ($-NH_2$), (2) a carboxyl group ($-COOH$), (3) a hydrogen atom, and (4) a variable **R group** (side chain) that gives each amino acid its distinct chemical identity. R groups fall into four broad polarity classes:

R-group polarity classes

- **Nonpolar / hydrophobic** — all-carbon-and-hydrogen R groups (e.g., alanine, valine, leucine, phenylalanine); cluster away from water.
- **Polar, uncharged** — R groups with polar but non-ionizing atoms such as $-OH$ or $-SH$ (e.g., serine, threonine, cysteine); can hydrogen-bond with water.
- **Acidic (negatively charged at physiological pH)** — R groups ending in a carboxyl that ionizes to $-COO^-$ (e.g., aspartate, glutamate).
- **Basic (positively charged at physiological pH)** — R groups containing amino/guanidinium/imidazole groups that ionize to a positive charge (e.g., lysine, arginine, histidine).

Ví dụ mẫu · Classifying R-group polarity

Classify each R group as nonpolar/hydrophobic, polar uncharged, acidic, or basic: (a) alanine, $-CH_3$; (b) serine, $-CH_2OH$; (c) glutamate, $-CH_2CH_2COO^-$; (d) lysine, $-(CH_2)_4NH_3^+$.

(a) Pure hydrocarbon, no polar atoms $\Rightarrow$ **nonpolar/hydrophobic**. **(b)** A hydroxyl group can hydrogen-bond with water but does not ionize at physiological pH $\Rightarrow$ **polar, uncharged**. **(c)** Already shown ionized as a carboxylate ($-COO^-$) $\Rightarrow$ **acidic, negatively charged**. **(d)** Already shown ionized as a protonated amine ($-NH_3^+$) $\Rightarrow$ **basic, positively charged**.

VN **GIẢI THÍCH TIẾNG VIỆT**

Mỗi amino acid có cùng "khung" gồm carbon trung tâm gắn với nhóm amino ($-NH_2$), nhóm carboxyl ($-COOH$), một nguyên tử H, và một **nhóm R** riêng biệt. Nhóm R quyết định amino acid đó thuộc loại nào trong 4 nhóm: **không phân cực/kỵ nước**, **phân cực không tích điện**, **acid (tích điện âm)**, hoặc **base (tích điện dương)** ở pH sinh lý. Tính chất của nhóm R là yếu tố quyết định amino acid đó sẽ nằm ở đâu khi protein cuộn gấp (bên trong kỵ nước hay bên ngoài ưa nước).

1.6.2 Peptide bonds and the four levels of protein structure

Amino acids join by dehydration synthesis between the carboxyl group of one and the amino group of the next, forming a **peptide bond** and releasing one water molecule per bond. A chain of amino acids linked this way is a **polypeptide**, with a free amino group at one end (the N-terminus) and a free carboxyl group at the other (the C-terminus).

Ví dụ mẫu · Polypeptide mass from monomer masses

In general, if n monomers (average mass m) join by dehydration synthesis, the resulting polymer's mass is approximately

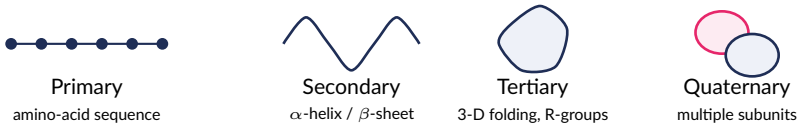
$$\text{mass} \approx nm - 18(n-1),$$

since one water molecule ($\approx$ 18.02 g/mol) is released per bond formed, and a chain of n monomers has $n-1$ bonds. Using actual amino acid masses, find the mass of the tetrapeptide Gly–Ala–Val–Leu, given free amino acid masses Gly $=$ 75.07, Ala $=$ 89.09, Val $=$ 117.15, Leu $=$ 131.17 g/mol.

Sum of monomer masses: $75.07 + 89.09 + 117.15 + 131.17 = 412.48$ g/mol. Number of peptide bonds formed: $n - 1 = 4 - 1 = 3$, releasing $3 \times 18.02 = 54.06$ g/mol worth of water.

$$\text{Tetrapeptide mass} \approx 412.48 - 54.06 = 358.42 \text{ g/mol}.$$

The polypeptide's exact sequence of amino acids is its **primary structure**. Local, repeating segments of the backbone fold into regular shapes stabilized by hydrogen bonds between backbone atoms (not R groups): the coiled α**-helix** and the pleated β**-sheet** are the two common **secondary structures**. The polypeptide as a whole then folds into a specific overall three-dimensional shape — its **tertiary structure** — driven by interactions among R groups: hydrophobic R groups cluster in the molecule's interior away from water, while hydrogen bonds, ionic bonds between charged R groups, and covalent **disulfide bridges** between cysteine sulfhydryl groups lock the shape in place. Some proteins are functional only as an assembly of two or more separate polypeptide chains (subunits); this level of organization is **quaternary structure** (e.g., hemoglobin, four subunits).



The four levels of protein structure: primary (amino-acid sequence, peptide bonds); secondary (local backbone H-bonding into α-helices/β-sheets); tertiary (overall 3-D fold of one polypeptide, driven by R-group interactions); quaternary (assembly of ≥ 2 polypeptide subunits, e.g., hemoglobin).

Four levels, one hierarchy: primary (sequence) → secondary (local backbone H-bonds: α-helix, β-sheet) → tertiary (overall 3-D fold of one chain, via R-group hydrophobic/ionic/H-bond/disulfide interactions) → quaternary (assembly of multiple folded chains). Each level depends on the one before it — the primary sequence ultimately dictates all higher-order structure.

VN **GIẢI THÍCH TIẾNG VIỆT**

Protein có 4 bậc cấu trúc: **bậc 1** (trình tự amino acid, nối bằng liên kết peptide); **bậc 2** (gấp cục bộ nhờ liên kết hydro giữa các nguyên tử *khung* — tạo xoắn α hoặc phiến gấp nếp β); **bậc 3** (hình dạng 3 chiều tổng thể của *một* chuỗi polypeptide, do tương tác giữa các nhóm R — kỵ nước, ion, hydro, cầu disulfide); **bậc 4** (nhiều chuỗi polypeptide riêng biệt kết hợp thành một protein chức năng, ví dụ hemoglobin gồm 4 tiểu đơn vị).

1.6.3 Denaturation and structure-function relationships

A protein functions correctly only when folded into its specific three-dimensional shape (its **native conformation**). Extreme heat, extreme pH, or certain chemicals can disrupt the weak interactions (hydrogen bonds, ionic bonds, hydrophobic interactions, and even disulfide bridges) that hold secondary, tertiary, and quaternary structure together, causing the protein to unfold and lose function

— a process called **denaturation**. Because denaturation does not break the strong covalent peptide bonds of the primary structure, the amino acid sequence itself remains intact; some denatured proteins can even refold correctly (renature) if normal conditions are restored, though many — like a cooked egg white — cannot.

The link between a protein's specific shape and its biological role is one of the central themes of biology: an **enzyme**'s active site is shaped to bind a specific substrate; an **antibody**'s variable region is shaped to bind a specific antigen; a **structural protein** such as collagen (a triple helix) or keratin (a coiled-coil) is shaped to resist mechanical stress. In every case, altering the shape — whether by mutation or denaturation — compromises the specific function.

(!) Lỗi thường gặp: Đừng nhầm **biến tính (denaturation)** với việc phá vỡ cấu trúc bậc 1. Biến tính chỉ phá vỡ các liên kết *yếu* giữ cấu trúc bậc 2, 3, 4 (liên kết hydro, ion, tương tác kỵ nước, và cả cầu disulfide) — protein mất hình dạng và mất chức năng, nhưng **trình tự amino acid (bậc 1) vẫn nguyên vẹn** vì liên kết peptide (liên kết cộng hoá trị) không bị phá vỡ. Ví dụ lòng trắng trứng khi luộc chín bị biến tính (đục, đông cứng) nhưng trình tự amino acid trong mỗi phân tử protein không hề thay đổi.

1.7 Macromolecules as Fuel: Energy Content

Carbohydrates, proteins, and fats can all be oxidized by cellular respiration to release usable chemical energy, but not at equal rates per gram. Carbohydrates and proteins each yield about 4 kcal (Calories) per gram, while fats yield about 9 kcal per gram — more than double — because a fat's hydrocarbon-rich, highly reduced structure (many C–H bonds, few oxygen atoms) holds far more energy to be released upon oxidation than the already partially-oxidized carbon skeletons of carbohydrates and proteins.

Ví dụ mẫu · Calories from a nutrition label

A granola bar's nutrition label lists 25 g carbohydrate, 5 g protein, and 6 g fat per bar. Using 4 kcal/g (carbohydrate), 4 kcal/g (protein), and 9 kcal/g (fat), calculate the total food energy per bar.

$$(25\text{ g})(4\ \tfrac{\text{kcal}}{\text{g}}) + (5\text{ g})(4\ \tfrac{\text{kcal}}{\text{g}}) + (6\text{ g})(9\ \tfrac{\text{kcal}}{\text{g}}) = 100 + 20 + 54 = 174\ \text{kcal per bar.}$$

1.8 Nucleic Acids

1.8.1 Nucleotide structure: DNA versus RNA

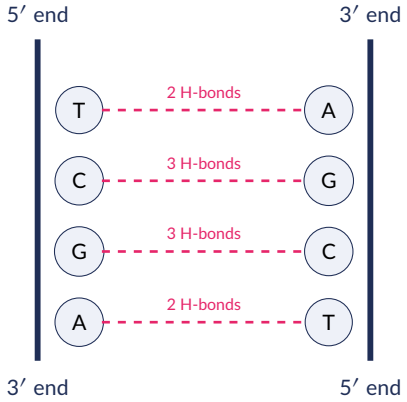
Nucleic acids — DNA and RNA — are polymers of **nucleotides**. Each nucleotide has three parts: (1) a five-carbon (pentose) sugar, (2) a phosphate group attached to the sugar's $5'$ carbon, and (3) a nitrogenous base attached to the sugar's $1'$ carbon. Nitrogenous bases fall into two structural families: **purines** (double-ringed: adenine, guanine) and **pyrimidines** (single-ringed: cytosine, thymine, uracil).

Feature	DNA	RNA
Sugar	Deoxyribose (no $-$OH at $2'$ carbon)	Ribose (has $-$OH at $2'$ carbon)
Bases	A, T, G, C	A, U, G, C (uracil replaces thymine)
Strandedness	Typically double-stranded	Typically single-stranded
Primary role	Long-term storage of genetic information	Gene expression (mRNA, tRNA, rRNA, etc.)

(!) Lỗi thường gặp: Hai lỗi thường gặp khi so sánh DNA và RNA: (1) nhầm đường — DNA dùng **deoxyribose** (thiếu nhóm $-$OH ở carbon số $2'$), RNA dùng **ribose** (có đủ nhóm $-$OH ở $2'$) — chính nhóm $-$OH này khiến RNA kém bền hơn DNA về mặt hoá học; (2) nhầm base — RNA có **uracil (U)** thay cho **thymine (T)** của DNA, còn ba base còn lại (A, G, C) giống nhau ở cả hai loại acid nucleic.

1.8.2 The antiparallel double helix, base pairing, and Chargaff's rule

Successive nucleotides in a strand are joined by **phosphodiester bonds** between the phosphate group on one nucleotide's $5'$ carbon and the sugar's $3'$-hydroxyl of the next, creating a repeating sugar-phosphate backbone with bases projecting to the side and giving each single strand an inherent $5' \to 3'$ directionality. In double-stranded DNA, two such strands wind around each other into a **double helix**, running **antiparallel** — one strand $5' \to 3'$, the complementary strand $3' \to 5'$ — held together by hydrogen bonds between bases on opposite strands according to strict **Watson–Crick base-pairing rules**: **adenine (A) pairs with thymine (T)** (or uracil, U, in RNA) via **2** hydrogen bonds, and **guanine (G) pairs with cytosine (C)** via **3** hydrogen bonds. Because a purine always pairs with a pyrimidine, the helix has a uniform width along its entire length. This strict complementarity is also the basis of **Chargaff's rule**: in double-stranded DNA, $\%\text{A} = \%\text{T}$ and $\%\text{G} = \%\text{C}$ (so total purines equal total pyrimidines), regardless of species.



Schematic antiparallel DNA double helix (drawn as a ladder): two sugar–phosphate backbones run in opposite $5' \to 3'$ directions. A pairs with T via 2 hydrogen bonds; G pairs with C via 3 hydrogen bonds, so G–C-rich regions are more thermally stable.

Base-pairing rules: A–T (DNA) or A–U (RNA), 2 hydrogen bonds; G–C, 3 hydrogen bonds. **Chargaff's rule:** in double-stranded DNA, $\%\text{A} = \%\text{T}$ and $\%\text{G} = \%\text{C}$. More G–C pairs $\Rightarrow$ more hydrogen bonds per unit length $\Rightarrow$ higher melting/denaturation temperature.

Ví dụ mẫu · Hydrogen bonds and Chargaff's rule together

A 20-base-pair region of double-stranded DNA is found to be 40% adenine. Using Chargaff's rule, find the number of A–T and G–C pairs in this region, then calculate the total number of hydrogen bonds holding it together.

The region has 20 base pairs $= 40$ individual bases total. Since $\%\text{A} = 40\%$ of all bases, the number of A bases $= 0.40 \times 40 = 16$; each A base belongs to exactly one A–T pair, so there are **16 A–T pairs**. By Chargaff's rule $\%\text{T} = \%\text{A} = 40\%$, consistent with 16 T bases. The remaining $20 - 16 =$ **4** pairs must be **G–C pairs** ($\%\text{G} = \%\text{C} = 10\%$ each, since $4/40 = 10\%$).

Total hydrogen bonds: $(16\ \text{A–T pairs})(2\ \text{H-bonds}) + (4\ \text{G–C pairs})(3\ \text{H-bonds}) = 32 + 12 =$ **44**

hydrogen bonds. Because this region is A–T-rich (80%), it would separate (melt) at a lower temperature than an equally long, more G–C-rich region.

VN **GIẢI THÍCH TIẾNG VIỆT**

Hai mạch DNA chạy **ngược chiều nhau (antiparallel)**: một mạch $5' \to 3'$, mạch kia $3' \to 5'$. Base bắt cặp theo nguyên tắc bổ sung: **A–T** (2 liên kết hydro) và **G–C** (3 liên kết hydro) — luôn là purine (A hoặc G) bắt cặp với pyrimidine (T/U hoặc C) nên bề rộng chuỗi xoắn kép luôn đồng nhất. **Quy tắc Chargaff**: $\%\text{A} = \%\text{T}$ và $\%\text{G} = \%\text{C}$ ở mọi loài. Vùng DNA giàu G–C có nhiều liên kết hydro hơn trên mỗi đơn vị chiều dài nên bền nhiệt hơn (nhiệt độ nóng chảy/biến tính cao hơn) vùng giàu A–T.

1.9 Problem Bank

Bài tập luyện tập

Each water molecule in liquid water can form up to how many hydrogen bonds with neighboring water molecules?

(A) 1
(B) 2
(C) 4
(D) 6

Lời giải chi tiết

Each water molecule has 2 hydrogens (each can donate one hydrogen bond) and 2 lone pairs on oxygen (each can accept one hydrogen bond), for a maximum of $2+2=4$ hydrogen bonds. **(C)**.

Bài tập luyện tập

Water is pulled up narrow xylem vessels against gravity through a combination of water molecules adhering to the polar vessel walls and cohering to each other. This combined phenomenon is called:

(A) Surface tension
(B) Capillary action
(C) Osmosis
(D) Specific heat

Lời giải chi tiết

Capillary action is precisely the combination of adhesion (water–wall attraction) and cohesion (water–water attraction) that lets water rise in a narrow tube. **(B)**.

Bài tập luyện tập

A small pond containing 1.0×10^7 g of water absorbs 2.1×10^8 J of solar heat energy during a sunny afternoon. Using $c_{\text{water}} = 4.184$ J/(g $\cdot^\circ$ C), calculate the pond's temperature increase (ignore evaporation and heat loss).

Lời giải chi tiết

Apply $q = mc\Delta T \Rightarrow \Delta T = \dfrac{q}{mc} = \dfrac{2.1 \times 10^8}{(1.0 \times 10^7)(4.184)} = \dfrac{2.1 \times 10^8}{4.184 \times 10^7} \approx 5.0^\circ$C. A body of soil or rock of the same mass, having a much lower specific heat, would warm far more for the same energy input — illustrating why large bodies of water buffer environmental temperature so effectively.

Bài tập luyện tập

Water striders can walk across the surface of a pond without breaking through mainly because of:

(A) The low density of liquid water

(B) Surface tension arising from cohesive hydrogen bonding at the air–water interface

(C) Water's high boiling point

(D) Capillary action

Lời giải chi tiết

Cohesive hydrogen bonds among surface water molecules create an elastic, film-like surface tension strong enough to support the light weight of a water strider's legs. **(B)**.

Bài tập luyện tập

Gastric juice has a pH of about 2; black coffee has a pH of about 5. How many times greater is the hydrogen ion concentration $[H^+]$ of gastric juice compared to black coffee?

(A) 3 times

(B) 30 times

(C) 300 times

(D) 1000 times

Lời giải chi tiết

The pH difference is $5 - 2 = 3$ units. Since pH is a base-10 logarithmic scale, each unit corresponds to a tenfold change in $[H^+]$: $10^3 = 1000$. Gastric juice has about $1000\times$ the $[H^+]$ of black coffee. **(D)**.

Bài tập luyện tập

A person hyperventilates, exhaling CO_2 faster than it is metabolically produced. Using the bicarbonate buffer equilibrium $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$, predict and explain what happens to blood pH.

Lời giải chi tiết

By Le Chatelier's principle, continuously removing CO_2 (exhaling it faster than it forms) depletes the left-hand side of the equilibrium, so the reaction shifts *left* to partially replace it: $H^+ + HCO_3^-$ is drawn back through H_2CO_3 toward $CO_2 + H_2O$. This consumes free H^+ ions, so $[H^+]$ falls and **blood pH rises** — a condition called respiratory alkalosis. (This is the mirror image of the earlier example, where adding H^+ from lactic acid shifted the equilibrium *right*, consuming HCO_3^- and generating CO_2 to be exhaled.)

Bài tập luyện tập

Iodine is an essential trace element in the human diet because it is a required structural component of:

(A) Hemoglobin
(B) Chlorophyll
(C) Thyroid hormones (e.g., thyroxine)
(D) ATP

Lời giải chi tiết

Iodine is incorporated directly into thyroid hormones such as thyroxine; dietary iodine deficiency impairs thyroid hormone production. **(C)**.

Bài tập luyện tập

A carbon atom is double-bonded to an oxygen atom at the very end of a carbon chain (i.e., that carbon is also bonded to a hydrogen). This functional group is a(n):

(A) Ketone
(B) Aldehyde
(C) Carboxyl
(D) Hydroxyl

Lời giải chi tiết

A carbonyl group at the terminal (end) position of a carbon skeleton is an aldehyde; the same carbonyl at an internal position (flanked by two carbons) is a ketone. **(B)**.

Bài tập luyện tập

Of the seven functional groups discussed (hydroxyl, carbonyl, carboxyl, amino, phosphate, sulfhydryl, methyl), which become negatively charged at physiological pH, and why?

Lời giải chi tiết

Carboxyl ($-\text{COOH} \rightarrow -\text{COO}^- + \text{H}^+$) and **phosphate** ($-\text{OPO}_3\text{H}_2 \rightarrow -\text{OPO}_3^{2-} + 2\text{H}^+$) both become negatively charged, because both are acidic groups that readily donate (ionize away) their H^+ near neutral pH, leaving the group with a net negative charge.

Bài tập luyện tập

Which best explains why carbon, rather than another element such as silicon (also tetravalent), forms the structural backbone of life's molecules?

(A) Silicon is far too rare in the universe to be biologically useful
(B) Carbon forms strong, kinetically stable single, double, and triple bonds with itself and other atoms across the range of temperatures compatible with life, enabling stable long chains, branches, and rings
(C) Silicon cannot bond to oxygen at all
(D) Carbon has more total electrons than silicon

Lời giải chi tiết

Carbon's bonds (C–C, C–H, C=C, etc.) are strong yet kinetically stable at biological temperatures, allowing durable chains, branches, and rings; heavier group-14 elements like silicon form comparatively weaker, less stable analogous bonds. **(B)**.

Bài tập luyện tập

Eight monosaccharides join end-to-end by dehydration synthesis to form a single linear polysaccharide chain. How many water molecules are released in the process?

Lời giải chi tiết

A linear chain of n monomers has $n-1$ bonds. Here $n=8$, so $n-1=7$ glycosidic bonds form, releasing 7 water molecules.

Bài tập luyện tập

Complete hydrolysis of a linear polysaccharide made of 250 glucose monomers requires how many water molecules, and how many free glucose molecules are produced?

Lời giải chi tiết

A linear chain of 250 monomers contains $250-1=249$ glycosidic bonds. Hydrolysis consumes exactly one H_2O per bond broken, so 249 water molecules are consumed, releasing all 250 glucose monomers as free sugar.

Bài tập luyện tập

Humans can digest starch but cannot digest cellulose, even though both are polymers of glucose, because:

(A) Starch and cellulose are made of chemically different monomers

(B) Human digestive enzymes (amylase) hydrolyze α-1,4 glycosidic bonds but not the β-1,4 bonds of cellulose

(C) Cellulose contains nitrogen atoms that block digestion

(D) Starch is a protein while cellulose is a carbohydrate

Lời giải chi tiết

Both are glucose polymers, but starch uses α-glycosidic linkages (which human amylase can hydrolyze) while cellulose uses β-glycosidic linkages (which human digestive enzymes cannot hydrolyze, since they lack cellulase). **(B)**.

Bài tập luyện tập

Two unknown compounds are analyzed for elemental composition by mass: Compound X is 40.0% C, 6.7% H, 53.3% O; Compound Y is 77% C, 12% H, 11% O. Identify which compound is more likely a carbohydrate and which is more likely a lipid, and justify your answer using the H:O ratio.

Lời giải chi tiết

Compound X has an H:O mass ratio close to that of water ($2:1$ by atoms; here consistent with the general carbohydrate formula $C_n(H_2O)_n$) and matches glucose ($C_6H_{12}O_6$) almost exactly — it is the **carbohydrate**. Compound Y has a much higher proportion of C and H and a much lower proportion of O, typical of a lipid's long hydrocarbon chains with relatively few oxygen atoms — it is the **lipid** (consistent with a triglyceride such as triolein). The lower oxygen content of lipids means their carbon skeleton is more reduced, which is also why lipids release more energy per gram (9 kcal/g) than carbohydrates (4 kcal/g) upon oxidation.

Bài tập luyện tập

Which polysaccharide is the most heavily branched, an adaptation that provides many free ends for rapid glucose mobilization during high energy demand?

(A) Cellulose
(B) Amylose
(C) Glycogen
(D) Chitin

Lời giải chi tiết

Glycogen, the animal storage polysaccharide (liver and muscle), is far more branched than plant starch, exposing many more ends from which enzymes can rapidly add or remove glucose units. **(C)**.

Bài tập luyện tập

Name two distinct biological structures built largely from chitin, and explain what modification to the glucose monomer distinguishes chitin from cellulose.

Lời giải chi tiết

Chitin forms the **exoskeletons of arthropods** (insects, crustaceans) and the **cell walls of fungi**. Its monomer is **N-acetylglucosamine**, a glucose derivative in which a nitrogen-containing acetylamino group replaces the hydroxyl at carbon 2; like cellulose, the monomers are linked by β-1,4 glycosidic bonds, giving similar structural rigidity plus extra strength from the added nitrogenous side groups.

Bài tập luyện tập

Rank the following 18-carbon fatty acids from *lowest* to *highest* melting point: (I) fully saturated, (II) monounsaturated (one *cis* double bond), (III) polyunsaturated (three *cis* double bonds).

(A) I $<$ II $<$ III
(B) III $<$ II $<$ I
(C) II $<$ I $<$ III
(D) All equal — saturation does not affect melting point

Lời giải chi tiết

More double bonds mean more rigid kinks in the chain, preventing tight packing and lowering the melting point. Polyunsaturated (III, most kinks) has the lowest melting point, then monounsaturated (II), then fully saturated (I, straightest chain, highest melting point): III $<$ II $<$ I. **(B)**.

Bài tập luyện tập

Compare the structure of a triglyceride and a phospholipid, and explain why phospholipids — but not triglycerides — spontaneously form bilayers in water.

Lời giải chi tiết

A triglyceride is glycerol esterified to **three** fatty acids, making it entirely nonpolar/hydrophobic throughout. A phospholipid is glycerol esterified to only **two** fatty acids, with a phosphate-containing polar head group in place of the third — making it **amphipathic** (hydrophilic head, hydrophobic tails). In water, phospholipids spontaneously orient so hydrophobic tails avoid water and polar heads face the surrounding water, forming a bilayer; triglycerides, lacking any polar head, instead coalesce into nonpolar fat droplets rather than bilayers.

Bài tập luyện tập

The four-ring carbon skeleton shared by all steroids, including cholesterol and steroid hormones, consists of:

(A) Four six-membered rings

(B) Three five-membered rings and one six-membered ring

(C) Three six-membered rings and one five-membered ring

(D) Two six-membered and two five-membered rings

Lời giải chi tiết

The steroid nucleus consists of three fused six-membered carbon rings and one five-membered ring. **(C)**.

Bài tập luyện tập

A snack bar's nutrition label lists 22 g carbohydrate, 6 g protein, and 9 g fat per serving. Using 4 kcal/g (carbohydrate), 4 kcal/g (protein), and 9 kcal/g (fat), calculate the total Calories per serving.

Lời giải chi tiết

$$(22)(4) + (6)(4) + (9)(9) = 88 + 24 + 81 = 193 \text{ kcal per serving.}$$

Bài tập luyện tập

Leucine's R group, $-CH_2CH(CH_3)_2$, is an all-carbon/hydrogen branched chain. This R group is best classified as:

(A) Polar, uncharged

(B) Nonpolar, hydrophobic

(C) Acidic, negatively charged

(D) Basic, positively charged

Lời giải chi tiết

An R group made only of carbon and hydrogen has no polar or ionizable atoms, so it is nonpolar and hydrophobic. **(B)**.

Bài tập luyện tập

Calculate the molar mass of a tripeptide formed from phenylalanine (165.19 g/mol), cysteine (121.16 g/mol), and glutamine (146.15 g/mol).

Lời giải chi tiết

Sum of free amino acid masses: $165.19 + 121.16 + 146.15 = 432.50$ g/mol. A tripeptide has $n - 1 = 2$ peptide bonds, releasing $2 \times 18.02 = 36.04$ g/mol of water:

$$432.50 - 36.04 = 396.46 \text{ g/mol}.$$

Bài tập luyện tập

The primary structure of a protein refers to:

(A) The linear sequence of amino acids joined by peptide bonds

(B) The folding of the backbone into α-helices and β-sheets

(C) The overall three-dimensional shape of a single polypeptide

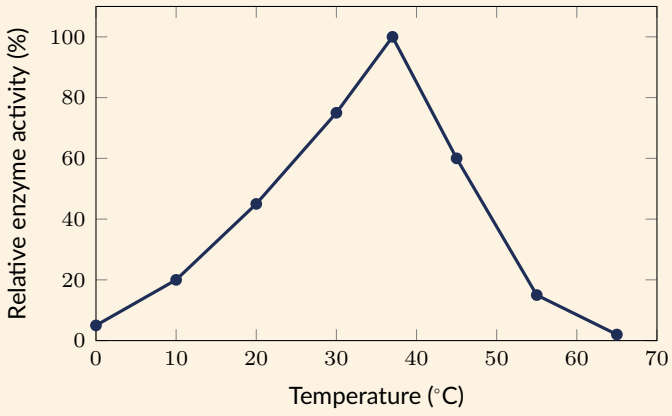
(D) The assembly of multiple polypeptide subunits

Lời giải chi tiết

Primary structure is simply the amino acid sequence, held together by peptide bonds — the most basic level of protein structure, upon which all higher levels depend. **(A)**.

Bài tập luyện tập

The graph below shows the activity of a human digestive enzyme as a function of temperature.



(a) Identify the approximate optimal temperature and explain why activity is low below it. (b) Explain, in terms of protein structure, why activity collapses above about 45°C.

Lời giải chi tiết

(a) Optimal temperature is about 37°C, human body temperature. Below this optimum, molecules move more slowly with less kinetic energy, so enzyme and substrate collide less frequently and less effectively, lowering the reaction rate. **(b)** Above about 45°C, heat disrupts the weak hydrogen bonds, ionic interactions, and hydrophobic interactions that hold the enzyme's secondary and tertiary structure (and therefore its active site) in shape — with-

out breaking the covalent peptide backbone. This denaturation misshapes the active site so the substrate can no longer bind, collapsing activity even though the primary structure remains intact.

Bài tập luyện tập

Pepsin (a stomach enzyme) and trypsin (a small-intestine enzyme) are both proteases, yet pepsin's activity peaks around pH 2 while trypsin's peaks around pH 8. Explain, in terms of protein structure, why placing pepsin in a solution of pH 8 would essentially inactivate it.

Lời giải chi tiết

pH determines the ionization state of acidic and basic R groups; each enzyme's tertiary structure — and therefore its active-site shape — is stabilized by a specific pattern of ionic bonds and hydrogen bonds that depends on those R groups being in their native protonation state at the enzyme's normal physiological pH. Shifting pepsin from pH 2 to pH 8 changes the protonation of many of its ionizable R groups, disrupting the ionic and hydrogen bonds that maintain its tertiary structure. The protein denatures, its active site loses its complementary shape, and it can no longer bind substrate effectively — consistent with pepsin and trypsin each being adapted to the very different pH environments of the stomach and small intestine.

Bài tập luyện tập

Hemoglobin is composed of four separate polypeptide subunits (two α and two β chains) that assemble into one functional protein. This is an example of which level of protein structure?

(A) Primary
(B) Secondary
(C) Tertiary
(D) Quaternary

Lời giải chi tiết

The assembly of multiple, independently-folded polypeptide chains into one functional protein is quaternary structure. **(D)**.

Bài tập luyện tập

Complete the comparison of DNA and RNA: (a) the sugar in each; (b) the base found in RNA but not DNA, and vice versa; (c) the typical strandedness of each.

Lời giải chi tiết

(a) DNA contains **deoxyribose** (no $-$OH at the $2'$ carbon); RNA contains **ribose** (has $-$OH at the $2'$ carbon). **(b)** RNA contains **uracil** instead of thymine; DNA contains **thymine**, not uracil (adenine, guanine, and cytosine occur in both). **(c)** DNA is typically **double-stranded** (antiparallel double helix); RNA is typically **single-stranded** (though it often folds back on itself).

Bài tập luyện tập

A sample of double-stranded DNA is found to be 22% adenine. Using Chargaff's rule, determine the percentages of thymine, guanine, and cytosine.

Lời giải chi tiết

By Chargaff's rule, $\%\text{T} = \%\text{A} = 22\%$. The remaining bases total $100\% - 22\% - 22\% = 56\%$, split evenly between G and C ($\%\text{G} = \%\text{C}$): $\%\text{G} = \%\text{C} = 28\%$.

Bài tập luyện tập

A 10-base-pair region of double-stranded DNA contains 6 G–C pairs and 4 A–T pairs. (a) How many total hydrogen bonds hold this region together? (b) Would this region separate (melt) at a higher or lower temperature than an equal-length region with 4 G–C and 6 A–T pairs? Explain.

Lời giải chi tiết

(a) $(6\text{ G–C})(3\text{ H-bonds}) + (4\text{ A–T})(2\text{ H-bonds}) = 18 + 8 = 26$ hydrogen bonds. **(b) Higher** temperature — more G–C pairs means more hydrogen bonds per base pair (3 vs. 2) plus stronger base-stacking interactions, so more thermal energy is required to separate the strands. This is the basis for GC-content correlating with DNA melting temperature.

Bài tập luyện tập

In the DNA double helix, the two strands are described as "antiparallel" because:

(A) They are held together only by ionic bonds, not hydrogen bonds

(B) One strand runs $5' \to 3'$ while the complementary strand runs $3' \to 5'$ within the same helix

(C) The two strands are not actually base-paired to one another

(D) Both strands run in the same $5' \to 3'$ direction

Lời giải chi tiết

The two complementary strands of the double helix run in opposite chemical directions, one $5' \to 3'$ and the other $3' \to 5'$ — this is what "antiparallel" means. **(B)**.

Bài tập luyện tập

Describe the three components of a single DNA nucleotide, and explain how successive nucleotides are joined to form one strand.

Lời giải chi tiết

A DNA nucleotide consists of (1) a deoxyribose sugar, (2) a phosphate group attached to the sugar's $5'$ carbon, and (3) one of four nitrogenous bases (A, T, G, or C) attached to the sugar's $1'$ carbon. Successive nucleotides are joined by **phosphodiester bonds**, formed between the phosphate group on one nucleotide's $5'$ carbon and the free $3'$-hydroxyl of the sugar on the next nucleotide, producing the repeating sugar-phosphate backbone with bases projecting out to the side.

Bài tập luyện tập

Which pairing of monomer → polymer is *incorrect*?

(A) Glucose → starch
(B) Amino acid → protein
(C) Nucleotide → nucleic acid
(D) Glycerol → triglyceride

Lời giải chi tiết

A triglyceride is one glycerol molecule joined (by dehydration synthesis) to three fatty acids — glycerol is not a repeating monomer unit in a polymer chain the way glucose, amino acids, and nucleotides are. Lipids, unlike carbohydrates, proteins, and nucleic acids, are not true polymers built from a single repeating monomer. **(D)**.

Cell Structure and Function

Mục tiêu Unit: Thuyết tế bào; tế bào nhân sơ và nhân thực; cấu trúc – chức năng các bào quan; tỉ lệ diện tích bề mặt trên thể tích (SA:V); mô hình khảm động của màng sinh chất; vận chuyển thụ động (khuếch tán, khuếch tán tăng cường, thẩm thấu, thế nước); trương lực và cân bằng nước; vận chuyển chủ động (bơm Na^+/K^+, đồng vận chuyển); nhập bào – xuất bào; hệ thống màng nội bào; và thuyết nội cộng sinh.

2.1 Cell Theory and the Diversity of Cellular Life

2.1.1 Cell theory

Modern biology rests on the **cell theory**, built from the work of Matthias Schleiden, Theodor Schwann, and Rudolf Virchow in the nineteenth century. It has three parts:

Cell theory

1. All living organisms are composed of one or more cells.
2. The cell is the basic unit of structure, function, and organization in all organisms.
3. All cells arise only from pre-existing cells (*omnis cellula e cellula*) — cells are not spontaneously generated.

VN **GIẢI THÍCH TIẾNG VIỆT**

Thuyết tế bào có ba nội dung cốt lõi: (1) mọi sinh vật sống đều được cấu tạo từ một hoặc nhiều tế bào; (2) tế bào là đơn vị cấu trúc và chức năng cơ bản của sự sống; (3) tế bào chỉ được sinh ra từ tế bào đã tồn tại trước đó (không tự phát sinh). Đây là nền tảng lý thuyết cho toàn bộ chương trình Sinh học tế bào.

2.1.2 Prokaryotic and eukaryotic cells

All cells share a plasma membrane, cytoplasm, ribosomes, and DNA as genetic material, but life divides into two fundamentally different cellular architectures.

Prokaryotic cells (Bacteria and Archaea) lack a membrane-bound nucleus and lack membrane-bound organelles. Their DNA is a single circular chromosome located in a region called the **nucleoid** (not enclosed by a membrane). Prokaryotes are small (1–10 μm), contain $70S$ ribosomes, and most have a rigid **cell wall** (peptidoglycan in bacteria) outside the plasma membrane; many also have a capsule, flagella, and/or pili.

Eukaryotic cells (animals, plants, fungi, protists) have a membrane-bound **nucleus** enclosing linear DNA wrapped around histone proteins, and an extensive system of membrane-bound organelles that compartmentalize the cytoplasm. Eukaryotic cytosolic ribosomes are $80S$ (a $60S$ and a $40S$ subunit); eukaryotic cells are generally larger (10–100 μm) than prokaryotic cells.

Feature	Prokaryotic cell	Eukaryotic cell
Nucleus	Absent (DNA in nucleoid)	Present, membrane-bound
DNA	Single circular chromosome	Multiple linear chromosomes with histones
Ribosomes	$70S$	$80S$ (cytosolic); $70S$ in mitochondria/chloroplasts
Membrane-bound organelles	Absent	Present (ER, Golgi, mitochondria, etc.)
Typical size	1–10 μm	10–100 μm
Cell wall	Usually present (peptidoglycan)	Present in plants (cellulose) and fungi (chitin); absent in animals

VN **GIẢI THÍCH TIẾNG VIỆT**

Tế bào nhân sơ (vi khuẩn, vi khuẩn cổ) KHÔNG có nhân thật (màng nhân) và KHÔNG có bào quan có màng bao bọc; ADN dạng vòng nằm tự do trong vùng nhân (nucleoid). **Tế bào nhân thực** (động vật, thực vật, nấm, nguyên sinh vật) có nhân thật với ADN dạng thẳng quấn quanh protein histone, và có hệ thống bào quan có màng giúp phân chia tế bào chất thành nhiều "phòng chức năng" riêng biệt. Kích thước ribosome ($70S$ so với $80S$) là một dấu hiệu phân biệt quan trọng — và sẽ quay lại ở phần thuyết nội cộng sinh.

2.2 Subcellular Components and Organelles

Eukaryotic cells subdivide their internal volume among distinct organelles, each with a structure matched precisely to its function.

2.2.1 The nucleus and ribosomes: information and protein synthesis

The **nucleus** is enclosed by a double-membrane **nuclear envelope** perforated by **nuclear pores**, which regulate the passage of RNA and proteins between the nucleus and cytoplasm. Inside, DNA is organized as **chromatin**; a darker region, the **nucleolus**, is where ribosomal RNA is transcribed and ribosomal subunits are assembled. The nucleus is the site of DNA replication and transcription, and therefore controls gene expression for the entire cell.

Ribosomes are not membrane-bound organelles; each is a complex of ribosomal RNA and protein that catalyzes translation (protein synthesis) by reading mRNA and joining amino acids. **Free ribosomes** in the cytosol make proteins that function in the cytosol itself, while ribosomes bound to the rough ER make proteins destined for secretion, the plasma membrane, or other organelles.

2.2.2 The endomembrane organelles: ER and Golgi apparatus

The **rough endoplasmic reticulum (rough ER)** is a network of membranous tubules and sacs continuous with the nuclear envelope, studded on its cytosolic face with ribosomes. It folds and chemically modifies (e.g., begins glycosylation of) proteins synthesized by its bound ribosomes and packages them into transport vesicles.

The **smooth endoplasmic reticulum (smooth ER)** lacks ribosomes. It synthesizes lipids and steroid hormones, detoxifies drugs and metabolic wastes (abundant in liver cells), and stores Ca^{2+} ions (as sarcoplasmic reticulum in muscle cells, essential for triggering contraction).

The **Golgi apparatus** is a stack of flattened membranous sacs (cisternae) with a receiving (*cis*) face near the ER and a shipping (*trans*) face near the plasma membrane. It further modifies, sorts, and tags proteins and lipids arriving from the ER, then packages them into vesicles addressed to their correct final destination.

2.2.3 Energy-converting organelles: mitochondria and chloroplasts

Mitochondria are bounded by a double membrane; the inner membrane folds into **cristae**, which greatly increase the surface area available for the electron transport chain, while the fluid-filled **matrix** contains the enzymes of the citric acid cycle. Mitochondria are the primary site of aerobic ATP production and are present in nearly all eukaryotic cells.

Chloroplasts (found in plants and algae) are also bounded by a double membrane and contain a third internal membrane system: flattened, chlorophyll-containing sacs called **thylakoids**, stacked into **grana** and bathed in a fluid **stroma**. Chloroplasts are the site of photosynthesis, converting light energy into chemical energy.

Both organelles carry their own small **circular DNA** and their own $70S$ **ribosomes**, distinct from the cell's nuclear genome and $80S$ cytosolic ribosomes — a fact central to the endosymbiotic theory (Section 1.10).

2.2.4 Degradation, storage, and structural organelles

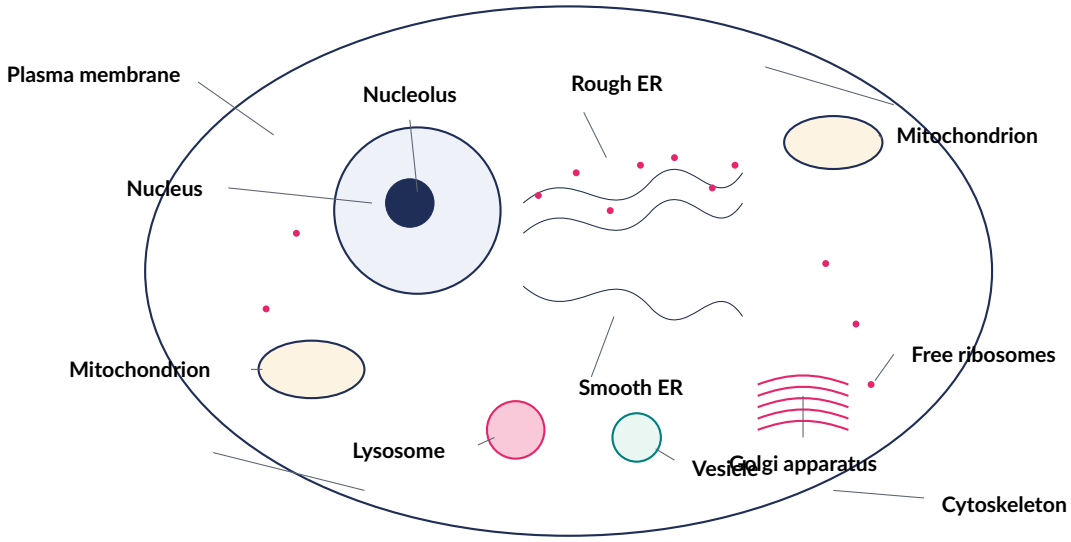
Lysosomes are membrane-bound sacs of hydrolytic (**acid hydrolase**) enzymes, active at the acidic pH (≈ 4.5–5) maintained inside them. They digest macromolecules delivered by endocytosis, recycle a cell's own damaged organelles (**autophagy**), and are especially prominent in animal cells such as macrophages.

Vacuoles are large membrane-bound sacs used for storage. Plant cells typically have one large **central vacuole** occupying up to 90% of cell volume, which stores water, ions, and pigments, and generates **turgor pressure** against the cell wall (Section 1.5). Freshwater protists such as *Paramecium* use a contractile vacuole to pump out excess water that continuously enters by osmosis.

The **cytoskeleton** is an internal protein scaffold with three main filament types: **microfilaments** (actin, ≈ 7 nm, involved in cell shape, movement, and cytokinesis), **intermediate filaments** (rope-like proteins that give mechanical strength and anchor organelles in place), and **microtubules** (tubulin, ≈ 25 nm, forming the mitotic spindle and serving as tracks for motor proteins such as kinesin and dynein, and forming the core of cilia and flagella).

The **cell wall** is a rigid layer outside the plasma membrane in plants (cellulose), fungi (chitin), and most prokaryotes (peptidoglycan in bacteria), but is absent in animal cells. It provides structural support, maintains cell shape, and — critically for osmotic balance — resists the internal pressure buildup that would otherwise cause the cell to burst when water enters (Section 1.6).

Organelle	Structure	Function
Nucleus	Double membrane, nuclear pores, chromatin, nucleolus	Houses DNA; controls transcription/replication
Ribosome	rRNA + protein, no membrane	Translation (protein synthesis)
Rough ER	Membrane tubules studded with ribosomes	Folds/modifies secreted & membrane proteins
Smooth ER	Membrane tubules, no ribosomes	Lipid synthesis, detoxification, Ca^{2+} storage
Golgi apparatus	Stack of flattened cisternae	Modifies, sorts, tags, and ships proteins/lipids
Mitochondrion	Double membrane, cristae, matrix, own DNA & $70S$ ribosomes	Aerobic ATP production
Chloroplast	Double membrane + thylakoids/grana in stroma, own DNA & $70S$ ribosomes	Photosynthesis
Lysosome	Membrane sac of acid hydrolases	Digestion, autophagy
Vacuole	Large membrane sac (central vacuole in plants)	Storage, turgor pressure, osmoregulation
Cytoskeleton	Microfilaments, intermediate filaments, microtubules	Shape, movement, transport tracks
Cell wall	Rigid layer outside plasma membrane	Support; resists osmotic lysis



A generalized animal (eukaryotic) cell, schematic and not to scale. Organelle numbers are reduced for clarity; a plant cell would additionally show a cell wall, a large central vacuole, and chloroplasts.

VN **GIẢI THÍCH TIẾNG VIỆT**

Cách nhớ nhanh: **nhân** = "trung tâm điều khiển" (chứa ADN); **ribosome** = "xưởng lắp ráp protein"; **lưới nội chất hạt** = "nơi gấp/chỉnh sửa protein tiết ra"; **lưới nội chất trơn** = "nơi tổng hợp lipid, khử độc"; **Golgi** = "trung tâm đóng gói và dán nhãn địa chỉ"; **ty thể** = "nhà máy điện" (hô hấp hiếu khí); **lục lạp** = "nhà máy quang hợp" (chỉ ở thực vật/tảo); **lysosome** = "trạm tiêu hoá nội bào"; **không bào** = "kho chứa + tạo áp suất trương"; **khung xương tế bào** = "bộ khung nâng đỡ + đường ray vận chuyển"; **thành tế bào** = "áo giáp bảo vệ, chống vỡ do nước".

2.3 Cell Size and the Surface-Area-to-Volume Ratio

A cell must exchange nutrients, gases, and wastes with its environment across its plasma membrane, while its metabolic demand (oxygen consumption, waste production) scales with its **volume**. Because

volume grows with the cube of a cell's linear dimension while surface area grows only with the square, the ratio of surface area to volume (**SA:V**) *falls* as a cell gets larger. This single geometric fact is one of the most important constraints on cell size, shape, and multicellularity in all of biology.

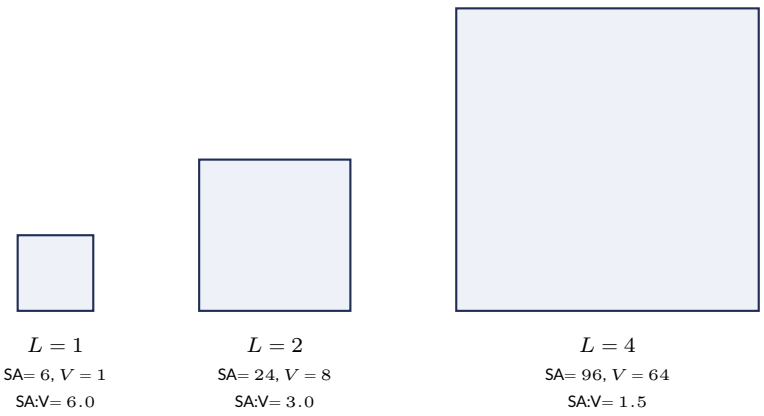
For a **cube** of side length L: surface area SA $= 6L^2$, volume $V = L^3$, so $\dfrac{\text{SA}}{V} = \dfrac{6}{L}$. For a **sphere** of radius r: SA $= 4\pi r^2$, $V = \frac{4}{3}\pi r^3$, so $\dfrac{\text{SA}}{V} = \dfrac{3}{r}$. In both cases, SA:V is inversely proportional to the linear size of the cell — it falls as the cell grows.

Ví dụ mẫu · SA:V ratio for cubes of increasing size

Compute the surface area, volume, and SA:V ratio for cubical cells of side length 1, 2, and 4 cm.

L (cm)	SA $= 6L^2$ (cm^2)	$V = L^3$ (cm^3)	SA:V
1	6	1	6.0
2	24	8	3.0
4	96	64	1.5

Doubling the side length from 1 to 2 cm multiplies surface area by 4 but volume by 8, so SA:V is cut in half ($6 \to 3$); doubling again ($2 \to 4$ cm) halves it again ($3 \to 1.5$). A cell that grew to macroscopic size (centimeters) would have far too little membrane surface, relative to its metabolic volume, to import nutrients and O_2 or export wastes fast enough to stay alive — which is exactly why living cells remain microscopic and large organisms are built from enormous numbers of small cells (multicellularity) rather than a few giant ones.



Squares represent the cross-section of cubical cells with side length $L = 1$, 2, and 4 cm. As L increases, volume ($\propto L^3$) outgrows surface area ($\propto L^2$), so the SA:V ratio falls.

Cells and organisms counteract a low SA:V ratio by folding or extending their exchange surfaces rather than growing a smooth surface larger — increasing surface area without a matching increase in volume.

Ví dụ mẫu · Surface amplification by root hairs

A root epidermal cell's absorptive plasma membrane, if perfectly smooth, would have surface area 500 μm^2 for a cell volume of 2000 μm^3 (initial SA:V $= 500/2000 = 0.25$). A slender root-hair extension increases this absorptive surface area by a factor of 5, to 2500 μm^2, while adding negligible extra volume. Find the new SA:V ratio.

$$\text{New SA:V} = \frac{2500\ \mu\text{m}^2}{2000\ \mu\text{m}^3} = 1.25\ \mu\text{m}^{-1},$$

exactly $5\times$ the original ratio (0.25). The same principle explains intestinal microvilli, the highly folded inner mitochondrial membrane (cristae), and the many thin lamellae of a fish gill: each increases exchange surface area steeply without a proportional increase in volume.

VN **GIẢI THÍCH TIẾNG VIỆT**

Tỉ lệ diện tích bề mặt trên thể tích (SA:V) là lý do cốt lõi khiến tế bào phải nhỏ. Khi kích thước tế bào tăng, thể tích (nhu cầu trao đổi chất) tăng theo luỹ thừa 3, còn diện tích màng (khả năng trao đổi chất) chỉ tăng theo luỹ thừa 2 — nên tỉ lệ SA:V giảm dần. Đây là lý do sinh vật lớn phải cấu tạo từ **nhiều tế bào nhỏ** (đa bào) thay vì một tế bào khổng lồ, và là lý do các cấu trúc như **vi nhung mao** (microvilli) ở ruột non, **lông hút** ở rễ cây, hay **mào** (cristae) trong ty thể đều có hình dạng gấp nếp để tăng diện tích bề mặt trao đổi mà không làm tăng đáng kể thể tích.

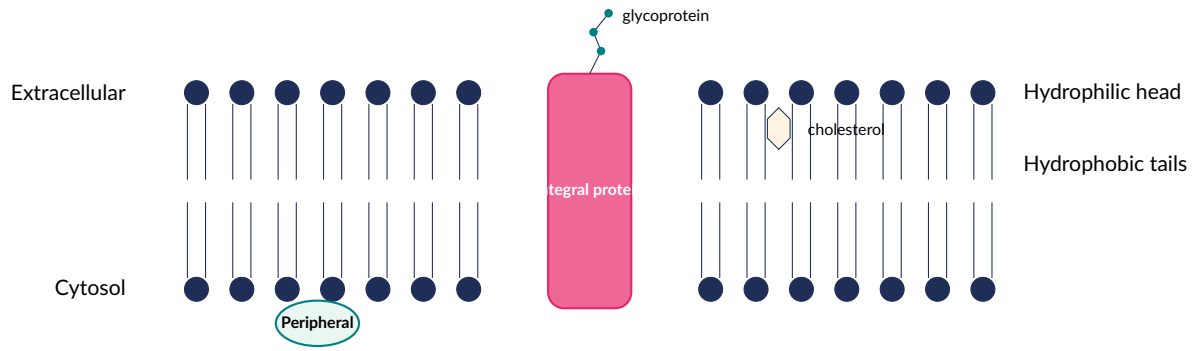
2.4 The Plasma Membrane: Fluid Mosaic Model

The plasma membrane is described by the **fluid mosaic model** (Singer and Nicolson, 1972): a **phospholipid bilayer** in which diverse proteins are embedded, all free to drift laterally.

Fluid mosaic model

Each **phospholipid** has a hydrophilic phosphate "head" and two hydrophobic fatty-acid "tails." In water, phospholipids spontaneously arrange into a bilayer with heads facing the aqueous extracellular fluid and cytosol, and tails facing each other in the water-free interior. **Integral (transmembrane) proteins** span the bilayer; **peripheral proteins** attach loosely to one face without penetrating it. The membrane is **fluid** because phospholipids and many proteins move laterally within their layer, and a **mosaic** because of the varied assortment of proteins studded throughout it.

Cholesterol, wedged between phospholipid tails in animal cell membranes, acts as a fluidity buffer: at high temperature it restrains excess phospholipid movement (reducing fluidity), while at low temperature it prevents phospholipids from packing tightly together and solidifying (maintaining fluidity). **Glycoproteins** and **glycolipids** — proteins and lipids with short carbohydrate chains attached on the extracellular face — function in cell-cell recognition, acting like an identification tag that allows immune cells, for instance, to distinguish "self" from "non-self."



Fluid mosaic model of the plasma membrane: a phospholipid bilayer (hydrophilic heads outward, hydrophobic tails inward) with an integral protein carrying an extracellular glycoprotein chain, a peripheral protein on the cytosolic face, and cholesterol nestled within the bilayer.

Ví dụ mẫu · Cholesterol and membrane fluidity

Predict how the fluidity of an animal cell's plasma membrane responds to a temperature drop from $37\,^{\circ}$C to $10\,^{\circ}$C, (a) in a hypothetical membrane with no cholesterol, and (b) in a real membrane containing cholesterol.

(a) Without cholesterol, cooling allows the fatty-acid tails of adjacent phospholipids to pack closely together through van der Waals interactions; the bilayer stiffens and can solidify into a gel-like state, impairing the function of embedded transport and signaling proteins.
(b) With cholesterol interspersed among the phospholipids, cholesterol's rigid ring structure interferes with this tight packing at low temperature, keeping the membrane fluid enough for normal protein function. At high temperature, the same cholesterol molecules instead restrain phospholipid movement, preventing the membrane from becoming excessively fluid. Cholesterol therefore **narrows the range of fluidity** the membrane experiences across a range of temperatures.

VN **GIẢI THÍCH TIẾNG VIỆT**

"Khảm động" (fluid mosaic) nghĩa là: **khảm** — màng là một bức tranh ghép gồm nhiều loại protein khác nhau cắm rải rác trong lớp phospholipid kép; **động** — các phân tử phospholipid và nhiều protein có thể trượt ngang tự do trong lớp màng, không đứng yên. **Cholesterol** đóng vai trò "bộ đệm ổn định độ linh động": ở nhiệt độ thấp nó ngăn màng bị đông cứng, ở nhiệt độ cao nó ngăn màng bị lỏng lẻo quá mức. **Glycoprotein/glycolipid** ở mặt ngoài tế bào hoạt động như "thẻ căn cước" giúp tế bào nhận diện nhau (ví dụ: hệ miễn dịch phân biệt tế bào của cơ thể với tế bào lạ).

2.4.1 Membrane permeability: what crosses freely

The hydrophobic core of the bilayer makes the plasma membrane **selectively permeable**: some substances cross it directly and rapidly, while others require a transport protein.

Crosses freely (no protein needed): small nonpolar/hydrophobic molecules such as O_2, CO_2, N_2, and lipid-soluble hormones (e.g., steroid hormones); very small uncharged polar molecules such as H_2O cross slowly by simple diffusion (and much faster through dedicated **aquaporin** channels).

Requires a transport protein: large molecules (glucose, amino acids, nucleotides) and any charged or strongly polar species (ions such as Na^+, K^+, Cl^-, H^+, Ca^{2+}) are repelled by the hydrophobic interior of the bilayer and must be shuttled across by a specific channel or carrier protein.

VN **GIẢI THÍCH TIẾNG VIỆT**

Nguyên tắc chọn lọc của màng: phân tử **nhỏ, không phân cực / kỵ nước** (O_2, CO_2, hormone steroid) đi xuyên qua lớp lipid kép một cách trực tiếp và dễ dàng. Phân tử **lớn, phân cực, hoặc mang điện tích** (glucose, amino acid, các ion như Na^+, K^+) bị lớp đuôi kỵ nước ở giữa màng "chặn lại" và bắt buộc phải đi qua một **protein vận chuyển** chuyên biệt.

2.5 Passive Transport Across Membranes

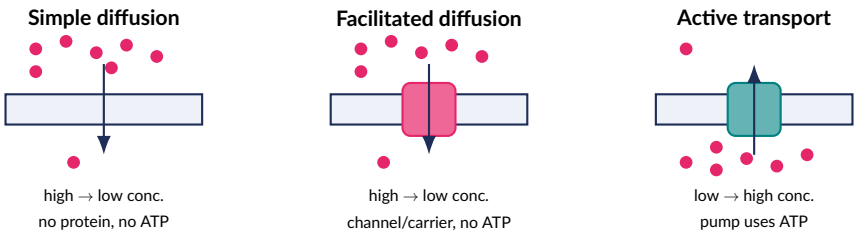
Passive transport moves a substance down its concentration (or electrochemical) gradient — from high to low concentration — and requires *no* input of metabolic energy, because the gradient itself is the energy source.

2.5.1 Simple and facilitated diffusion

In **simple diffusion**, small nonpolar molecules move directly through the lipid bilayer, from a region of higher concentration to a region of lower concentration, until equilibrium is reached. In **facilitated diffusion**, polar or charged solutes that cannot cross the bilayer unassisted still move down their gradient, but only with the help of a transport protein:

- **Channel proteins** form a hydrophilic pore through the membrane (e.g., aquaporins for water; ion channels, which may be gated — voltage-gated or ligand-gated — opening only under specific conditions).
- **Carrier proteins** bind their specific solute and undergo a conformational change that shuttles it across (e.g., GLUT transporters for glucose).

(!) Lỗi thường gặp: Facilitated diffusion still counts as **passive** transport, even though it requires a protein. The defining test for "passive" is not whether a protein is involved, but whether the solute moves *down* its concentration/electrochemical gradient without ATP hydrolysis. A protein is required here only because the solute is too polar, charged, or large to cross the lipid bilayer directly — not because energy must be spent to move it.



Passive transport (simple and facilitated diffusion) moves solutes down their concentration gradient with no energy input; active transport moves solutes against their gradient and requires ATP hydrolysis.

Ví dụ mẫu · Diffusion rate and the concentration gradient

By Fick's law, the net rate of diffusion is directly proportional to the size of the concentration gradient across the membrane (all else — temperature, surface area, membrane permeability — held constant). O_2 diffusing across an alveolar membrane moves at 40 mL/min when the partial-pressure difference between alveolar air and blood is 60 mmHg. Predict the new diffusion rate if the gradient increases to 90 mmHg (e.g., during exercise, as blood O_2 is used up faster).

$$\text{rate}_2 = \text{rate}_1 \times \frac{\Delta P_2}{\Delta P_1} = 40 \text{ mL/min} \times \frac{90}{60} = 60 \text{ mL/min}.$$

A $1.5\times$ increase in gradient produces a $1.5\times$ increase in diffusion rate — the hallmark of a simple, unassisted, non-saturating diffusion process.

Ví dụ mẫu · Simple diffusion vs. a saturable carrier

Compare O_2 entering a red blood cell (simple diffusion) with glucose entering the same cell via GLUT1 carrier proteins (facilitated diffusion) as external concentration keeps rising. Why does O_2 uptake keep climbing roughly in proportion to its gradient, while glucose uptake through GLUT1 levels off (saturates) at high external glucose concentration?

O_2 dissolves directly in the lipid bilayer and crosses at any point on the membrane, so there

is effectively no upper limit on how many molecules can cross per second as the gradient grows. Glucose, however, must bind a *finite* number of GLUT1 carrier proteins in the membrane; once every carrier is continuously occupied and cycling, adding more external glucose cannot increase the rate further — the transport rate has reached its maximum (T_{max}), and the rate-vs-concentration curve flattens into a plateau. This carrier saturation is a defining signature of any transport process (facilitated diffusion or active transport) that depends on a limited number of protein transporters, and distinguishes it from unassisted simple diffusion.

2.5.2 Osmosis and water potential

Osmosis is the diffusion of water across a selectively permeable membrane, from a region of higher *water* concentration (lower solute concentration) to a region of lower water concentration (higher solute concentration).

(!) Lỗi thường gặp: **Osmosis is not a separate phenomenon from diffusion — it *is* diffusion**, specifically the diffusion of water molecules across a selectively permeable membrane. Every osmosis question is a diffusion question about one particular solute: water. Do not treat "diffusion" and "osmosis" as two unrelated transport types on an exam; osmosis is the special case where the diffusing substance is water itself.

To predict the direction of water movement precisely — including in walled plant cells, where physical pressure matters — biologists use **water potential** (Ψ, the Greek letter psi), measured in bars. Water always moves from a region of *higher* Ψ to a region of *lower* Ψ.

$$\Psi = \Psi_p + \Psi_s, \qquad \Psi_s = -iCRT$$

where Ψ_p is **pressure potential** (physical pressure on the solution; positive when a cell wall pushes back against a swelling cell, i.e., turgor pressure); Ψ_s is **solute potential** (osmotic potential), which is always ≤ 0 for a solution (solutes "tie up" water molecules and lower its free energy); i is the **ionization constant** (number of particles the solute dissociates into: $i = 1$ for sucrose, $i = 2$ for NaCl, $i = 3$ for $CaCl_2$); C is molar concentration (mol/L); $R = 0.0831$ L·bar/(mol·K); T is temperature in kelvin (°C + 273). By convention, pure free water at atmospheric pressure has $\Psi = 0$.

Ví dụ mẫu · Solute potential of an open solution

Find Ψ_s and Ψ for a 0.30 M sucrose solution in an open beaker at $27\,^{\circ}$C ($T = 300$ K). Sucrose does not ionize, so $i = 1$; an open beaker has $\Psi_p = 0$.

$$\Psi_s = -iCRT = -(1)(0.30)(0.0831)(300) = -7.48 \text{ bar}.$$
$$\Psi = \Psi_p + \Psi_s = 0 + (-7.48) = -7.48 \text{ bar}.$$

Ví dụ mẫu · Comparing two solutions, and a walled cell at turgor

(a) Two open beakers, both at $25\,^{\circ}$C ($T = 298$ K), are separated by a selectively permeable membrane: Beaker A holds 0.10 M NaCl ($i = 2$); Beaker B holds 0.20 M NaCl ($i = 2$). Predict the direction of net water movement.

$$\Psi_A = -iCRT = -(2)(0.10)(0.0831)(298) = -4.95 \text{ bar} \;\; (\Psi_p = 0 \Rightarrow \Psi_A = -4.95).$$

$$\Psi_B = -(2)(0.20)(0.0831)(298) = -9.90 \text{ bar} \quad (\Psi_p = 0 \Rightarrow \Psi_B = -9.90).$$

Water moves from the higher (less negative) potential to the lower potential: from **A to B** — that is, from the more dilute toward the more concentrated solution.

(b) A walled plant cell with internal solute potential $\Psi_s = -6$ bar is placed in pure water ($\Psi = 0$) and allowed to reach equilibrium. Find the pressure (turgor) potential the wall develops at equilibrium.

At equilibrium the cell's Ψ equals the surrounding water's Ψ: $\Psi_{\text{cell}} = 0$. Since $\Psi_{\text{cell}} = \Psi_p + \Psi_s$:

$$0 = \Psi_p + (-6) \implies \Psi_p = +6 \text{ bar}.$$

Net water entry raises internal pressure until the wall pushes back with $\Psi_p = +6$ bar, exactly canceling the pull of $\Psi_s = -6$ bar — at that point $\Psi_{\text{cell}} = \Psi_{\text{outside}}$ and net water flow stops, leaving the cell firm and turgid rather than bursting.

(!) Lỗi thường gặp: The most common Ψ_s error is a **sign mistake**: $\Psi_s = -iCRT$ always carries a leading minus sign, because dissolved solute can only lower water potential relative to pure water — never raise it. A second common error is forgetting the ionization constant i: a 0.1 M NaCl solution has *double* the solute potential magnitude of a 0.1 M sucrose solution at the same temperature, because NaCl dissociates into two particles per formula unit ($i = 2$) while sucrose does not dissociate at all ($i = 1$).

VN **GIẢI THÍCH TIẾNG VIỆT**

Thẩm thấu là sự khuếch tán của nước qua màng bán thấm, từ nơi thế nước cao đến nơi thế nước thấp. **Thế nước** $\Psi = \Psi_p + \Psi_s$ gồm hai thành phần: **thế áp suất** Ψ_p (áp lực vật lý — dương khi thành tế bào đẩy ngược lại tế bào đang trương nước) và **thế thẩm thấu** Ψ_s (luôn ≤ 0, vì chất tan làm giảm "năng lượng tự do" của nước). Công thức $\Psi_s = -iCRT$ luôn có dấu **âm**, và hệ số i (số hạt phân li) rất dễ bị bỏ sót khi tính với các chất điện li như NaCl. **Nước luôn di chuyển từ nơi Ψ cao đến nơi Ψ thấp** — đây là nguyên lý duy nhất cần nhớ để giải mọi bài toán thế nước.

2.6 Tonicity and Osmoregulation

Tonicity describes the effect a surrounding solution has on a cell's water balance, by comparing solute concentration outside the cell to that inside.

Solution	Animal cell (no wall)	Plant cell (has wall)
Isotonic (equal solute conc.)	No net water movement; normal shape	No net water movement; flaccid (not turgid)
Hypertonic (more solute outside)	Water exits; cell shrinks (**crenation**)	Water exits; membrane pulls away from wall (**plasmolysis**)
Hypotonic (less solute outside)	Water enters; cell swells and may burst (**lysis**)	Water enters; wall resists, cell becomes firm (**turgid**)

(!) Lỗi thường gặp: Students frequently reverse the direction of water flow. Remember: water moves toward the side with *more* solute (lower water potential) — so a cell placed in a **hyper**tonic solution *loses* water (shrinks), and a cell placed in a **hypo**tonic solution *gains* water

(swells). A useful anchor: "hyper" = solution has the higher (greater) solute concentration ⇒ it pulls water *out of* the cell.

(!) Lỗi thường gặp: Do not assume a plant cell placed in a hypotonic solution behaves like an animal cell. An animal cell has no wall and can lyse (burst) as water keeps entering. A plant cell's rigid cellulose wall resists expansion: internal pressure potential rises until it balances the solute potential difference, water movement stops, and the cell simply becomes turgid — it does *not* burst under normal hypotonic conditions. This is precisely why a wilted plant regains rigidity ("perks up") after watering.

Ví dụ mẫu · Same hypotonic solution, two different outcomes

A red blood cell (animal cell, no wall) and an *Elodea* leaf cell (plant cell, has a cellulose wall) are both placed in distilled water (strongly hypotonic to both). Predict and explain the outcome for each.

Red blood cell: water enters continuously by osmosis because solute concentration is higher inside than in the surrounding distilled water, and nothing but the plasma membrane resists the resulting pressure buildup. The membrane cannot withstand unlimited internal pressure, so the cell swells and undergoes **lysis** (bursts).

Elodea leaf cell: water also enters by osmosis, and the cell begins to swell — but the rigid cell wall resists further expansion. Internal pressure potential Ψ_p rises as the protoplast pushes against the wall, until Ψ_p exactly offsets the negative Ψ_s inside the cell and $\Psi_{\text{cell}} = \Psi_{\text{outside}} = 0$. Net water entry then stops with the cell **turgid** (firm), not burst. The cell wall is therefore essential for allowing plant cells to tolerate hypotonic environments that would destroy an unwalled animal cell.

Osmoregulation is the active maintenance of solute/water balance. Freshwater protists such as *Paramecium* live in a strongly hypotonic environment and continuously take on water by osmosis; a **contractile vacuole** collects this excess water and actively expels it, preventing lysis. Multicellular animals regulate the tonicity of extracellular fluid using specialized organs (e.g., kidneys), keeping the internal environment close to isotonic for individual cells.

VN **GIẢI THÍCH TIẾNG VIỆT**

Đẳng trương (isotonic): nồng độ chất tan trong và ngoài tế bào bằng nhau, không có sự di chuyển nước ròng. **Ưu trương** (hypertonic): dung dịch bên ngoài có nồng độ chất tan CAO hơn trong tế bào → nước đi RA khỏi tế bào → tế bào động vật teo lại, tế bào thực vật **co nguyên sinh** (màng tách khỏi thành). **Nhược trương** (hypotonic): dung dịch bên ngoài có nồng độ chất tan THẤP hơn trong tế bào → nước đi VÀO tế bào → tế bào động vật có thể vỡ (tan bào), còn tế bào thực vật chỉ **trương nước** (turgid) nhờ có thành tế bào chống đỡ, không bị vỡ. **Không bào co bóp** (contractile vacuole) giúp các sinh vật đơn bào nước ngọt bơm nước thừa ra ngoài để tránh bị vỡ.

2.7 Active Transport

Active transport moves a solute *against* its concentration (or electrochemical) gradient — from low to high concentration — which is thermodynamically unfavorable and therefore requires an input of metabolic energy, typically ATP.

Primary active transport uses the energy released by ATP hydrolysis directly to power a conformational change in a pump protein. The classic example is the Na^+/K^+ **pump (**Na^+/K^+**-ATPase)**, found in the plasma membrane of essentially all animal cells: for each ATP hydrolyzed, it exports 3

Na^+ ions and imports 2 K^+ ions, both moving against their respective gradients. This maintains the steep Na^+ and K^+ gradients that neurons use to generate action potentials, and — because it moves 3 positive charges out for every 2 it brings in — it directly contributes a small net negative charge to the cell interior (it is "electrogenic"), on top of its larger role in sustaining the electrochemical gradients on which secondary active transport and nerve signaling depend.

Secondary active transport (cotransport) uses the electrochemical gradient built up by a primary pump (very often the Na^+ gradient) to drive a *second* solute against its own gradient, without directly hydrolyzing ATP itself. A **symporter** moves both solutes in the same direction across the membrane (e.g., the Na^+/glucose symporter in intestinal epithelial cells, which pulls glucose into the cell against its gradient as Na^+ flows down its gradient); an **antiporter** moves them in opposite directions (e.g., the Na^+/H^+ antiporter). Cotransport is still ultimately powered by ATP, since the Na^+ gradient it depends on was itself built by the ATP-driven Na^+/K^+ pump.

Ví dụ mẫu · Na^+/K^+ pump stoichiometry

After a burst of neuronal signaling, a neuron must export 1.5×10^5 Na^+ ions per second to restore its resting gradient. Given the pump's fixed stoichiometry of 3 Na^+ out and 2 K^+ in per ATP hydrolyzed, find (a) the rate of ATP hydrolysis and (b) the rate of K^+ import.

(a) $\dfrac{1.5 \times 10^5 \text{ Na}^+/\text{s}}{3 \text{ Na}^+/\text{ATP}} = 5.0 \times 10^4$ ATP/s.

(b) 5.0×10^4 ATP/s $\times$ 2 K^+/ATP $= 1.0 \times 10^5$ K^+ ions imported per second.

VN **GIẢI THÍCH TIẾNG VIỆT**

Vận chuyển chủ động di chuyển chất tan NGƯỢC chiều gradient nồng độ, nên bắt buộc cần năng lượng (thường là ATP) — khác với vận chuyển thụ động (khuếch tán, khuếch tán tăng cường, thẩm thấu) luôn đi THEO chiều gradient và không cần năng lượng. **Bơm Na^+/K^+** là ví dụ kinh điển của **vận chuyển chủ động sơ cấp** (dùng ATP trực tiếp): mỗi ATP thuỷ phân bơm 3 Na^+ ra ngoài và 2 K^+ vào trong. **Vận chuyển chủ động thứ cấp** (đồng vận chuyển) không dùng ATP trực tiếp mà "mượn" năng lượng từ gradient đã được bơm sơ cấp tạo ra trước đó (ví dụ: đồng vận chuyển Na^+/glucose ở ruột non).

2.8 Bulk Transport: Endocytosis and Exocytosis

Molecules too large for any membrane transport protein — whole macromolecules, particles, or even entire cells — cross the plasma membrane packaged inside vesicles, in a process that always requires ATP.

Endocytosis brings material into the cell as the plasma membrane invaginates and pinches off to form a vesicle:

- **Phagocytosis** ("cell eating"): the cell engulfs large particles or entire cells (e.g., a macrophage engulfing a bacterium), forming a large vesicle (phagosome) that typically fuses with a lysosome for digestion.
- **Pinocytosis** ("cell drinking"): the cell nonspecifically takes in extracellular fluid and any dissolved solutes via small vesicles.
- **Receptor-mediated endocytosis**: specific molecules bind receptor proteins clustered on the membrane surface (often at clathrin-coated pits), triggering vesicle formation; this is far more selective and efficient than pinocytosis (e.g., uptake of LDL cholesterol particles via LDL receptors).

Exocytosis is the reverse process: an intracellular vesicle fuses with the plasma membrane, releasing its contents to the outside (e.g., secretion of hormones, digestive enzymes, or neurotransmitters at a synapse).

VN **GIẢI THÍCH TIẾNG VIỆT**

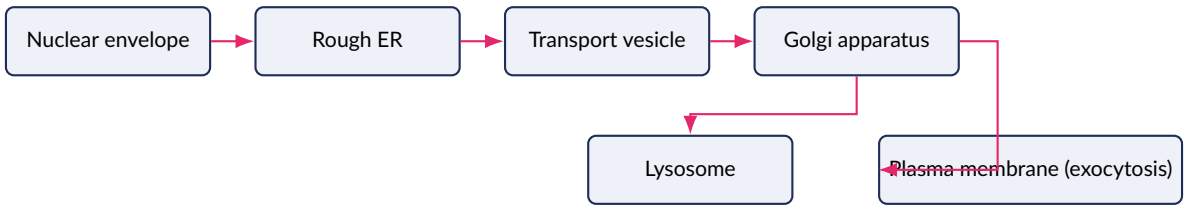
Nhập bào (endocytosis) là quá trình màng tế bào lõm vào để "nuốt" vật chất vào bên trong dưới dạng túi (vesicle), gồm ba kiểu: **thực bào** (nuốt hạt/tế bào lớn), **ẩm bào** (hút dịch ngoại bào không chọn lọc), và **nhập bào qua trung gian thụ thể** (chọn lọc cao nhờ thụ thể đặc hiệu). **Xuất bào** (exocytosis) là quá trình ngược lại: túi nội bào hợp nhất với màng sinh chất để giải phóng chất ra ngoài (ví dụ: bài tiết hormone, enzyme tiêu hoá, chất dẫn truyền thần kinh). Cả hai đều cần năng lượng ATP vì liên quan đến sự biến dạng chủ động của màng và bộ khung xương tế bào.

2.9 Cell Compartmentalization and the Endomembrane System

Eukaryotic cells divide their interior into distinct membrane-bound compartments — the **endomembrane system** — that work together as a coordinated production and delivery pathway for proteins and lipids.

Endomembrane pathway

Proteins destined for secretion or for insertion into a membrane typically travel: **nuclear envelope** (continuous with) → **rough ER** (synthesis, folding, initial modification) → **transport vesicle** → **Golgi apparatus** (further modification, sorting, tagging with an address) → **vesicle** → final destination: the **plasma membrane** (secreted by exocytosis, or inserted as a membrane protein) or a **lysosome** (as a digestive enzyme).



Vesicle trafficking through the endomembrane system: proteins made on the rough ER are packaged into vesicles, processed and sorted through the Golgi apparatus, and delivered either to lysosomes or to the plasma membrane for secretion.

Compartmentalization dramatically increases a eukaryotic cell's efficiency in two related ways. First, it creates **localized chemical environments** tailored to specific reactions — for example, lysosomes maintain an acidic interior (pH ≈ 4.5–5) ideal for their hydrolytic enzymes, sharply different from the near-neutral cytosol (pH ≈ 7.2), and mitochondria maintain a proton gradient across the inner membrane that would be impossible without a bounded compartment. Second, it allows **simultaneous, incompatible reactions** to proceed at once in the same cell without interfering with each other — for example, powerful digestive enzymes are safely confined within lysosomes rather than roaming free in the cytosol, where they would degrade the cell's own proteins.

VN **GIẢI THÍCH TIẾNG VIỆT**

Hệ thống màng nội bào (endomembrane system) hoạt động như một dây chuyền sản xuất: màng nhân → lưới nội chất hạt (tổng hợp và gấp protein) → túi vận chuyển → bộ máy Golgi (chỉnh sửa, phân loại, gắn "địa chỉ") → túi vận chuyển → đích cuối cùng (màng sinh chất để xuất bào, hoặc lysosome). Việc chia tế bào thành nhiều "ngăn" có màng bao riêng biệt giúp: (1) tạo ra các **môi trường hoá học cục bộ** phù hợp cho từng loại phản ứng (ví dụ pH acid trong lysosome khác hẳn pH trung tính của bào tương); (2) cho phép các phản ứng **không tương thích xảy ra đồng thời** mà không gây hại lẫn nhau (enzyme tiêu hoá mạnh được "nhốt" an toàn trong lysosome thay vì trôi nổi tự do trong bào tương).

2.10 Origins of Compartmentalization: Endosymbiotic Theory

Why do mitochondria and chloroplasts look and behave so differently from every other eukaryotic organelle? The **endosymbiotic theory** proposes that both organelles originated as free-living prokaryotes engulfed by an ancestral host cell roughly 1.5–2 billion years ago (mitochondria, from an aerobic bacterium) and later (≈ 1 billion years ago, chloroplasts, from a photosynthetic cyanobacterium), establishing a permanent mutualistic partnership rather than being digested.

Evidence for the endosymbiotic theory:

- **Double membrane**: the outer membrane derives from the host cell's engulfing vesicle; the inner membrane derives from the original prokaryote's own plasma membrane.
- **Own circular DNA**: a single circular chromosome, unassociated with histones — structurally like a bacterial chromosome, not like the linear, histone-wrapped nuclear chromosomes of the host.
- **Own $70S$ ribosomes**: matching the size and composition of bacterial ribosomes, distinct from the host's cytosolic $80S$ ribosomes, and sensitive to antibiotics (e.g., streptomycin) that specifically target bacterial-type ribosomes.
- **Binary-fission-like division**: mitochondria and chloroplasts replicate on their own schedule, independent of the host cell's mitotic cycle, by pinching in two much like bacterial binary fission.
- **Comparable size to bacteria**: both organelles are roughly 1–5 μm, the same size range as typical free-living prokaryotic cells.

Ví dụ mẫu · Applying the evidence for endosymbiosis

A biologist isolates an unknown organelle from a eukaryotic cell and observes: (1) it is bounded by two membranes; (2) it contains a small circular DNA molecule distinct from the cell's nuclear genome; (3) it contains $70S$ ribosomes; (4) it divides independently of the host cell cycle by a pinching mechanism resembling bacterial binary fission. Evaluate whether these observations support an endosymbiotic origin, and identify one additional feature that would distinguish a mitochondrion from a chloroplast.

All four observations match the predictions of endosymbiotic theory: the double membrane is consistent with an engulfing host vesicle plus the original prokaryote's own membrane; the circular, histone-free DNA and $70S$ ribosomes are bacterial hallmarks, not eukaryotic nuclear/-cytosolic ones; and independent, fission-like division is exactly how free-living bacteria reproduce, not how host organelles are built during mitosis. To distinguish the two: the presence of **thylakoid membranes stacked into grana, a stroma, and chlorophyll** would identify a **chloroplast** (photosynthetic), whereas **cristae** (folds of the inner membrane) and a matrix containing citric-acid-cycle enzymes, with no chlorophyll, would identify a **mitochondrion**.

VN **GIẢI THÍCH TIẾNG VIỆT**

Thuyết nội cộng sinh cho rằng ty thể và lục lạp vốn là các vi khuẩn sống tự do, bị một tế bào tổ tiên "nuốt" vào nhưng không bị tiêu hoá mà tồn tại cộng sinh bên trong, dần trở thành bào quan. Bằng chứng gồm: **màng kép** (màng ngoài từ túi nuốt của tế bào chủ, màng trong từ chính vi khuẩn); **ADN vòng riêng** không liên kết với histone (giống vi khuẩn, khác ADN nhân); **ribosome** $70S$ riêng (giống vi khuẩn, khác ribosome $80S$ trong bào tương); **phân chia kiểu trực phân** độc lập với chu kỳ tế bào của vật chủ; và **kích thước tương đương vi khuẩn**. Đây là lý do ty thể và lục lạp là hai bào quan duy nhất mang bộ gen riêng ngoài nhân tế bào.

2.11 Practice Problems

Bài tập luyện tập

Which statement is a correct part of the cell theory?

(A) Cells can arise spontaneously from non-living matter under the right conditions.

(B) All living organisms are composed of one or more cells, and all cells arise from pre-existing cells.

(C) Only eukaryotic organisms are composed of cells.

(D) Prokaryotic cells are not considered true cells because they lack a nucleus.

Lời giải chi tiết

Cell theory states that all organisms are made of cells and that cells arise only from pre-existing cells, never spontaneously. Prokaryotes are true cells; they simply lack a membrane-bound nucleus. **(B)**.

Bài tập luyện tập

A researcher observes an unknown microorganism under an electron microscope and notes: no membrane-bound nucleus, a single circular chromosome in an unbound nucleoid region, and $70S$ ribosomes. This organism is most likely:

(A) A plant cell

(B) A prokaryote

(C) A fungal cell

(D) An animal cell

Lời giải chi tiết

The absence of a membrane-bound nucleus, a single circular (unbound) chromosome, and $70S$ ribosomes are all defining prokaryotic features; eukaryotic cells (plant, fungal, animal) have a membrane-bound nucleus and $80S$ cytosolic ribosomes. **(B)**.

Bài tập luyện tập

List two structural differences and one size difference between a typical prokaryotic cell and a typical eukaryotic cell.

Lời giải chi tiết

Structural: (1) prokaryotes lack a membrane-bound nucleus (DNA is in an unbound nucleoid), while eukaryotes have a true nucleus; (2) prokaryotes lack membrane-bound organelles (no ER, Golgi, mitochondria, etc.), while eukaryotes have an extensive endomembrane system and other membrane-bound organelles. Size: prokaryotic cells are typically 1–10 μm, while eukaryotic cells are typically 10–100 μm, roughly an order of magnitude larger.

Bài tập luyện tập

Which organelle is correctly paired with its primary function?

(A) Smooth ER — protein synthesis via bound ribosomes
(B) Golgi apparatus — modifies, sorts, and packages proteins and lipids for delivery
(C) Lysosome — synthesizes ATP through aerobic respiration
(D) Nucleolus — stores hydrolytic digestive enzymes

Lời giải chi tiết

The Golgi apparatus receives material from the ER, chemically modifies and tags it, and packages it into vesicles addressed to its correct destination. Smooth ER (not rough ER) lacks ribosomes and instead makes lipids; lysosomes digest macromolecules, they do not make ATP; the nucleolus assembles ribosomal subunits, it does not store digestive enzymes. **(B)**.

Bài tập luyện tập

A liver cell that specializes in detoxifying drugs would be expected to have an unusually large amount of which organelle?

(A) Rough endoplasmic reticulum
(B) Smooth endoplasmic reticulum
(C) Lysosomes
(D) Central vacuole

Lời giải chi tiết

Smooth ER carries out lipid synthesis and detoxification of drugs and metabolic wastes; liver cells, which perform heavy detoxification, are characteristically packed with smooth ER. **(B)**.

Bài tập luyện tập

Explain, in terms of structure, why the inner membrane of a mitochondrion is folded into cristae rather than being smooth.

Lời giải chi tiết

The electron transport chain proteins responsible for aerobic ATP production are embedded in the inner mitochondrial membrane. Folding this membrane into cristae greatly increases its surface area without increasing the mitochondrion's overall volume, allowing many more electron transport chain complexes (and thus a higher rate of ATP synthesis) to be packed into the same organelle — the same surface-area-amplification principle that governs intestinal microvilli and root hairs.

Bài tập luyện tập

Which of the following would be found in BOTH a mitochondrion and a chloroplast?

(A) Thylakoid membranes
(B) Chlorophyll
(C) Circular DNA and $70S$ ribosomes
(D) Cristae

Lời giải chi tiết

Both mitochondria and chloroplasts carry their own circular DNA and their own $70S$ ribosomes — a shared legacy of their endosymbiotic bacterial origins. Thylakoids and chlorophyll are specific to chloroplasts; cristae are specific to mitochondria. **(C)**.

Bài tập luyện tập

A spherical cell has radius $r = 3$ μm. Calculate its surface area, volume, and SA:V ratio. (SA $= 4\pi r^2$, $V = \frac{4}{3}\pi r^3$.)

Lời giải chi tiết

SA $= 4\pi(3)^2 = 4\pi(9) = 36\pi \approx 113.1$ μm^2.
$V = \frac{4}{3}\pi(3)^3 = \frac{4}{3}\pi(27) = 36\pi \approx 113.1$ μm^3.
SA:V $= \dfrac{36\pi}{36\pi} = 1.0$ (equivalently, using SA:V $= 3/r = 3/3 = 1.0$ μm^{-1}).

Bài tập luyện tập

If the radius of the spherical cell above doubles to $r = 6$ μm, find the new SA:V ratio and state, with a reason, whether the cell's exchange capacity per unit volume has improved or worsened.

Lời giải chi tiết

SA:V $= 3/r = 3/6 = 0.5$ μm^{-1}. The ratio has been cut in half (from 1.0 to 0.5). Because metabolic demand scales with volume ($\propto r^3$) while exchange capacity scales with surface area ($\propto r^2$), doubling the radius means the cell now has only half as much membrane surface available per unit of metabolic demand — its exchange capacity per unit volume has **worsened**.

Bài tập luyện tập

A cube-shaped cell has side length $L = 3$ mm. (a) Compute its SA, V, and SA:V ratio. (b) A second, similar cell has side length $L = 6$ mm. By what factor has the SA:V ratio changed?

Lời giải chi tiết

(a) SA $= 6L^2 = 6(9) = 54$ mm^2; $V = L^3 = 27$ mm^3; SA:V $= 54/27 = 2.0$.
(b) For $L = 6$: SA:V $= 6/L = 6/6 = 1.0$. The ratio fell from 2.0 to 1.0, a factor of $\frac{1}{2}$ — consistent with SA:V $= 6/L$ being inversely proportional to L: doubling L always halves the SA:V ratio.

Bài tập luyện tập

Explain, using the concept of SA:V ratio, why large multicellular organisms are built from enormous numbers of small cells rather than from a smaller number of very large cells.

Lời giải chi tiết

Volume (and therefore metabolic demand for nutrients, O_2, and waste removal) scales with the cube of a cell's linear dimension, while the surface area of the plasma membrane available for exchange scales only with the square. As a hypothetical cell grew larger, its SA:V ratio would keep falling (SA:V $\propto 1/L$), so eventually its membrane surface could not supply nutrients or remove wastes fast enough to sustain its interior. Building a large body from vast numbers of small cells — each individually kept below this size limit — instead lets every cell retain a sufficiently high SA:V ratio for its own exchange needs, while overall organism size is achieved by cell *number*, not cell *size*.

Bài tập luyện tập

Which structure is best described by the fluid mosaic model as providing the membrane's "fluidity"?

(A) The rigid cellulose cell wall outside the membrane
(B) The lateral movement of phospholipids and many proteins within the bilayer
(C) Covalent cross-links locking proteins in a fixed position
(D) The nuclear envelope's double-membrane structure

Lời giải chi tiết

"Fluid" in the fluid mosaic model refers to the fact that phospholipids and many embedded proteins are not fixed in place but drift laterally within their layer of the bilayer. A rigid cell wall and covalent cross-links would prevent, not enable, fluidity; the nuclear envelope is a separate structure. **(B)**.

Bài tập luyện tập

A membrane protein that binds a hormone on the extracellular surface and triggers an internal response, but never enters the hydrophobic core of the membrane, is best classified as:

(A) An integral (transmembrane) protein
(B) A peripheral protein
(C) A phospholipid
(D) A glycolipid

Lời giải chi tiết

A protein that stays on one face of the membrane without spanning the hydrophobic core is a peripheral protein, by definition; an integral/transmembrane protein spans the bilayer. **(B)**.

Bài tập luyện tập

Explain the role of glycoproteins on the extracellular surface of the plasma membrane, and explain why this role depends on their location specifically on the outer (extracellular) face rather than the inner (cytosolic) face.

Lời giải chi tiết

Glycoproteins (proteins with attached carbohydrate chains) function in cell-cell recognition, acting as identity markers that let other cells and the immune system distinguish this cell as "self" versus "non-self" or as belonging to a particular cell type. This function requires the carbohydrate chains to be displayed on the *outer* surface, where they are accessible to receptors on neighboring cells and immune cells; a marker facing only the cytosol could not be "read" by anything outside the cell.

Bài tập luyện tập

Which of the following crosses the plasma membrane by simple diffusion, without requiring any transport protein?

(A) Glucose
(B) A Na^+ ion
(C) CO_2
(D) An amino acid

Lời giải chi tiết

CO_2 is small and nonpolar, so it dissolves directly in and crosses the hydrophobic lipid bilayer without assistance. Glucose and amino acids are too large/polar, and Na^+ is charged — all three require a transport protein. **(C)**.

Bài tập luyện tập

Baseline: a solute diffuses across a membrane at 12 mmol/min when the concentration difference across the membrane is 8 mM. Assuming the rate remains directly proportional to the concentration gradient, predict the rate when the gradient is increased to 20 mM.

Lời giải chi tiết

Rate is proportional to the gradient: $\text{rate}_2 = \text{rate}_1 \times \dfrac{\Delta C_2}{\Delta C_1} = 12 \times \dfrac{20}{8} = 12 \times 2.5 = 30$ mmol/min.

Bài tập luyện tập

A membrane transport protein shows a rate-vs-concentration curve that rises steeply at low external solute concentration but flattens into a plateau at high concentration, unlike simple diffusion, whose rate keeps rising linearly. Explain this difference.

Lời giải chi tiết

Simple diffusion has no upper limit because solute molecules can cross the lipid bilayer at essentially any point, so raising the gradient keeps raising the rate proportionally. A carrier-mediated process (facilitated diffusion or active transport), however, depends on a *finite* number of transport protein molecules in the membrane. At low concentration, most carriers are unoccupied and available, so rate rises steeply with concentration; at high concentration, every carrier becomes continuously occupied and cycling, and the transport rate reaches a maximum (T_{max}) that cannot be exceeded no matter how much higher the external concentration climbs — producing the characteristic plateau (saturation curve).

Bài tập luyện tập

Which of the following is true of facilitated diffusion?

(A) It requires ATP because a protein is involved.

(B) It moves solutes against their concentration gradient.

(C) It is a form of passive transport that requires a channel or carrier protein because the solute cannot cross the lipid bilayer unassisted.

(D) It only occurs in prokaryotic cells.

Lời giải chi tiết

Facilitated diffusion moves solutes down their concentration gradient (passive) and needs no ATP; a protein is required only because the solute (polar, charged, or large) cannot cross the hydrophobic bilayer directly. It occurs in both prokaryotic and eukaryotic cells. **(C)**.

Bài tập luyện tập

Find Ψ_s for a 0.50 M glucose solution (glucose does not ionize, $i = 1$) at $22\,^\circ$C ($T = 295$ K), in an open beaker.

Lời giải chi tiết

$\Psi_s = -iCRT = -(1)(0.50)(0.0831)(295) = -(0.50)(24.51) = -12.25$ bar. Since the beaker is open, $\Psi_p = 0$, so $\Psi = \Psi_s = -12.25$ bar.

Bài tập luyện tập

Find Ψ_s for a 0.20 M $CaCl_2$ solution ($i = 3$, since $CaCl_2 \rightarrow Ca^{2+} + 2Cl^-$) at $20\,^\circ$C ($T = 293$ K), in an open beaker.

Lời giải chi tiết

$\Psi_s = -iCRT = -(3)(0.20)(0.0831)(293) = -(0.60)(24.35) = -14.61$ bar. With $\Psi_p = 0$, $\Psi = -14.61$ bar.

Bài tập luyện tập

Two adjacent, open ($\Psi_p = 0$) solutions at $25\,^\circ$C ($T = 298$ K) are separated by a selectively permeable membrane: Solution X is 0.40 M sucrose ($i = 1$); Solution Y is 0.15 M NaCl ($i = 2$). Calculate Ψ for each and predict the direction of net water movement.

Lời giải chi tiết

$\Psi_X = -(1)(0.40)(0.0831)(298) = -9.90$ bar.
$\Psi_Y = -(2)(0.15)(0.0831)(298) = -(0.30)(24.76) = -7.43$ bar.
Since $\Psi_Y\ (-7.43) > \Psi_X\ (-9.90)$, water moves from the higher potential to the lower potential: net water movement is from **Y to X**.

Bài tập luyện tập

A walled plant cell has internal solute potential $\Psi_s = -4$ bar and is currently fully turgid with pressure potential $\Psi_p = +4$ bar. It is then placed in an open 0.10 M sucrose solution at $27\,^\circ$C ($T = 300$ K, $i = 1$). Will the cell gain water, lose water, or stay the same? Justify with a calculation.

Lời giải chi tiết

Cell's current $\Psi_{\text{cell}} = \Psi_p + \Psi_s = 4 + (-4) = 0$ bar.
Solution's $\Psi_{\text{sol}} = \Psi_s = -(1)(0.10)(0.0831)(300) = -2.49$ bar (open container, $\Psi_p = 0$).
Since $\Psi_{\text{cell}}\ (0) > \Psi_{\text{sol}}\ (-2.49)$, water moves from the cell into the solution — the cell will **lose water** (pressure potential will fall as the cell loses turgor, potentially approaching plasmolysis if it continues).

Bài tập luyện tập

A plant physiologist reports a cell's overall water potential as $\Psi = -2$ bar but is unsure whether the cell is under positive or negative pressure. Explain why Ψ alone (without also knowing

Ψ_s) cannot determine the sign of Ψ_p, and give a numerical example illustrating two different (Ψ_p, Ψ_s) pairs that both produce $\Psi = -2$ bar.

Lời giải chi tiết

Because $\Psi = \Psi_p + \Psi_s$ is a sum, infinitely many combinations of Ψ_p and Ψ_s can add to the same total. For example: $\Psi_p = +3$ bar, $\Psi_s = -5$ bar gives $\Psi = -2$ bar (a turgid cell in a fairly concentrated internal solution); equally, $\Psi_p = 0$, $\Psi_s = -2$ bar also gives $\Psi = -2$ bar (a flaccid cell in a more dilute internal solution). Both cells would exchange water identically with a $\Psi = -2$ bar environment, even though their internal pressure and solute states are very different — which is why Ψ_s (and, for walled cells, Ψ_p) must be reported separately, not just the total Ψ.

Bài tập luyện tập

An animal cell is placed in a solution and is observed to shrink and shrivel. This solution is:

(A) Isotonic to the cell
(B) Hypertonic to the cell
(C) Hypotonic to the cell
(D) Impossible to determine

Lời giải chi tiết

Shrinking means the cell lost water, which happens when the surrounding solution has a higher solute concentration (lower water potential) than the cell's interior — that is, the solution is hypertonic to the cell. **(B)**.

Bài tập luyện tập

Why does a plant cell placed in a hypertonic solution show *plasmolysis* (the plasma membrane visibly pulling away from the cell wall), rather than simply becoming smaller and flaccid the way an animal cell does?

Lời giải chi tiết

In a hypertonic solution, water leaves the cell by osmosis and the protoplast (plasma membrane plus cytoplasm) shrinks. Unlike an animal cell, a plant cell's rigid cell wall does *not* shrink along with the protoplast — the wall keeps its original size and shape. As the protoplast continues to lose water and contract, it detaches from the surrounding wall, leaving a visible gap between membrane and wall: this separation is plasmolysis, and it is only possible because the cell wall stays rigid while the membrane-bound cytoplasm shrinks independently of it.

Bài tập luyện tập

A *Paramecium* living in a freshwater pond continuously takes on water by osmosis because pond water is strongly hypotonic to its cytoplasm. Explain the mechanism it uses to avoid lysis, and explain why a marine (saltwater) protist typically does not need this same mechanism.

Lời giải chi tiết

Paramecium uses a **contractile vacuole** that collects the excess water continuously entering by osmosis and actively pumps it back out of the cell, preventing the internal pressure buildup that

would otherwise cause lysis. A marine protist living in seawater experiences a much smaller (or no) osmotic gradient — seawater's solute concentration is close to (or higher than) that of the cell's cytoplasm — so little or no net water enters by osmosis, and a contractile vacuole to expel excess water is largely unnecessary.

Bài tập luyện tập

Which best describes the difference between primary and secondary active transport?

(A) Primary active transport moves solutes down their gradient; secondary moves them against their gradient.

(B) Primary active transport uses ATP directly; secondary active transport uses an existing electrochemical gradient (itself built by a primary pump) to move a second solute against its gradient.

(C) Primary active transport occurs only in plants; secondary active transport occurs only in animals.

(D) There is no meaningful difference; both terms describe the same process.

Lời giải chi tiết

Primary active transport (e.g., the Na^+/K^+ pump) hydrolyzes ATP directly to move a solute against its gradient. Secondary active transport (cotransport) does not hydrolyze ATP itself; instead it harnesses the electrochemical gradient of one solute (built up by a primary pump) to move a second solute against its own gradient, via a symporter or antiporter. **(B)**.

Bài tập luyện tập

The Na^+/K^+ pump exports 3 Na^+ and imports 2 K^+ per ATP hydrolyzed. A cell must export 9.0×10^6 Na^+ ions per minute to maintain its resting gradient. Calculate (a) the number of ATP molecules hydrolyzed per minute and (b) the number of K^+ ions imported per minute.

Lời giải chi tiết

(a) $\dfrac{9.0 \times 10^6}{3} = 3.0 \times 10^6$ ATP hydrolyzed per minute.
(b) $3.0 \times 10^6 \times 2 = 6.0 \times 10^6$ K^+ ions imported per minute.

Bài tập luyện tập

Explain why the Na^+/K^+ pump is described as "electrogenic," and explain how this pump's activity indirectly supports secondary active transport of glucose in intestinal epithelial cells.

Lời giải chi tiết

The pump exports 3 positive (Na^+) charges for every 2 positive (K^+) charges it imports, so each cycle removes one net positive charge from the cell — directly contributing to a more negative interior, which is what "electrogenic" means. This same pump also keeps Na^+ concentration much lower inside the cell than outside. The Na^+/glucose symporter in intestinal epithelial cells uses this steep inward Na^+ gradient as an energy source: as Na^+ flows back down its gradient through the symporter, the symporter simultaneously drags glucose into the cell against its own gradient — a process that depends entirely on the gradient the Na^+/K^+ pump built using ATP.

Bài tập luyện tập

A macrophage engulfs an entire bacterium by extending its plasma membrane around the bacterium and pinching off a large vesicle. This process is:

(A) Pinocytosis
(B) Phagocytosis
(C) Exocytosis
(D) Facilitated diffusion

Lời giải chi tiết

Engulfing a large particle or whole cell via membrane invagination is phagocytosis ("cell eating"); pinocytosis is nonspecific fluid uptake, exocytosis releases material from the cell, and facilitated diffusion is a passive transport-protein-mediated process, not a bulk vesicle process. **(B)**.

Bài tập luyện tập

A liver cell needs to take up circulating LDL cholesterol particles very selectively, without taking in large volumes of unrelated extracellular fluid. Which bulk transport process best matches this requirement, and why is it more efficient for this purpose than pinocytosis?

Lời giải chi tiết

Receptor-mediated endocytosis is the best match: LDL particles bind specific LDL receptor proteins clustered on the membrane (often in clathrin-coated pits), and only after binding does the membrane invaginate and pinch off a vesicle. This is more efficient than pinocytosis because pinocytosis takes in extracellular fluid and its solutes nonspecifically, wasting energy internalizing unwanted material; receptor-mediated endocytosis instead concentrates only the target molecule (bound to its receptor) before triggering vesicle formation, achieving high selectivity for the same energetic cost.

Bài tập luyện tập

Trace the path a digestive enzyme protein takes from the moment its mRNA is translated to the moment it is packaged inside a lysosome, naming every organelle/structure involved in order.

Lời giải chi tiết

The mRNA is translated by a ribosome bound to the **rough ER**, where the growing polypeptide is threaded into the ER lumen and begins folding and initial modification. The protein is then packaged into a **transport vesicle** that buds off the rough ER and travels to the **Golgi apparatus**, entering at the *cis* face. As it passes through the Golgi's stacked cisternae, it is further modified and specifically tagged for lysosomal delivery. It exits the *trans* face of the Golgi in a new vesicle that is targeted directly to a **lysosome**, with which it fuses, delivering the finished digestive enzyme into the lysosome's acidic interior.

Bài tập luyện tập

Explain why keeping digestive (hydrolytic) enzymes confined within lysosomes, rather than free in the cytosol, is an example of how compartmentalization increases a eukaryotic cell's efficiency.

Lời giải chi tiết

Hydrolytic enzymes are powerful and largely non-specific about which macromolecules they break down; if released directly into the cytosol they would begin digesting the cell's own proteins, membranes, and organelles indiscriminately, which would be lethal. By confining them within the lysosome's own membrane-bound, acidic compartment, the cell allows these enzymes to function at full efficiency (they are, in fact, optimized for the lysosome's low internal pH) while the rest of the cell's contents remain completely protected — an incompatible reaction (uncontrolled protein digestion) is made possible only because it is spatially isolated from everything it would otherwise damage.

Bài tập luyện tập

Which of the following is NOT evidence supporting the endosymbiotic origin of mitochondria and chloroplasts?

(A) Both organelles are bounded by a double membrane.

(B) Both organelles contain their own circular DNA and $70S$ ribosomes.

(C) Both organelles divide by a process resembling bacterial binary fission, independent of the host cell cycle.

(D) Both organelles are connected directly to the endomembrane system via vesicle trafficking from the Golgi apparatus.

Lời giải chi tiết

Mitochondria and chloroplasts are notably *not* part of the vesicle-trafficking endomembrane system — they replicate and manage their own protein synthesis largely independently, which is itself part of the evidence that they originated separately as free-living prokaryotes rather than budding off from the ER/Golgi pathway like the rest of the endomembrane system. **(D)**.

Bài tập luyện tập

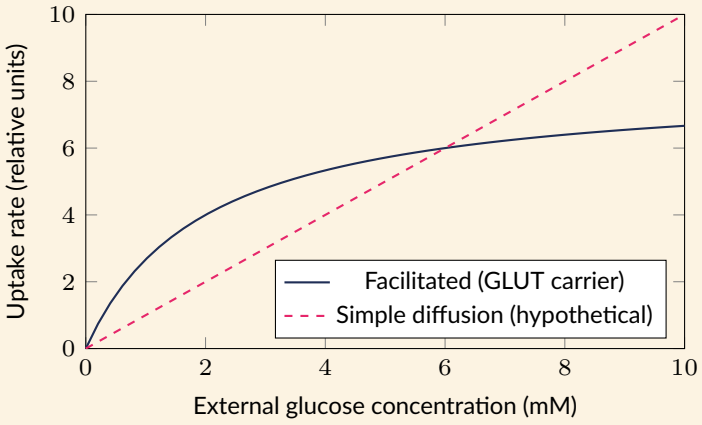
A student argues that because mitochondria are found inside eukaryotic cells and are essential to those cells' survival, they cannot possibly have once been free-living organisms. Evaluate this argument using evidence from endosymbiotic theory.

Lời giải chi tiết

The argument confuses *current* interdependence with *original* independence — endosymbiotic theory does not claim mitochondria are currently free-living, only that they descend from ancestors that once were. Multiple independent lines of structural evidence support this ancestry despite the organelle's now-permanent integration into the host cell: its double membrane (host vesicle plus original bacterial membrane), its own circular, histone-free DNA (unlike nuclear chromosomes), its own $70S$ ribosomes (bacterial-type, distinct from the cell's $80S$ cytosolic ribosomes and sensitive to antibacterial antibiotics), its independent fission-like division schedule, and its bacteria-comparable size. Over roughly 1.5–2 billion years, the relationship became obligate and mutually dependent (the organelle now relies on many host-encoded proteins, and the host relies on the organelle for ATP), but that later loss of independence does not erase the structural evidence of where mitochondria originally came from.

Bài tập luyện tập

The graph below shows the rate of glucose uptake into a cell via GLUT-type carrier proteins as external glucose concentration increases, compared with the (hypothetical) uptake rate if glucose could cross by simple diffusion instead.



(a) Describe the shape of each curve. (b) At low glucose concentration (e.g., 1 mM), which pathway moves more glucose per unit time? (c) At high glucose concentration (e.g., 9 mM), which pathway moves more glucose per unit time, and why?

Lời giải chi tiết

(a) The simple-diffusion curve (dashed) is a straight line through the origin — rate rises linearly and without limit as concentration increases. The facilitated-diffusion curve (solid) rises steeply at first but bends over and flattens toward a plateau (saturation) at high concentration.
(b) At low concentration (e.g., 1 mM), the facilitated curve lies above the diffusion line (reading the graph, the carrier-mediated rate is noticeably higher than the simple-diffusion rate at this point), because carrier proteins are efficient at capturing and transporting solute even at low concentration.
(c) At high concentration (e.g., 9 mM), the diffusion line has caught up to and exceeds the now-plateaued facilitated curve, because simple diffusion has no saturation limit while every GLUT carrier is already continuously occupied and cannot transport glucose any faster no matter how much external concentration keeps rising — the facilitated pathway is capped at its T_{max}.

Bài tập luyện tập

A cell biologist treats cells with a drug that specifically destroys all Golgi apparatus stacks, leaving the rough ER and lysosomes intact. Predict what would happen to (a) newly synthesized secretory proteins and (b) the delivery of newly made digestive enzymes to lysosomes.

Lời giải chi tiết

(a) Secretory proteins would still be correctly synthesized and initially folded on the rough ER and packaged into transport vesicles, but with no Golgi apparatus to receive, further modify, sort, and address-tag them, those vesicles would have nowhere correct to go — proteins normally destined for secretion would likely accumulate undelivered (or be secreted without their normal Golgi-added modifications and correct sorting) rather than being properly released by exocytosis.
(b) Newly made lysosomal enzymes are also normally tagged for lysosomal delivery while pass-

ing through the Golgi; without the Golgi, this tagging step could not occur, so newly synthesized digestive enzymes could not be correctly routed to lysosomes — existing lysosomes would persist (since they are not destroyed by the drug) but would gradually stop receiving fresh enzymes, eventually impairing the cell's digestive/autophagic capacity.

Cellular Energetics

Mục tiêu Unit: Cấu trúc và cơ chế hoạt động của enzyme (vị trí hoạt động, mô hình khớp cảm ứng, năng lượng hoạt hoá E_a); các yếu tố ảnh hưởng đến hoạt tính enzyme (nhiệt độ, pH, nồng độ cơ chất, đồng yếu tố, chất ức chế cạnh tranh/không cạnh tranh, điều hoà dị lập thể); cấu trúc và vai trò của ATP, năng lượng tự do (ΔG), phản ứng oxi hoá – khử và các chất mang electron (NAD^+/NADH, FAD/$FADH_2$); quang hợp (cấu trúc lục lạp, pha sáng, chu trình Calvin, các yếu tố giới hạn tốc độ); và hô hấp tế bào hiếu khí – kỵ khí (đường phân, oxi hoá pyruvate, chu trình Krebs, chuỗi truyền electron, hoá thẩm thấu, lên men).

3.1 Enzymes: Structure and Mechanism

3.1.1 Active site, substrate specificity, and the induced-fit model

Nearly every chemical reaction inside a cell is catalyzed by an **enzyme**, almost always a protein (a small number of RNA molecules, called **ribozymes**, also catalyze reactions). An enzyme's three-dimensional folded shape creates a pocket or groove called the **active site**, where a specific reactant molecule — the **substrate** — binds. The precise arrangement of amino-acid side chains lining the active site gives every enzyme **substrate specificity**: an enzyme's active site is shaped (and chemically charged/polar in the right pattern) to bind only one substrate or a small family of closely related substrates, much as a tool is shaped for one particular job.

Induced fit

The active site is not a rigid, pre-formed mould that a substrate simply drops into (the older "lock-and-key" idea). Instead, the modern **induced-fit model** describes the active site as flexible: when the substrate makes initial contact, the enzyme's active site changes shape slightly, molding itself more snugly around the substrate. This conformational adjustment brings catalytic side chains into optimal position and often strains particular bonds in the substrate, helping to convert it into the transition state.

Once bound, the substrate is held in the **enzyme–substrate complex**. The enzyme converts substrate to product and releases it, and the enzyme itself is left chemically unchanged at the end of the reaction — it is not consumed and can catalyze the same reaction repeatedly.

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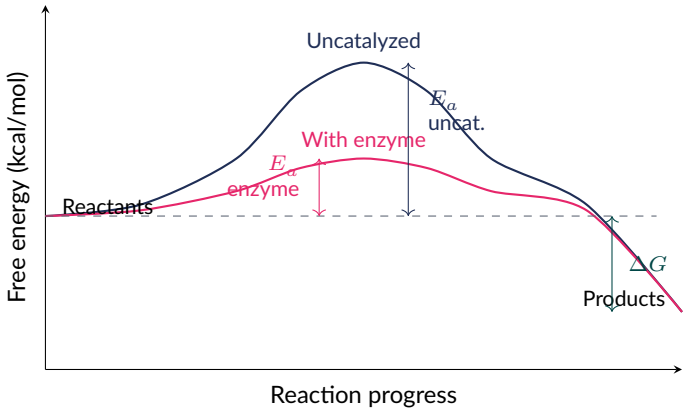
Vị trí hoạt động (active site) là "túi" đặc biệt trên bề mặt enzyme, có hình dạng và tính chất hoá học khớp với một cơ chất (substrate) nhất định — đây là cơ sở của **tính đặc hiệu cơ chất**. Theo **mô hình khớp cảm ứng (induced fit)**, vị trí hoạt động KHÔNG phải là khuôn cứng nhắc có sẵn hình dạng của cơ chất (như mô hình "ổ khoá – chìa khoá" cũ), mà thay đổi hình dạng một chút khi cơ chất gắn vào, ôm khít lấy cơ chất và đưa các nhóm hoá học xúc tác vào đúng vị trí để phản ứng xảy ra. Sau phản ứng, enzyme trở lại hình dạng ban đầu và có thể tái sử dụng nhiều lần vì bản thân nó không bị biến đổi hay tiêu hao.

3.1.2 Activation energy: how enzymes speed up reactions

Even a reaction that releases energy overall (is exergonic) usually does not happen spontaneously at a noticeable rate, because reactant molecules must first absorb enough energy to reach an unstable, high-energy **transition state** before they can rearrange into products. The energy input needed to reach the transition state is the **activation energy**, E_a. Enzymes are biological **catalysts**: they speed up reactions by **lowering the activation energy**, providing an alternative reaction pathway that requires less energy input to reach the transition state — for example, by orienting substrates precisely, straining particular bonds, providing a favorable microenvironment, or transiently forming/breaking covalent bonds with the substrate.



Free-energy diagram for the same exergonic reaction, without (navy) and with (pink) enzyme catalysis. The enzyme lowers the activation energy E_a (the height of the transition-state peak above the reactants) but leaves the free-energy difference ΔG between reactants and products — and therefore the reaction's spontaneity and equilibrium point — completely unchanged.

An enzyme changes the **rate** at which a reaction reaches equilibrium (by lowering E_a), but it never changes *whether* a reaction is thermodynamically favorable. ΔG, the equilibrium constant, and the reaction's overall spontaneity are all fixed by the identities of reactants and products, not by the presence of a catalyst. An enzyme speeds up the forward and reverse reactions by exactly the same factor.

Ví dụ mẫu · Reading an activation-energy diagram

Using the diagram above, the uncatalyzed reaction rises from a reactant baseline of 8 kcal/mol to a transition-state peak of 16 kcal/mol, while the catalyzed curve peaks at only 11 kcal/mol from the same baseline. Both curves end at a product level of 3 kcal/mol.

(a) E_a(uncatalyzed) $= 16 - 8 = 8$ kcal/mol.
(b) E_a(enzyme) $= 11 - 8 = 3$ kcal/mol — the enzyme lowers E_a by $8 - 3 = 5$ kcal/mol.
(c) $\Delta G = 3 - 8 = -5$ kcal/mol for *both* curves — identical, confirming the enzyme does not change the reaction's overall energy release or spontaneity (both curves are exergonic by the same amount; only the height of the barrier in between differs).

(!) Lỗi thường gặp: Enzymes lower **activation energy (E_a)**, not the **free-energy change (ΔG)** of a reaction. A very common error is to say an enzyme "makes a reaction more exergonic" or "supplies energy" to a reaction — false on both counts. An enzyme cannot make an endergonic reaction spontaneous, and it does not change ΔG, the equilibrium constant, or which direction a reaction favors; it only makes the reaction (forward and reverse) reach that same equilibrium faster.

3.2 Environmental Effects on Enzyme Function and Regulation

Enzymes are proteins, so their activity depends sensitively on conditions that affect protein folding and molecular motion: temperature, pH, substrate availability, and the presence of regulatory molecules.

3.2.1 Temperature and pH

Every enzyme has an optimal temperature and an optimal pH at which its rate is maximal. As temperature rises toward the optimum, molecules move faster and collide more often with more kinetic energy, so reaction rate increases. Beyond the optimum, however, heat disrupts the weak bonds (hydrogen bonds, ionic interactions, hydrophobic interactions) that hold the enzyme's tertiary and quaternary structure together; the protein unfolds and loses its specific active-site shape — a process called **denaturation** — and catalytic activity drops sharply, often irreversibly. Most human enzymes have optima near body temperature ($\approx 37\,^{\circ}$C), while enzymes from thermophilic organisms (e.g., *Taq* polymerase from hot-spring bacteria) have much higher optima.

Similarly, each enzyme has an optimal pH range, reflecting the ionization states of amino-acid side chains needed for substrate binding and catalysis; pH values above or below that range disrupt ionic bonds and hydrogen bonds in the protein, again denaturing it. Digestive enzymes illustrate this well: **pepsin**, active in the acidic stomach, has an optimum near pH 1.5–2, while **trypsin**, active in the small intestine, has an optimum near pH 8.

	Below optimum	**Above optimum**
Cause	Low kinetic energy, fewer/slower collisions	Heat or extreme pH breaks bonds maintaining protein shape
Effect on rate	Rate is simply slow (reversible if conditions improve)	Denaturation — active site shape lost, often irreversible

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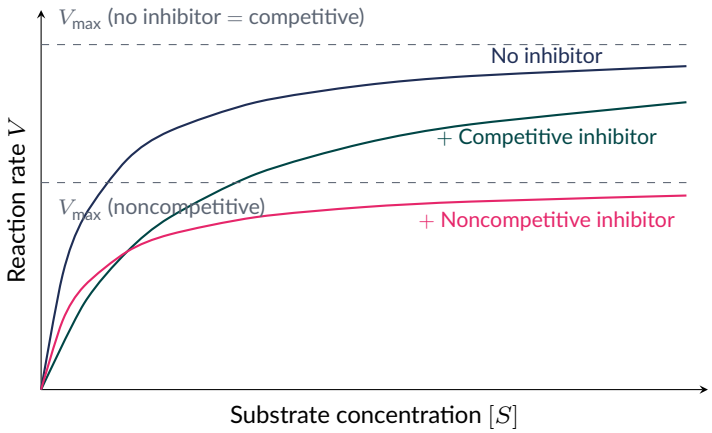
Enzyme có **nhiệt độ tối ưu** và **pH tối ưu** riêng. Dưới ngưỡng tối ưu, tốc độ phản ứng chậm chỉ vì động năng phân tử thấp — vẫn có thể tăng tốc trở lại khi tăng nhiệt độ (thuận nghịch). Trên ngưỡng tối ưu, nhiệt độ cao hoặc pH quá lệch sẽ phá vỡ các liên kết yếu (liên kết hydro, liên kết ion) giữ cấu trúc bậc ba của protein, khiến enzyme bị **biến tính (denaturation)** — mất hình dạng vị trí hoạt động, thường KHÔNG thể phục hồi. Ví dụ kinh điển: pepsin (dạ dày) hoạt động tốt nhất ở pH rất thấp (≈ 1.5–2), trong khi trypsin (ruột non) hoạt động tốt nhất ở pH kiềm (≈ 8) — mỗi enzyme thích nghi với môi trường nơi nó hoạt động.

3.2.2 Substrate concentration and saturation kinetics

At a fixed enzyme concentration, increasing substrate concentration $[S]$ increases reaction rate V, because more substrate molecules are available to collide with and bind free active sites. This increase is not unlimited: as $[S]$ continues to rise, a larger and larger fraction of enzyme molecules is occupied at any instant, and rate increases more slowly. Eventually, essentially all active sites are occupied continuously (the enzyme is **saturated**), and adding still more substrate cannot increase the rate further — the curve plateaus at the enzyme's **maximum velocity**, V_{max}, which is set by the enzyme's own turnover rate and its concentration, not by $[S]$.



Reaction rate versus substrate concentration. The uninhibited curve (navy) rises toward an asymptote at V_{max} as the enzyme becomes saturated. A competitive inhibitor (teal) can still be out-competed by enough substrate, reaching the *same* V_{max} but only at a much higher $[S]$ (higher apparent K_m). A noncompetitive inhibitor (pink) permanently removes catalytic capacity, lowering V_{max} itself no matter how much substrate is added.

Ví dụ mẫu · Identifying V_{max} and saturation

An enzyme assay measures rate V (in μmol/min) at increasing substrate concentration $[S]$ (in mM): $[S] = 1 \rightarrow V = 3.3$; $[S] = 6 \rightarrow V = 7.5$; $[S] = 15 \rightarrow V = 8.8$; $[S] = 30 \rightarrow V = 9.4$; $[S] = 60 \rightarrow V = 9.7$. Estimate V_{max} and explain the shape of the data.

As $[S]$ increases from 1 to 60 mM, V keeps rising but by smaller and smaller increments ($+4.2$, then $+1.3$, then $+0.6$, then $+0.3$), approaching a plateau near $V \approx 10$ μmol/min; this plateau value is V_{max}. The flattening occurs because, at high $[S]$, nearly every enzyme molecule's active site is occupied at all times — the enzyme is **saturated** — so the rate is limited by how fast each enzyme can process and release substrate (its turnover number), not by how much substrate is available. Only adding more enzyme (not more substrate) could raise the rate further.

3.2.3 Cofactors and coenzymes

Many enzymes require a non-protein "helper" molecule to be catalytically active. A **cofactor** is an inorganic ion (e.g., Mg^{2+}, Zn^{2+}, Fe^{2+}) that binds an enzyme and assists catalysis, often by stabilizing charge or participating directly in the reaction. A **coenzyme** is an organic cofactor, frequently derived from a vitamin — for example, **NAD⁺** (from niacin, vitamin B_3), **FAD** (from riboflavin, vitamin B_2), and **coenzyme A** (from pantothenic acid) all serve as coenzymes central to cellular respiration. An enzyme lacking its required cofactor (an **apoenzyme**) is catalytically inactive; the complete, active enzyme–cofactor complex is called a **holoenzyme**.

VN **GIẢI THÍCH TIẾNG VIỆT**

Đồng yếu tố (cofactor) là ion vô cơ (VD Mg^{2+}, Zn^{2+}) hỗ trợ enzyme hoạt động; **coenzyme** là đồng yếu tố hữu cơ, thường có nguồn gốc từ vitamin (VD NAD^+ từ vitamin B_3, FAD từ vitamin B_2) — đây là lý do thiếu vitamin có thể làm rối loạn chuyển hoá tế bào. Enzyme thiếu đồng yếu tố (**apoenzyme**) không có hoạt tính; enzyme đầy đủ đồng yếu tố (**holoenzyme**) mới hoạt động được.

3.2.4 Enzyme inhibition: competitive and noncompetitive

An **inhibitor** is a molecule that decreases enzyme activity. AP Biology distinguishes two reversible mechanisms.

Competitive vs. noncompetitive inhibition

A **competitive inhibitor** structurally resembles the normal substrate and binds directly in the **active site**, physically blocking substrate from binding. Because it competes with substrate for the same site, its effect can be *overcome* by adding enough substrate to out-compete the inhibitor for access to active sites — so V_{max} is still reachable (unchanged), but a higher $[S]$ is needed to reach any given rate (the apparent K_m increases).

A **noncompetitive inhibitor** (a common type of **allosteric** inhibitor) binds a different site on the enzyme — an **allosteric site**, away from the active site — changing the enzyme's overall shape, including the active site, so that it binds substrate poorly or catalyzes inefficiently even when substrate is bound. Because it does not compete for the active site, adding more substrate cannot reverse its effect: V_{max} is lowered (since some fraction of enzyme is always disabled), while the apparent K_m for the still-functional enzyme is roughly unchanged.

Ví dụ mẫu · Comparing effects on V_{max} and apparent K_m

Referring to the kinetics figure above: the uninhibited curve reaches $V_{max} = 10$ at high $[S]$. Compare what happens with (a) a competitive inhibitor and (b) a noncompetitive inhibitor.

(a) **Competitive inhibitor** (teal curve): the curve still climbs to the *same* $V_{max} = 10$, but only after a much larger $[S]$ — the apparent K_m has increased (more substrate is needed to reach half of V_{max}). This matches direct competition for the active site: enough excess substrate statistically out-competes the inhibitor.

(b) **Noncompetitive inhibitor** (pink curve): the curve saturates at a *lower* $V_{max} = 6$, and no amount of added substrate brings it back up to 10 — the ceiling itself has been lowered because a fraction of enzyme molecules are permanently distorted by the inhibitor bound at an allosteric site, regardless of $[S]$.

(!) Lỗi thường gặp: A competitive inhibitor's effect **can** be overcome by adding a large excess of substrate (restoring the original V_{max}, just at a higher $[S]$), because it is competing for the very same active site as the substrate. A noncompetitive/allosteric inhibitor's effect **cannot** be overcome by more substrate, because it acts at a completely different site and lowers V_{max} itself. If a question states that excess substrate restores full enzyme rate, that describes competitive inhibition; if excess substrate fails to restore the original maximum rate, that describes noncompetitive inhibition.

VN **GIẢI THÍCH TIẾNG VIỆT**

Phân biệt hai kiểu ức chế: **ức chế cạnh tranh (competitive)** — chất ức chế có hình dạng giống cơ chất, tranh giành trực tiếp vị trí hoạt động; có thể bị "đánh bại" nếu tăng đủ nhiều nồng độ cơ chất, nên V_{max} không đổi nhưng K_m biểu kiến tăng (cần nhiều cơ chất hơn mới đạt được cùng tốc độ). **Ức chế không cạnh tranh / dị lập thể (noncompetitive/allosteric)** — chất ức chế gắn vào một vị trí khác (vị trí dị lập thể), làm biến dạng cả vị trí hoạt động; KHÔNG thể khắc phục bằng cách tăng cơ chất, nên V_{max} bị giảm hẳn.

3.2.5 Allosteric regulation and feedback inhibition

Many enzymes are regulated allosterically even in the absence of an inhibitor drug or toxin — this is a normal, essential part of metabolic control. Such enzymes typically have multiple subunits and can shift between an active (relaxed) and inactive (tense) overall conformation. An **allosteric activator** binds an allosteric site and stabilizes the enzyme's active conformation, increasing activity; an **allosteric inhibitor** stabilizes the inactive conformation, decreasing activity.

The most important biological application is **feedback inhibition** (end-product inhibition): the final product of a multi-step metabolic pathway allosterically inhibits an enzyme that acts earlier in that same pathway — usually the first, "committed" step. As the end product accumulates, it shuts down its own pathway; as the end product is used up (its concentration falls), inhibition is relieved and the pathway resumes. This self-limiting design prevents cells from wastefully overproducing a metabolite and lets metabolism respond dynamically to cellular need.

VN **GIẢI THÍCH TIẾNG VIỆT**

Điều hoà dị lập thể (allosteric regulation): chất hoạt hoá dị lập thể giữ enzyme ở dạng hoạt động, chất ức chế dị lập thể giữ enzyme ở dạng không hoạt động — thường gắn vào vị trí khác vị trí hoạt động và làm thay đổi hình dạng toàn bộ enzyme. **Ức chế ngược (feedback inhibition)** là ví dụ quan trọng nhất: sản phẩm cuối cùng của một con đường chuyển hoá quay lại ức chế enzyme ở bước đầu con đường đó, giống như một "van tự động" — khi sản phẩm dư thừa, con đường tự tắt; khi sản phẩm được tiêu thụ hết, con đường lại mở ra. Đây là cách tế bào tiết kiệm nguyên liệu và năng lượng, tránh sản xuất dư thừa không cần thiết.

3.3 ATP, Free Energy, and Redox Reactions

3.3.1 ATP structure, hydrolysis, and the ATP/ADP cycle

Adenosine triphosphate (ATP) is the cell's primary short-term energy currency. Structurally, ATP consists of the nitrogenous base **adenine**, the five-carbon sugar **ribose**, and a chain of **three phosphate groups** attached to the sugar, linked to each other by high-energy phosphoanhydride bonds.

ATP hydrolysis

Hydrolyzing the bond to the terminal (outermost) phosphate group,

$$\text{ATP} + \text{H}_2\text{O} \longrightarrow \text{ADP} + \text{P}_\text{i} + \text{energy},$$

releases roughly 7.3 kcal/mol (≈ 30.5 kJ/mol) under standard conditions — an **exergonic** reaction ($\Delta G \approx -7.3$ kcal/mol). Energy is released chiefly because the three closely packed, negatively charged phosphate groups in ATP repel each other electrostatically; removing one phosphate relieves this strain, and the freed inorganic phosphate (P_i) is more stable (better resonance-stabilized) on its own.

Because ATP hydrolysis is exergonic, cells use it to power an enormous range of endergonic cellular work: biosynthesis of macromolecules, active transport across membranes, and mechanical work (e.g., muscle contraction, motor proteins). ADP and P_i are then re-combined back into ATP — an endergonic reaction requiring an energy input — chiefly through cellular respiration. This continuous interconversion is the **ATP/ADP cycle**: a working cell hydrolyzes and regenerates its entire ATP pool on a timescale of seconds to minutes, meaning ATP is not stored in large quantities but is instead constantly recycled.

VN **GIẢI THÍCH TIẾNG VIỆT**

ATP gồm ba phần: bazơ nitơ **adenine**, đường **ribose** (5 carbon), và **ba nhóm phosphate** nối tiếp nhau. Ba nhóm phosphate mang điện tích âm rất gần nhau nên đẩy nhau mạnh — khi thuỷ phân cắt bỏ nhóm phosphate cuối (tạo ADP + P_i), lực đẩy này được giải phóng dưới dạng năng lượng (≈ -7.3 kcal/mol, phản ứng toả năng lượng). Tế bào liên tục "sạc lại" ADP thành ATP (chủ yếu qua hô hấp tế bào) rồi lại thuỷ phân — đây là **chu trình ATP/ADP** — nên ATP hoạt động như "tiền mặt" năng lượng ngắn hạn của tế bào, không phải kho dự trữ năng lượng dài hạn (vai trò đó thuộc về tinh bột, glycogen, lipid).

3.3.2 Free energy and coupled reactions

The **Gibbs free energy change**, ΔG, of a reaction measures whether that reaction can proceed spontaneously and how much usable energy it releases or requires.

> $\Delta G < 0$: **exergonic** — energy is released, the reaction is spontaneous as written.
> $\Delta G > 0$: **endergonic** — energy must be supplied, the reaction is nonspontaneous as written.
> $\Delta G = 0$: the system is at **equilibrium**; no net free energy is available to do work in either direction.

Cells constantly need to run endergonic reactions — building macromolecules, pumping ions against their gradient, and so on. They accomplish this through **energy coupling**: pairing an exergonic reaction (most often ATP hydrolysis) with an endergonic reaction, so that the overall (net) ΔG of the combined, coupled process is negative. Mechanically, this is usually achieved by **phosphorylation** — an enzyme transfers ATP's terminal phosphate group onto a substrate molecule, temporarily raising that substrate's own free energy and making it much more reactive (primed to undergo the desired endergonic step).

Ví dụ mẫu · Coupling ATP hydrolysis to an endergonic reaction

The first step of glycolysis, phosphorylating glucose to glucose-6-phosphate, is endergonic on its own: glucose $+$ P_i $\rightarrow$ glucose-6-phosphate $+$ H_2O, $\Delta G = +3.3$ kcal/mol. Show how coupling this to ATP hydrolysis makes the overall reaction favorable, and compute the net ΔG.

Instead of using free P_i, the enzyme *hexokinase* transfers the phosphate directly from ATP:

$$\text{glucose} + \text{ATP} \longrightarrow \text{glucose-6-phosphate} + \text{ADP}.$$

This is equivalent to adding the two half-reactions: phosphorylation of glucose ($\Delta G = +3.3$ kcal/mol) plus ATP hydrolysis ($\Delta G = -7.3$ kcal/mol):

$$\Delta G_{\text{net}} = (+3.3) + (-7.3) = -4.0 \text{ kcal/mol}.$$

The coupled reaction is now exergonic overall ($\Delta G_{\text{net}} < 0$) and proceeds spontaneously, even though phosphorylating glucose by itself never would. This is the general strategy cells use throughout metabolism: an endergonic step "borrows" free energy from the strongly exergonic hydrolysis of ATP.

VN **GIẢI THÍCH TIẾNG VIỆT**

Năng lượng tự do (ΔG) cho biết một phản ứng có tự xảy ra được hay không: $\Delta G < 0$ (toả năng lượng, exergonic) $\Rightarrow$ tự xảy ra; $\Delta G > 0$ (thu năng lượng, endergonic) $\Rightarrow$ cần được cung cấp năng lượng mới xảy ra. Tế bào "ghép cặp" (couple) phản ứng thu năng lượng với phản ứng thuỷ phân ATP (rất toả năng lượng) — thường bằng cách chuyển nhóm phosphate từ ATP sang chất nền (phosphoryl hoá) — để tổng ΔG của cả quá trình ghép cặp trở nên âm, giúp phản ứng vốn không tự xảy ra được trở nên khả thi.

3.3.3 Oxidation–reduction reactions and electron carriers

Much of cellular metabolism, especially energy metabolism, consists of **oxidation–reduction (redox) reactions**: reactions in which electrons are transferred from one molecule to another.

> **Oxidation** is the *loss* of electrons (often as part of a hydrogen atom); **reduction** is the *gain* of electrons. Mnemonic: **OIL RIG** — Oxidation Is Loss, Reduction Is Gain. Oxidation and reduction always occur together, as a pair: the electrons lost by the oxidized species are exactly the electrons gained by the reduced species.

Because free electrons cannot simply float around the cell, specialized **electron carriers** shuttle high-energy electrons (and associated protons) from one reaction to another. The two central carriers in cellular respiration and photosynthesis are:

Carrier	Reaction	Role
$NAD^+/NADH$	$NAD^+ + 2e^- + 2H^+ \rightleftharpoons NADH + H^+$	Main electron carrier of glycolysis, pyruvate oxidation, and the Krebs cycle
$FAD/FADH_2$	$FAD + 2e^- + 2H^+ \rightleftharpoons FADH_2$	Electron carrier of one Krebs-cycle step (succinate dehydrogenase)

When these carriers pick up electrons (becoming NADH or $FADH_2$), they are themselves being *reduced*; when they later donate those electrons to the electron transport chain, they are *oxidized* back to NAD^+/FAD and can be reused. NADH carries its electrons at a higher energy level than $FADH_2$ (it donates them earlier, at Complex I of the electron transport chain, whereas $FADH_2$ donates them further downstream, at Complex II) — this is why, as accounted for below, NADH ultimately yields more ATP than $FADH_2$.

Ví dụ mẫu · Identifying oxidation and reduction

In lactic acid fermentation, pyruvate is converted to lactate: pyruvate + NADH + H^+ → lactate + NAD^+. Identify which species is oxidized and which is reduced.

NADH is oxidized: it goes from carrying two extra electrons (as NADH) to losing them (becoming NAD^+).
Pyruvate is reduced: it gains those electrons (along with a hydrogen), becoming lactate.
This pairing is required — electrons removed from NADH must be accepted by something, and here that something is pyruvate.

VN **GIẢI THÍCH TIẾNG VIỆT**

Quy tắc **OIL RIG**: **oxi hoá** = mất electron; **khử** = nhận electron. Hai chất mang điện tử quan trọng nhất trong hô hấp tế bào là NAD^+/NADH và $FAD/FADH_2$ — chúng "vận chuyển" electron năng lượng cao từ đường phân, oxi hoá pyruvate, và chu trình Krebs đến chuỗi truyền electron. NADH mang electron ở mức năng lượng cao hơn $FADH_2$ (do đi vào chuỗi truyền electron ở vị trí sớm hơn), nên mỗi NADH cuối cùng tạo ra được nhiều ATP hơn mỗi $FADH_2$.

3.4 Photosynthesis

3.4.1 Overview equation and chloroplast structure

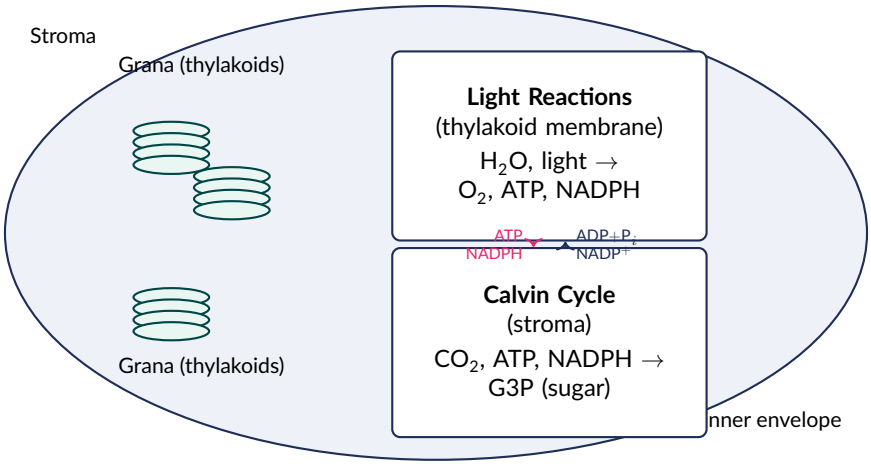
Photosynthesis converts light energy into the chemical energy of organic molecules, occurring in plants, algae, and cyanobacteria. Its overall summary equation is

$$6\,CO_2 + 6\,H_2O \xrightarrow{\text{light energy}} C_6H_{12}O_6 + 6\,O_2.$$

This single equation actually combines two coupled sets of reactions that occur in different compartments of the **chloroplast**: the **light-dependent reactions** and the **Calvin cycle** (light-independent reactions).

Chloroplast structure

A chloroplast is bounded by a double membrane (outer and inner envelope). Inside, a third membrane system — the **thylakoid membrane** — forms flattened, interconnected sacs; stacks of thylakoid discs are called **grana** (singular: granum). The fluid surrounding the thylakoids, inside the inner envelope, is the **stroma**. The light reactions occur in/across the thylakoid membrane; the Calvin cycle occurs in the stroma.



Chloroplast structure and the coupling of the two stages of photosynthesis. The light reactions (thylakoid membrane) consume H_2O and light to release O_2 and produce ATP and NADPH; the Calvin cycle (stroma) consumes CO_2 along with that ATP and NADPH to build sugar (G3P), returning ADP, P_i, and $NADP^+$ for reuse by the light reactions.

VN **GIẢI THÍCH TIẾNG VIỆT**

Lục lạp có màng kép bao ngoài (màng ngoài, màng trong), bên trong là hệ thống **màng thylakoid** xếp thành từng chồng gọi là **grana**, và chất dịch bao quanh thylakoid gọi là **stroma**. **Pha sáng** diễn ra trên màng thylakoid, tạo ra ATP và NADPH; hai chất này sau đó được **chu trình Calvin** trong stroma sử dụng để cố định CO_2 thành đường. Hai giai đoạn này được **ghép cặp chặt chẽ**: pha sáng "nạp năng lượng" (ATP, NADPH) cho chu trình Calvin, còn chu trình Calvin trả lại ADP và $NADP^+$ để pha sáng tái sử dụng.

3.4.2 The light-dependent reactions

The light reactions capture light energy and convert it into the chemical energy of ATP and NADPH, releasing O_2 as a byproduct. Two pigment–protein complexes embedded in the thylakoid membrane, **Photosystem II (PSII)** and **Photosystem I (PSI)**, work in series (electrons flow PSII → PSI, sometimes called the "Z-scheme").

Light reactions, step by step

1. Light striking **PSII** (reaction center P_{680}) excites an electron to a higher energy level; this high-energy electron is passed to an electron transport chain in the thylakoid membrane.
2. PSII replaces its lost electron by splitting water — **photolysis**: $2\,H_2O \rightarrow 4\,H^+ + 4e^- + O_2$. This is the source of the O_2 released by photosynthesis (and, ultimately, of most atmospheric oxygen).
3. As electrons move down the electron transport chain (plastoquinone → cytochrome b_6f → plastocyanin) toward PSI, the energy released pumps H^+ from the stroma into the thylakoid lumen, building a steep proton gradient.

4. **Chemiosmosis**: protons flow back down their gradient through **ATP synthase** embedded in the thylakoid membrane, driving synthesis of ATP from ADP + P_i (**photophosphorylation**).
5. Light striking **PSI** (reaction center P_{700}) re-energizes the electrons it receives from the chain, passing them to ferredoxin and then to the enzyme $NADP^+$ reductase, which combines them with H^+ and $NADP^+$ to form **NADPH**.

Overall, the light reactions consume H_2O and light energy and produce O_2, ATP, and NADPH — the ATP and NADPH then power the Calvin cycle.

VN **GIẢI THÍCH TIẾNG VIỆT**

Trình tự pha sáng: ánh sáng kích thích **PSII**, electron năng lượng cao đi vào chuỗi truyền electron; PSII "vá lại" electron đã mất bằng cách **phân giải nước (photolysis)** — đây là nguồn gốc của O_2 thải ra. Electron di chuyển qua chuỗi truyền electron tới **PSI**, quá trình này bơm H^+ vào xoang thylakoid tạo gradien nồng độ; gradien này được dùng để tổng hợp ATP qua **hoá thẩm thấu (chemiosmosis)** nhờ enzyme ATP synthase. PSI hấp thụ ánh sáng lần nữa, "nạp lại" năng lượng cho electron, rồi chuyển electron đó cho $NADP^+$ để tạo **NADPH**. Kết quả: pha sáng tạo ra O_2 (thải ra), ATP, và NADPH (dùng cho chu trình Calvin).

3.4.3 The Calvin cycle

The **Calvin cycle** occurs in the stroma and uses the ATP and NADPH generated by the light reactions to convert CO_2 into organic sugar. It runs continuously in three phases.

The three phases of the Calvin cycle

1. Carbon fixation. The enzyme **RuBisCO** (ribulose-1,5-bisphosphate carboxylase/oxygenase) attaches a CO_2 molecule to **RuBP** (ribulose-1,5-bisphosphate, a 5-carbon sugar), forming an unstable 6-carbon intermediate that immediately splits into two molecules of **3-phosphoglycerate (3-PGA)**, each 3 carbons.

2. Reduction. Each 3-PGA is phosphorylated by ATP, then reduced using electrons from NADPH, forming **glyceraldehyde-3-phosphate (G3P)**.

3. Regeneration. For every 3 turns of the cycle (fixing $3\,CO_2$ and producing 6 G3P), 5 of the 6 G3P molecules are recycled, using additional ATP, to regenerate 3 RuBP so the cycle can continue; the remaining 1 G3P is the net product, exported for use in building glucose and other organic molecules.

Net stoichiometry to synthesize **one glucose** molecule (6 carbons = two G3P): the Calvin cycle must turn **6** times, fixing $6\,CO_2$, and consuming 18 ATP and 12 NADPH overall.

Ví dụ mẫu · Photosynthesis stoichiometry

A plant produces 9.01 g of glucose ($C_6H_{12}O_6$, molar mass 180.16 g/mol) via photosynthesis. Using the overall equation $6\,CO_2 + 6\,H_2O \rightarrow C_6H_{12}O_6 + 6\,O_2$, find (a) the moles of CO_2 fixed and (b) the mass of O_2 released.

Moles of glucose:

$$n(\text{glucose}) = \frac{9.01\ \text{g}}{180.16\ \text{g/mol}} = 0.0500\ \text{mol}.$$

(a) The balanced equation shows a $6:1$ mole ratio of CO_2 to glucose:

$$n(CO_2) = 6 \times 0.0500 = 0.300\ \text{mol} \quad (\text{mass} = 0.300 \times 44.01 = 13.2\ \text{g}).$$

(b) The mole ratio of O_2 to glucose is also $6:1$:

$$n(O_2) = 6 \times 0.0500 = 0.300 \text{ mol}, \qquad \text{mass} = 0.300 \times 32.00 = 9.60 \text{ g}.$$

Producing 9.01 g of glucose therefore requires fixing 13.2 g of CO_2 and releases 9.60 g of O_2.

(!) Lỗi thường gặp: Do not confuse the two stages' locations or requirements: the **light reactions** occur in/across the **thylakoid membrane** and directly require light and H_2O; the **Calvin cycle** occurs in the **stroma** and directly requires CO_2, ATP, and NADPH — not photons of light themselves. The Calvin cycle is sometimes loosely called the "light-independent reactions," but it is still indirectly dependent on light, because it cannot run without the ATP and NADPH that only the light reactions supply. In a plant kept in darkness, the Calvin cycle stops within seconds, once the existing ATP/NADPH supply is used up.

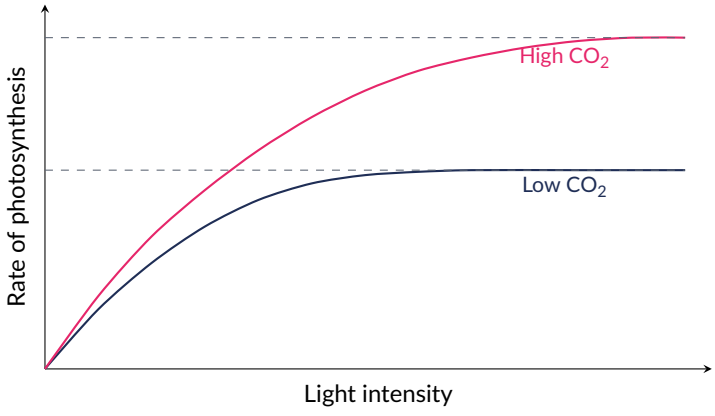
VN **GIẢI THÍCH TIẾNG VIỆT**

Chu trình Calvin gồm 3 giai đoạn: (1) **cố định carbon** — RuBisCO gắn CO_2 vào RuBP tạo 3-PGA; (2) **khử** — dùng ATP và NADPH biến 3-PGA thành G3P; (3) **tái tạo RuBP** — phần lớn G3P được dùng (tốn thêm ATP) để tái tạo RuBP, chỉ một phần nhỏ G3P được xuất ra để tổng hợp glucose và các phân tử hữu cơ khác. Cần 6 **vòng** chu trình (cố định $6\,CO_2$, tiêu tốn 18 ATP và 12 NADPH) để tạo ra **một phân tử glucose**.

3.4.4 Factors affecting the rate of photosynthesis

The overall rate of photosynthesis depends on light intensity, CO_2 concentration, and temperature. At any moment, the rate is set by whichever of these factors is in shortest supply relative to the others — the **limiting factor** (Blackman's law of limiting factors): increasing a factor that is *not* currently limiting has little effect on rate, while increasing the actual limiting factor raises the rate, until some other factor becomes limiting in turn.

- **Light intensity:** rate rises roughly proportionally with light intensity at low light, then **plateaus** at higher intensities once the light-capturing machinery is saturated (or once CO_2/temperature becomes limiting instead).
- CO_2 **concentration:** more CO_2 provides more substrate for RuBisCO and the Calvin cycle, raising the rate — up to a plateau where some other factor (light or temperature) becomes limiting.
- **Temperature:** because both stages of photosynthesis rely on enzymes (RuBisCO and many others), rate increases with temperature toward an optimum, then falls sharply as enzymes begin to denature at higher temperatures.



Rate of photosynthesis versus light intensity at two CO_2 concentrations. Both curves rise together at low light (light is limiting for both), but the low-CO_2 curve plateaus earlier and lower, because CO_2 supply — not light — becomes the limiting factor once light is abundant. Raising CO_2 lifts the plateau to a new, higher ceiling.

Ví dụ mẫu · Interpreting a limiting-factor plateau

In the figure above, both curves rise together at low light intensity, but the low-CO_2 curve flattens out at a light intensity of about 16 (arbitrary units) while the high-CO_2 curve keeps climbing until about 22. Explain why increasing light intensity beyond 16 fails to increase the rate under low-CO_2 conditions.

At low light intensity, light capture by the photosystems is the bottleneck for both curves, so both rise together — light is the limiting factor in this range. Once light intensity exceeds about 16 under low-CO_2 conditions, the light reactions can already supply ATP and NADPH faster than the Calvin cycle can consume them, because there is not enough CO_2 available for RuBisCO to fix — CO_2 has become the new limiting factor, so adding more light has no further effect. Consistent with this, supplying more CO_2 (pink curve) removes that bottleneck and allows the rate to keep rising to a higher plateau before light itself (or another factor, such as temperature) eventually becomes limiting again.

VN **GIẢI THÍCH TIẾNG VIỆT**

Yếu tố giới hạn (limiting factor): tốc độ quang hợp tại một thời điểm bị giới hạn bởi yếu tố nào đang **khan hiếm nhất** — cường độ ánh sáng, nồng độ CO_2, hoặc nhiệt độ. Tăng một yếu tố KHÔNG đang giới hạn sẽ không làm tăng tốc độ (đồ thị nằm ngang, "cao nguyên" — plateau); chỉ khi tăng đúng yếu tố đang giới hạn thì tốc độ mới tăng trở lại, cho đến khi một yếu tố khác trở thành yếu tố giới hạn mới.

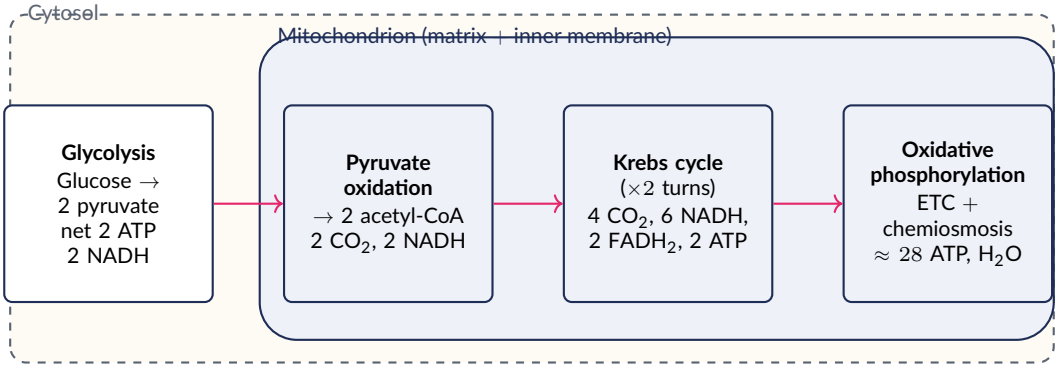
3.5 Cellular Respiration

3.5.1 Overview and glycolysis

Cellular respiration is the set of catabolic pathways that break down glucose (and other fuels) to harvest chemical energy as ATP. The overall equation for the complete aerobic oxidation of glucose is

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O + \text{energy (ATP)}.$$

Aerobic respiration proceeds in four linked stages: **glycolysis**, **pyruvate oxidation**, the **citric acid (Krebs) cycle**, and **oxidative phosphorylation**.



Overview of aerobic cellular respiration. Glycolysis occurs in the cytosol; pyruvate oxidation, the Krebs cycle, and oxidative phosphorylation occur inside the mitochondrion (matrix for the first two, inner membrane for the last).

Glycolysis ("sugar splitting") occurs in the **cytosol** and does not require oxygen. One glucose molecule (6 carbons) is split and rearranged into **two molecules of pyruvate** (3 carbons each), through a 10-step enzyme-catalyzed pathway. Although 2 ATP are invested early in the pathway (to phosphorylate glucose and fructose-6-phosphate), 4 ATP are generated later by **substrate-level phosphorylation** (an enzyme transfers a phosphate group directly from an intermediate onto ADP), for a **net** yield of 2 ATP. Glycolysis also produces 2 **NADH** (by oxidizing an intermediate and reducing NAD^+).

> **Glycolysis, net per glucose:** 1 glucose $\rightarrow$ 2 pyruvate $+$ net 2 ATP (substrate-level phosphorylation) $+$ 2 NADH. Occurs in the cytosol; does not require O_2.

3.5.2 Pyruvate oxidation

If oxygen is available, each pyruvate molecule is transported into the mitochondrial **matrix**, where the **pyruvate dehydrogenase complex** carries out the **pyruvate oxidation** (**link** or **transition**) reaction: pyruvate (3 carbons) loses one carbon as CO_2, and the remaining 2-carbon fragment is attached to coenzyme A to form **acetyl-CoA**, while NAD^+ is reduced to **NADH**.

$$\text{pyruvate} + \text{CoA} + \text{NAD}^+ \longrightarrow \text{acetyl-CoA} + \text{CO}_2 + \text{NADH}.$$

Because each glucose produced two pyruvate molecules, this reaction happens **twice** per glucose, yielding (per glucose) 2 acetyl-CoA, $2\,CO_2$, and 2 NADH. No ATP is produced in this step.

3.5.3 The citric acid (Krebs) cycle

Each acetyl-CoA (2 carbons) enters the **citric acid cycle** (Krebs cycle) in the mitochondrial matrix, combining with a 4-carbon molecule (oxaloacetate) to form citrate (6 carbons). Over a series of enzyme-catalyzed steps, the cycle releases $2\,CO_2$, regenerates oxaloacetate to accept the next acetyl-CoA, and harvests energy in the form of electron carriers and one ATP-equivalent.

> **Krebs cycle, per turn (per acetyl-CoA):** 3 NADH $+$ $1\,FADH_2$ $+$ 1 ATP (via GTP, substrate-level phosphorylation) $+$ $2\,CO_2$ released.
> Because each glucose yields 2 acetyl-CoA, the cycle turns **twice** per glucose: totals of 6 NADH, $2\,FADH_2$, 2 ATP, and $4\,CO_2$.

VN **GIẢI THÍCH TIẾNG VIỆT**

Chu trình Krebs (chu trình acid citric) diễn ra trong chất nền ty thể. Mỗi vòng (ứng với 1 acetyl-CoA) tạo ra 3 NADH, $1\,FADH_2$, 1 ATP, và giải phóng $2\,CO_2$. Vì mỗi glucose tạo ra 2 acetyl-CoA nên chu trình quay 2 **vòng** mỗi glucose — tổng cộng 6 NADH, $2\,FADH_2$, 2 ATP, và $4\,CO_2$. Đây là giai đoạn tạo ra **nhiều chất mang electron nhất** trong toàn bộ hô hấp tế bào, chuẩn bị "nguyên liệu" cho chuỗi truyền electron.

3.5.4 Oxidative phosphorylation: electron transport and chemiosmosis

The NADH and $FADH_2$ produced by glycolysis, pyruvate oxidation, and the Krebs cycle carry high-energy electrons to the **electron transport chain (ETC)**, a series of protein complexes embedded in the mitochondrial **inner membrane**. As electrons pass down the chain (through Complexes I–IV) toward **oxygen** — the final electron acceptor, which combines with electrons and H^+ to form H_2O — the energy released is used to actively pump H^+ ions from the matrix into the intermembrane space, building a steep electrochemical **proton gradient** (the proton-motive force).

In **chemiosmosis**, protons flow back down this gradient, through the enzyme **ATP synthase**, which uses that flow to phosphorylate ADP into ATP. Together, the electron transport chain and chemiosmosis constitute **oxidative phosphorylation**, which generates the great majority of ATP produced during aerobic respiration. Because NADH donates its electrons at an earlier, higher-energy

point in the chain (Complex I) than $FADH_2$ (which donates at Complex II), NADH drives more proton pumping — and therefore yields more ATP — per molecule than $FADH_2$.

VN **GIẢI THÍCH TIẾNG VIỆT**

Phosphoryl hoá oxi hoá (oxidative phosphorylation) = chuỗi truyền electron + hoá thẩm thấu. NADH và $FADH_2$ nhường electron cho chuỗi truyền electron trên màng trong ty thể; năng lượng giải phóng khi electron di chuyển qua các phức hệ được dùng để bơm H^+ vào khoang giữa hai màng, tạo građien nồng độ H^+. O_2 là chất nhận electron cuối cùng, kết hợp với electron và H^+ tạo thành H_2O. H^+ sau đó khuếch tán ngược qua ATP synthase (hoá thẩm thấu), tổng hợp phần lớn ATP của toàn bộ quá trình hô hấp tế bào. NADH nhường electron ở vị trí sớm hơn trong chuỗi nên bơm được nhiều H^+ hơn $FADH_2$, do đó tạo ra nhiều ATP hơn.

3.5.5 Full ATP yield accounting

Modern accounting uses approximate conversion factors of 2.5 **ATP per NADH** and 1.5 **ATP per** $FADH_2$ oxidized through the electron transport chain (these fractional values reflect that the proton gradient is a shared, continuously "leaky" resource, not a fixed integer number of ATP per carrier).

Ví dụ mẫu · Full ATP-yield accounting for one glucose

Tally the net ATP yield of complete aerobic respiration of one glucose molecule.

Stage	Substrate-level ATP	NADH	$FADH_2$
Glycolysis (cytosol)	$+2$	2	0
Pyruvate oxidation ($\times 2$)	0	2	0
Krebs cycle ($\times 2$ turns)	$+2$	6	2
Total	**4**	**10**	**2**

Oxidative phosphorylation:

$$10\ \text{NADH} \times 2.5\ \tfrac{\text{ATP}}{\text{NADH}} = 25\ \text{ATP}, \qquad 2\ \text{FADH}_2 \times 1.5\ \tfrac{\text{ATP}}{\text{FADH}_2} = 3\ \text{ATP}.$$

$$\text{Oxidative phosphorylation subtotal} = 25 + 3 = 28\ \text{ATP}.$$

Grand total (malate–aspartate shuttle, no loss):

$$4\ (\text{substrate-level}) + 28\ (\text{oxidative}) = \textbf{32 ATP}.$$

In many eukaryotic cells, however, the 2 NADH from glycolysis are made in the *cytosol*, and NADH itself cannot cross the inner mitochondrial membrane. Some cell types (e.g., skeletal muscle, brain) use the **glycerol-3-phosphate shuttle**, which hands those 2 electrons pairs to FAD instead of mitochondrial NAD^+ — so each of those 2 NADH is effectively worth only 1.5 ATP (like $FADH_2$) rather than 2.5 ATP, a loss of $2 \times (2.5 - 1.5) = 2$ ATP-equivalents:

$$32 - 2 = \textbf{30 ATP}.$$

Net ATP yield of aerobic respiration of one glucose molecule is therefore approximately 30–32 **ATP**, depending on which shuttle a given cell type uses (cells using the malate–aspartate shuttle, e.g. liver, heart, and kidney, achieve the higher value). This modern, carefully-accounted figure has replaced the older textbook estimate of 36–38 ATP, which assumed a fixed 3 ATP per NADH and 2 ATP per $FADH_2$ with no shuttle cost.

(!) Lỗi thường gặp: NADH and $FADH_2$ are **electron carriers**, not ATP themselves — never simply count them as "1 NADH $= 1$ ATP." Each must be converted using its ATP-equivalent factor (≈ 2.5 for NADH, ≈ 1.5 for $FADH_2$) through oxidative phosphorylation, and only **after** oxygen has accepted the final electrons in the electron transport chain. If oxygen (or the ETC) is unavailable, accumulated NADH and $FADH_2$ cannot be "cashed in" for ATP at all.

3.5.6 Anaerobic fermentation

When oxygen is unavailable, the electron transport chain stalls (no final electron acceptor), which in turn stops the Krebs cycle and pyruvate oxidation, because they depend on a continuous supply of NAD^+ (and FAD) — and that NAD^+ is normally regenerated only by handing electrons to the ETC. Glycolysis, however, can continue *without* oxygen, but only if its own NAD^+ supply is regenerated some other way; this is the job of **fermentation**.

Two common fermentation pathways

Lactic acid fermentation (in animal muscle cells during intense exercise, and some bacteria): pyruvate directly accepts electrons from NADH, forming **lactate** and regenerating NAD^+:

$$\text{pyruvate} + \text{NADH} + \text{H}^+ \longrightarrow \text{lactate} + \text{NAD}^+.$$

Alcohol (ethanol) fermentation (in yeast and some bacteria): pyruvate is first decarboxylated to acetaldehyde (releasing CO_2), and acetaldehyde then accepts electrons from NADH to form **ethanol**, again regenerating NAD^+:

$$\text{pyruvate} \longrightarrow \text{acetaldehyde} + \text{CO}_2, \qquad \text{acetaldehyde} + \text{NADH} + \text{H}^+ \longrightarrow \text{ethanol} + \text{NAD}^+.$$

In both pathways, the sole purpose is to regenerate NAD^+ so that glycolysis's NAD^+-requiring step (glyceraldehyde-3-phosphate dehydrogenase) can keep running. **No additional ATP is produced** by the fermentation step itself — the cell's total ATP yield from a fermenting glucose molecule is just glycolysis's net 2 ATP, because fermentation does not involve the electron transport chain or oxidative phosphorylation at all; the chemical energy remaining in lactate or ethanol is simply left unharvested.

Ví dụ mẫu · Fermentation versus aerobic respiration: ATP comparison

Explain, in terms of mechanism, why fermenting one glucose molecule yields only 2 ATP, while aerobic respiration of one glucose molecule yields roughly 30–32 ATP.

Glycolysis itself produces the same net 2 ATP (by substrate-level phosphorylation) whether or not oxygen is present. The huge difference comes entirely from what happens *afterward*: with oxygen, pyruvate is fully oxidized through pyruvate oxidation and the Krebs cycle, generating 10 NADH and 2 $FADH_2$ total, whose electrons then flow through the electron transport chain to power chemiosmosis and oxidative phosphorylation — the source of ≈ 28 of the ≈ 30–32 total ATP. Without oxygen, none of that can happen: there is no final electron acceptor for the ETC, so the Krebs cycle and pyruvate oxidation halt, and NADH is instead re-oxidized by the "shortcut" of fermentation (reducing pyruvate to lactate, or its derivative to ethanol) purely to regenerate NAD^+ for glycolysis. Fermentation harvests *none* of the substantial chemical energy still locked inside pyruvate/lactate/ethanol — it only keeps glycolysis's modest 2-ATP output running.

(!) Lỗi thường gặp: Fermentation is not a completely separate energy pathway — it is glycolysis *plus* a small NAD^+-regenerating step tacked on at the end. All of fermentation's net ATP (2 per

glucose) comes from glycolysis itself; the lactic acid or alcohol fermentation step produces **zero** additional ATP. Students sometimes mistakenly think fermentation is a completely different, independent way of making ATP — instead, its only job is regenerating NAD^+ so glycolysis does not stall.

VN **GIẢI THÍCH TIẾNG VIỆT**

Khi không có O_2, chuỗi truyền electron ngừng hoạt động (không có chất nhận electron cuối cùng), kéo theo chu trình Krebs và oxi hoá pyruvate cũng ngừng vì thiếu NAD^+ tái sinh. **Lên men** (lactic acid ở người/vi khuẩn, hoặc rượu ở nấm men) chỉ có MỘT nhiệm vụ: tái tạo lại NAD^+ từ NADH bằng cách chuyển electron cho pyruvate (hoặc dẫn xuất của nó), để đường phân có thể tiếp tục chạy. Lên men **KHÔNG** tạo thêm ATP nào — toàn bộ 2 ATP thu được vẫn chỉ đến từ đường phân. Đây là lý do lên men cho năng lượng ít hơn hô hấp hiếu khí rất nhiều (2 ATP so với ≈ 30–32 ATP mỗi glucose).

3.6 Practice Problems

Bài tập luyện tập

Which of the following best describes the induced-fit model of enzyme action?

(A) The active site is a rigid mould that fits only one exact substrate shape, like a lock and key.

(B) The active site changes shape slightly as it binds substrate, molding more closely around it.

(C) Substrates change their own shape permanently before binding any enzyme.

(D) Enzymes bind substrates randomly with no structural specificity at all.

Lời giải chi tiết

The induced-fit model describes a flexible active site that adjusts its conformation upon substrate binding, improving the fit and positioning catalytic groups correctly — not a rigid, pre-shaped lock. **(B)**.

Bài tập luyện tập

An enzyme lowers the activation energy of a reaction from 12 kcal/mol (uncatalyzed) to 4 kcal/mol (catalyzed). If the reactants sit at a free-energy level of 10 kcal/mol and the products sit at 6 kcal/mol, what is ΔG for the catalyzed reaction, and is it exergonic or endergonic?

Lời giải chi tiết

ΔG depends only on the free-energy difference between products and reactants, not on the pathway or the presence of a catalyst: $\Delta G = 6 - 10 = -4$ kcal/mol. Since $\Delta G < 0$, the reaction is **exergonic** (spontaneous). Note that ΔG would be exactly the same, -4 kcal/mol, for the uncatalyzed reaction too — the enzyme changed only the activation energy ($12 \to 4$ kcal/mol), not ΔG.

Bài tập luyện tập

A patient has a fever of $40\,^\circ$C, well above the normal optimum of many human enzymes ($\approx 37\,^\circ$C). Predict and explain the short-term effect on enzyme activity if the fever continues to

rise significantly further, to 42–$43\,^{\circ}$C.

Lời giải chi tiết

As temperature rises further above the optimum, the extra heat begins to disrupt the weak bonds (hydrogen bonds, ionic interactions) that maintain the enzyme's three-dimensional tertiary structure. The protein loses its specific shape — including the active site — a process called **denaturation**. Enzyme activity therefore falls sharply, and because denaturation is often irreversible, activity may not return even if temperature is later restored to normal — this is why sustained very high fevers are medically dangerous.

Bài tập luyện tập

Enzyme rate data at increasing substrate concentration ($[S]$ in mM, V in μmol/min): $[S] = 2, V = 4.0$; $[S] = 8, V = 10.7$; $[S] = 20, V = 14.5$; $[S] = 50, V = 16.7$; $[S] = 100, V = 17.5$. Estimate V_{max} and explain your reasoning.

Lời giải chi tiết

The rate increases with $[S]$ but by progressively smaller increments ($+6.7$, then $+3.8$, then $+2.2$, then $+0.8$), clearly leveling off. Extrapolating the trend, $V_{\text{max}} \approx 18\ \mu$mol/min — the plateau the curve is approaching as $[S] \to \infty$. This flattening reflects enzyme **saturation**: at high $[S]$, essentially every active site is occupied at all times, so the rate is capped by how quickly each enzyme molecule can process substrate, not by substrate availability.

Bài tập luyện tập

Which statement correctly distinguishes a cofactor from a coenzyme?

(A) A cofactor is always a vitamin-derived organic molecule; a coenzyme is always a metal ion.

(B) A cofactor is any non-protein helper (often an inorganic ion); a coenzyme is specifically an organic cofactor, often vitamin-derived.

(C) Cofactors and coenzymes are two names for exactly the same thing with no distinction.

(D) Only enzymes with quaternary structure require cofactors or coenzymes.

Lời giải chi tiết

"Cofactor" is the general term for a non-protein helper required for enzyme activity (which may be an inorganic ion, e.g. Mg^{2+}, or an organic molecule). "Coenzyme" specifically refers to an *organic* cofactor, frequently derived from a vitamin (e.g., NAD^{+} from niacin). **(B)**.

Bài tập luyện tập

A biochemist tests an enzyme inhibitor. Adding a very large excess of substrate fully restores the enzyme's original V_{max}, although a much higher $[S]$ is now needed to reach it. What type of inhibitor is this, and where does it most likely bind?

Lời giải chi tiết

Because the inhibitor's effect is fully reversed by a large excess of substrate, and only the apparent K_m (not V_{max}) is affected, this is a **competitive inhibitor**. It binds directly at the **active site**, competing with substrate for the same binding location — with enough substrate present, substrate molecules statistically out-compete the inhibitor for access to active sites, so the original V_{max} is still achievable.

Bài tập luyện tập

An allosteric inhibitor is added to an enzyme reaction. Which outcome would you expect, even after adding a very large excess of substrate?

(A) V_{max} returns fully to its uninhibited value.

(B) V_{max} remains lower than the uninhibited value, because the inhibitor does not compete for the active site.

(C) The reaction rate becomes exactly zero at all substrate concentrations.

(D) The enzyme's substrate specificity changes to a new substrate.

Lời giải chi tiết

Allosteric (noncompetitive) inhibitors bind a site distinct from the active site, distorting the enzyme's shape so that some fraction of enzyme molecules remain permanently less effective, regardless of substrate concentration. Because they are not competing directly for the active site, adding more substrate cannot displace them, so V_{max} stays reduced. **(B)**.

Bài tập luyện tập

In a biosynthetic pathway $A \xrightarrow{\text{enzyme 1}} B \xrightarrow{\text{enzyme 2}} C \xrightarrow{\text{enzyme 3}} D$, the end product D allosterically inhibits enzyme 1. Explain the biological advantage of this arrangement, and predict what happens to the pathway's flux as D accumulates versus as D is consumed by the cell.

Lời giải chi tiết

This is **feedback inhibition** (end-product inhibition). As D accumulates, it binds an allosteric site on enzyme 1 (the first, "committed" step of the pathway) and inhibits it, slowing or stopping further conversion of A to B — and therefore the whole pathway — before resources are wasted making more D than the cell needs. As the cell consumes D (its concentration falls), less enzyme 1 is inhibited, flux through the pathway resumes, and more D is made. This creates a self-regulating supply that automatically tracks cellular demand, conserving raw material (A) and energy.

Bài tập luyện tập

Which of the following is a correct structural description of ATP?

(A) Adenine + deoxyribose + two phosphate groups

(B) Guanine + ribose + three phosphate groups

(C) Adenine + ribose + three phosphate groups

(D) Uracil + ribose + three phosphate groups

Lời giải chi tiết

ATP (adenosine triphosphate) consists of the nitrogenous base adenine, the sugar ribose (not deoxyribose — that is DNA's sugar), and a chain of three phosphate groups. **(C)**.

Bài tập luyện tập

A cell needs to actively transport Na^+ ions against their concentration gradient, an endergonic process with $\Delta G = +5.5$ kcal/mol. If this is coupled to hydrolysis of one ATP ($\Delta G \approx -7.3$ kcal/mol), what is the net ΔG of the coupled process, and is active transport now possible?

Lời giải chi tiết

Coupling adds the two ΔG values: $\Delta G_{\text{net}} = (+5.5) + (-7.3) = -1.8$ kcal/mol. Since $\Delta G_{\text{net}} < 0$, the coupled process is exergonic overall and **is** spontaneous — ATP hydrolysis supplies more than enough free energy to drive the endergonic transport of Na^+ against its gradient. (This is exactly the strategy used by pumps such as the Na^+/K^+-ATPase.)

Bài tập luyện tập

Classify each process as exergonic or endergonic: (a) breakdown of glycogen into glucose monomers; (b) the Calvin cycle building G3P from CO_2; (c) ATP hydrolysis; (d) synthesis of a protein from amino acids.

Lời giải chi tiết

(a) **Exergonic** — catabolic breakdown of a macromolecule into smaller monomers releases free energy. (b) **Endergonic** — building organic sugar from CO_2 requires energy input (from ATP and NADPH), which is why the Calvin cycle cannot run without the light reactions. (c) **Exergonic** — $\Delta G \approx -7.3$ kcal/mol. (d) **Endergonic** — anabolic polymerization of amino acids into a protein requires energy input (ultimately from ATP hydrolysis at each peptide-bond-forming step).

Bài tập luyện tập

In the reaction FAD $+ 2\text{H} \rightarrow \text{FADH}_2$, which species is oxidized and which is reduced?

(A) FAD is oxidized; the hydrogen source is reduced.

(B) FAD is reduced (gains electrons/hydrogens); the hydrogen source is oxidized (loses them).

(C) Both species are oxidized simultaneously.

(D) Neither species changes oxidation state.

Lời giải chi tiết

FAD gains electrons (as part of the two hydrogen atoms) to become $FADH_2$ — a gain of electrons is **reduction**. Whatever donated those hydrogens/electrons is thereby **oxidized**. **(B)**.

Bài tập luyện tập

Explain why one molecule of NADH ultimately yields more ATP through oxidative phosphorylation than one molecule of $FADH_2$.

Lời giải chi tiết

NADH delivers its electrons to the electron transport chain at **Complex I**, an earlier and higher-energy entry point, so electrons from NADH pass through more of the proton-pumping complexes on their way to oxygen, pumping more H^+ into the intermembrane space. $FADH_2$ delivers its electrons further downstream, at **Complex II**, bypassing Complex I entirely, so fewer protons are pumped per $FADH_2$. Because ATP yield through chemiosmosis is proportional to the size of the proton gradient generated, NADH (≈ 2.5 ATP) yields more than $FADH_2$ (≈ 1.5 ATP).

Bài tập luyện tập

Which structure is the site of the Calvin cycle, and which is the site of the light-dependent reactions?

(A) Both occur in the thylakoid membrane.

(B) Light reactions occur in the stroma; Calvin cycle occurs on the thylakoid membrane.

(C) Light reactions occur on/across the thylakoid membrane; Calvin cycle occurs in the stroma.

(D) Both occur in the mitochondrial matrix.

Lời giải chi tiết

The light-dependent reactions take place in and across the **thylakoid membrane** (where the photosystems, electron transport chain, and ATP synthase are embedded); the Calvin cycle takes place in the **stroma**, the fluid surrounding the thylakoids. **(C)**.

Bài tập luyện tập

During the light reactions, water is split (photolysis). Identify the three products of this reaction and explain the ultimate fate of each.

Lời giải chi tiết

Photolysis, $2\,H_2O \rightarrow 4\,H^+ + 4e^- + O_2$, produces: (1) H^+ **ions**, which contribute to the proton gradient across the thylakoid membrane, driving ATP synthesis by chemiosmosis; (2) **electrons** (e^-), which replace those lost by PSII when it absorbed light, allowing PSII to continue functioning; (3) O_2, which is released as a byproduct (it plays no further role in photosynthesis itself and simply diffuses out of the leaf/cell — this is the source of the oxygen released by photosynthesis).

Bài tập luyện tập

RuBisCO catalyzes which specific reaction of the Calvin cycle?

(A) Reduction of 3-PGA to G3P using NADPH

(B) Regeneration of RuBP from G3P using ATP

(C) Attachment of CO_2 to RuBP, forming two molecules of 3-PGA

(D) Splitting of water to release O_2

Lời giải chi tiết

RuBisCO (ribulose-1,5-bisphosphate carboxylase/oxygenase) catalyzes carbon fixation: attaching CO_2 to the 5-carbon RuBP, forming an unstable 6-carbon intermediate that splits into two 3-carbon 3-PGA molecules. **(C)**.

Bài tập luyện tập

How many total turns of the Calvin cycle, and how much ATP and NADPH, are required to net-produce one glucose molecule ($C_6H_{12}O_6$)? Explain your reasoning in terms of carbon accounting.

Lời giải chi tiết

Glucose has 6 carbons, and each net G3P exported from the Calvin cycle has 3 carbons, so it takes **2 net G3P** molecules to build one glucose. Each net G3P requires **3** turns of the cycle (fixing $3\,CO_2$, using 9 ATP and 6 NADPH per net G3P). Therefore, producing one glucose requires $2 \times 3 = $ **6** total turns of the cycle, fixing $6\,CO_2$, and consuming $2 \times 9 = $ **18** ATP and $2 \times 6 = $ **12** NADPH.

Bài tập luyện tập

A greenhouse experiment measures photosynthetic rate at increasing light intensity, first at normal atmospheric CO_2 (0.04%) and then at an elevated CO_2 level. At normal CO_2, the rate plateaus at moderate light intensity; at elevated CO_2, the rate continues rising to a higher plateau before leveling off. If the elevated-CO_2 curve is now also run at two different temperatures ($20\,^\circ$C and $30\,^\circ$C, with light and CO_2 both kept abundant), predict what would be observed and explain why.

Lời giải chi tiết

With light and CO_2 both abundant (no longer limiting), **temperature** becomes the limiting factor, since both the light reactions' proteins and — especially — the Calvin cycle's enzymes (RuBisCO and others) are temperature-sensitive. We would expect the $30\,^\circ$C curve to plateau at a **higher** rate than the $20\,^\circ$C curve (assuming $30\,^\circ$C is still within the plant's optimal range), because warmer temperature (up to the optimum) increases enzyme-catalyzed reaction rates, allowing the Calvin cycle to fix CO_2 and regenerate RuBP faster. If temperature were pushed well beyond the enzymes' optimum (e.g., $45\,^\circ$C), the rate would instead **fall** sharply due to denaturation of RuBisCO and other enzymes.

Bài tập luyện tập

Which of the following correctly identifies where glycolysis occurs and its net ATP/NADH yield per glucose?

(A) Mitochondrial matrix; net 2 ATP, 2 NADH

(B) Cytosol; net 2 ATP, 2 NADH

(C) Cytosol; net 4 ATP, 0 NADH

(D) Mitochondrial matrix; net 30 ATP, 2 NADH

Lời giải chi tiết

Glycolysis occurs in the **cytosol**, does not require oxygen, and yields a **net** 2 ATP (from 4 produced by substrate-level phosphorylation minus 2 invested) plus 2 NADH per glucose. **(B)**.

Bài tập luyện tập

What are the direct products of pyruvate oxidation (the link/transition reaction) for a *single* pyruvate molecule, and how many times does this reaction occur per glucose?

Lời giải chi tiết

For one pyruvate: pyruvate + coenzyme A + $NAD^+ \rightarrow$ **1 acetyl-CoA** + **1** CO_2 + **1 NADH**. Since each glucose produces 2 pyruvate molecules via glycolysis, this reaction occurs **twice** per glucose, yielding 2 acetyl-CoA, $2\,CO_2$, and 2 NADH in total. No ATP is produced directly at this step.

Bài tập luyện tập

Per glucose molecule, how many total NADH, $FADH_2$, CO_2, and ATP (by substrate-level phosphorylation) are produced by the citric acid (Krebs) cycle, given that it must turn twice?

Lời giải chi tiết

Per turn: 3 NADH, $1\,FADH_2$, 1 ATP, $2\,CO_2$. For 2 turns (one per acetyl-CoA, two acetyl-CoA per glucose): **6** NADH, **2** $FADH_2$, **2** ATP, and **4** CO_2.

Bài tập luyện tập

Using the malate–aspartate shuttle (no ATP-equivalent loss) and the conversion factors 2.5 ATP/NADH and 1.5 ATP/$FADH_2$, calculate the net ATP yield of aerobic respiration for one glucose molecule, showing every component of the calculation.

Lời giải chi tiết

Totals per glucose: substrate-level ATP $= 2$ (glycolysis) $+2$ (Krebs) $= 4$; NADH $= 2$ (glycolysis) $+2$ (pyruvate oxidation) $+6$ (Krebs) $= 10$; $FADH_2 = 2$ (Krebs).
Oxidative phosphorylation ATP $= 10 \times 2.5 + 2 \times 1.5 = 25 + 3 = 28$.
Net total $= 4 + 28 =$ **32 ATP** per glucose (malate–aspartate shuttle, no shuttle loss).

Bài tập luyện tập

A skeletal-muscle cell uses the glycerol-3-phosphate shuttle, which delivers the electrons from cytosolic (glycolytic) NADH to mitochondrial FAD rather than NAD^+. Recompute the net ATP yield of aerobic respiration for one glucose molecule under this condition, and state how many total ATP-equivalents are "lost" to the shuttle compared with the malate–aspartate shuttle.

Lời giải chi tiết

With the glycerol-3-phosphate shuttle, the 2 NADH produced by glycolysis (in the cytosol) are each worth only 1.5 ATP (like $FADH_2$) instead of 2.5 ATP once their electrons enter the mitochondrion. Starting from the malate–aspartate-shuttle total of 32 ATP, the loss is

2 NADH $\times$ $(2.5 - 1.5$ ATP/NADH$) = 2 \times 1.0 =$ **2 ATP** lost. Net yield $= 32 - 2 =$ **30 ATP** per glucose. This is exactly why different cell types are commonly cited as yielding "30" versus "32" ATP per glucose — the difference is entirely due to which NADH shuttle is used to import cytosolic electrons into the mitochondrion.

Bài tập luyện tập

Cyanide is a poison that binds tightly to and blocks Complex IV (cytochrome c oxidase) of the electron transport chain, preventing electrons from being passed to oxygen. Predict, with reasoning, the effect of cyanide poisoning on (a) the proton gradient, (b) ATP synthase activity, (c) the Krebs cycle, and (d) the cell's total ATP output.

Lời giải chi tiết

(a) With Complex IV blocked, electrons can no longer flow all the way to O_2, so upstream complexes stop pumping H^+ as electron flow backs up; the **proton gradient collapses** as existing protons leak back down without being replenished. (b) With no proton gradient to drive it, **ATP synthase activity stops** — oxidative phosphorylation ceases almost entirely. (c) NAD^+ and FAD can no longer be regenerated (their reduced forms cannot be re-oxidized without a functioning ETC), so the **Krebs cycle (and pyruvate oxidation) grinds to a halt** for lack of the oxidized carriers they require. (d) The cell is left producing only the modest **net 2 ATP from glycolysis** (which can continue briefly only if some NAD^+ is regenerated, e.g. via fermentation-like reactions) — total ATP output collapses from ≈ 30–32 per glucose to essentially 2, which is why cyanide poisoning is rapidly lethal, especially to highly ATP-dependent tissues like the brain and heart.

Bài tập luyện tập

Which of the following correctly distinguishes substrate-level phosphorylation from oxidative phosphorylation?

(A) Substrate-level phosphorylation requires a proton gradient across a membrane; oxidative phosphorylation directly transfers a phosphate group from a substrate to ADP.

(B) Substrate-level phosphorylation directly transfers a phosphate group from a reaction intermediate to ADP; oxidative phosphorylation uses a proton gradient (chemiosmosis) generated by the electron transport chain.

(C) Both processes are identical mechanisms occurring in different locations.

(D) Only oxidative phosphorylation occurs in glycolysis.

Lời giải chi tiết

Substrate-level phosphorylation (occurring in glycolysis and the Krebs cycle) is a direct enzymatic transfer of a phosphate group from a high-energy intermediate onto ADP, forming ATP with no membrane or gradient involved. **Oxidative phosphorylation** generates ATP indirectly, via the electron transport chain building a proton gradient that ATP synthase then uses (chemiosmosis). **(B)**.

Bài tập luyện tập

Yeast cells are grown in a sealed flask with abundant glucose but no oxygen. Which product(s) would accumulate, and would the flask's total ATP yield per glucose be higher, lower, or the same compared to yeast grown aerobically with the same amount of glucose?

Lời giải chi tiết

Under anaerobic conditions, yeast perform **alcohol (ethanol) fermentation**: glycolysis proceeds normally, then pyruvate is decarboxylated to acetaldehyde (releasing CO_2), and acetaldehyde is reduced by NADH to **ethanol**, regenerating NAD^+. The flask would accumulate **ethanol and** CO_2. ATP yield per glucose would be **much lower** — only the net 2 ATP from glycolysis, versus ≈ 30–32 ATP under aerobic conditions — because without oxygen there is no electron transport chain activity and no oxidative phosphorylation; fermentation's ethanol-producing step generates no ATP of its own and exists solely to regenerate NAD^+.

Bài tập luyện tập

A student claims: "Lactic acid fermentation is a completely separate pathway from cellular respiration that produces its own ATP independent of glycolysis." Evaluate this claim.

Lời giải chi tiết

The claim is **incorrect**. Lactic acid fermentation is not independent of glycolysis — it is glycolysis *plus* one additional step (pyruvate + NADH → lactate + NAD^+) whose only purpose is to regenerate the NAD^+ that glycolysis needs to keep running. The lactate-forming step itself produces **zero** ATP. All ATP obtained during fermentation (net 2 per glucose) comes entirely from glycolysis's substrate-level phosphorylation, which occurs identically whether or not fermentation follows it.

Bài tập luyện tập

Which of the following organisms/tissues use lactic acid fermentation, and which use alcohol fermentation, when oxygen is limited?

(A) Human muscle cells use alcohol fermentation; yeast use lactic acid fermentation.

(B) Both always use alcohol fermentation exclusively.

(C) Human (and other animal) muscle cells and some bacteria use lactic acid fermentation; yeast and some bacteria use alcohol fermentation.

(D) Neither organism can survive without oxygen at all.

Lời giải chi tiết

Human/animal muscle cells (and some bacteria, e.g. those used to make yogurt) regenerate NAD^+ by reducing pyruvate directly to **lactate** (lactic acid fermentation). Yeast (and some bacteria) instead decarboxylate pyruvate and reduce the product to **ethanol** (alcohol fermentation), releasing CO_2 along the way. **(C)**.

Bài tập luyện tập

Explain, using free-energy reasoning, why the reaction $ADP + P_i \rightarrow ATP + H_2O$ does *not* occur spontaneously in the cell, and identify what type of process must be coupled to it to make it happen.

Lời giải chi tiết

This reaction is simply ATP hydrolysis run in reverse, so its ΔG is the opposite sign of hydrolysis: $\Delta G \approx +7.3$ kcal/mol — strongly **endergonic**, meaning it is nonspontaneous and will not proceed on its own. For ADP to be phosphorylated back into ATP, this endergonic reaction must be **coupled** to a sufficiently exergonic process that can supply at least 7.3 kcal/mol per mole. In the cell, this energy is ultimately supplied by **catabolic pathways** — most directly, chemiosmosis: the exergonic flow of H^+ down its electrochemical gradient through ATP synthase (during oxidative phosphorylation or photophosphorylation), or, in glycolysis and the Krebs cycle, the exergonic transfer of a phosphate group from a high-energy intermediate directly onto ADP (substrate-level phosphorylation).

Bài tập luyện tập

A researcher measures oxygen consumption in isolated mitochondria supplied with excess NADH and $ADP + P_i$, then adds a drug that makes the inner mitochondrial membrane "leaky" to protons (allowing H^+ to cross without passing through ATP synthase). Predict the effect on (a) the rate of electron transport/oxygen consumption and (b) the rate of ATP synthesis.

Lời giải chi tiết

This scenario describes an **uncoupler** (e.g., the drug DNP, historically studied for exactly this effect). (a) With the membrane now leaky to H^+, the proton gradient can no longer build up, so there is little resistance limiting the electron transport chain — electrons continue flowing to oxygen freely, so oxygen consumption **increases or stays high** (the ETC is no longer "backed up" by a steep gradient). (b) However, because protons leak back into the matrix directly through the membrane instead of through ATP synthase, chemiosmosis is short-circuited and **ATP synthesis drops sharply**, even while electron transport (and O_2 use) continues — a clear demonstration that electron transport and ATP synthesis, while normally linked, are mechanistically separate processes connected only by the proton gradient. (The energy that would have made ATP is instead released as heat, which is precisely how uncoupling proteins in brown fat generate heat.)

Cell Communication and Cell Cycle

Mục tiêu Unit: Tín hiệu tế bào (paracrine, synap, nội tiết, tiếp xúc trực tiếp qua gap junction/plasmodesmata); ba giai đoạn truyền tín hiệu (tiếp nhận – truyền tin – đáp ứng); thụ thể bắt cặp G-protein (GPCR) và thụ thể tyrosine kinase (RTK); khuếch đại tín hiệu; đột biến thụ thể và mối liên hệ với ung thư; cơ chế phản hồi âm và phản hồi dương; chu kỳ tế bào (G1, S, G2, nguyên phân, phân bào tế bào chất); và hệ thống kiểm soát chu kỳ tế bào (cyclin, CDK, p53, các điểm kiểm soát, và sự mất kiểm soát chu kỳ trong ung thư).

4.1 Cell Communication: An Overview

4.1.1 Why cells communicate

Every cell in a multicellular organism must coordinate its behavior with its neighbors and with the body as a whole. **Cell communication** (cell signaling) is the process by which a cell detects and responds to a chemical signal released by another cell. Signaling allows single-celled organisms (e.g., yeast searching for a mating partner) to coordinate behavior with others of their kind, and allows the trillions of cells in a multicellular organism to divide labor: coordinating growth, development, immune defense, tissue repair, and moment-to-moment physiological regulation such as heart rate and blood glucose level.

Core idea

Every act of cell signaling requires a **signal molecule** (ligand) released by a signaling cell and a complementary **receptor** on or in a target cell. Communication succeeds only if the target cell actually has the matching receptor – the same hormone circulating in the blood affects only the cells equipped to detect it.

VN GIẢI THÍCH TIẾNG VIỆT

Giao tiếp tế bào (cell communication/cell signaling) là quá trình một tế bào phát tín hiệu và tế bào đích nhận diện, phản ứng lại tín hiệu đó. Điều kiện tiên quyết là tế bào đích phải có **thụ thể (receptor)** phù hợp với **phân tử tín hiệu (ligand)** – nếu không có thụ thể tương thích, tế bào sẽ "điếc" với tín hiệu đó dù tín hiệu có mặt xung quanh nó. Đây là lý do vì sao cùng một hormone trong máu chỉ tác động lên một số loại tế bào nhất định (tế bào đích), chứ không phải toàn bộ cơ thể.

4.1.2 Local signaling: paracrine and synaptic signaling

When target cells lie close to the signaling cell, communication is fast and localized.

Paracrine signaling: a cell secretes local regulator molecules (e.g., growth factors, cytokines) that diffuse through the extracellular fluid and act on nearby cells. Because the signal is broken down quickly and diffusion is slow over distance, only cells in the immediate vicinity are affected. Example: growth factors released by a cell that stimulate nearby cells to divide during wound healing.

Synaptic signaling: a specialized form of local, short-range signaling used by neurons. An electrical signal (action potential) travels down the neuron to its tip, triggering release of a chemical

neurotransmitter into the narrow gap (synapse) between the neuron and its target cell. The neurotransmitter diffuses the short synaptic distance and binds receptors on the target cell (another neuron, a muscle fiber, or a gland cell), producing a rapid response.

4.1.3 Long-distance signaling: endocrine (hormonal) signaling

When the signaling and target cells are far apart, multicellular organisms use **endocrine signaling**. Specialized endocrine cells secrete **hormones** into body fluids, most commonly the bloodstream in animals. Because blood circulates throughout the entire body, a hormone reaches essentially every cell – but only **target cells**, which carry the matching receptor, respond. Endocrine signals travel farther and act more slowly than paracrine or synaptic signals (seconds to hours, rather than milliseconds), and their effects tend to be broader and longer-lasting (e.g., insulin regulating blood glucose throughout the body, or thyroid hormone setting the metabolic rate of virtually every tissue).

VN **GIẢI THÍCH TIẾNG VIỆT**

Ba kiểu tín hiệu theo khoảng cách: **tín hiệu cận tiết (paracrine)** – tế bào tiết chất điều hòa cục bộ khuếch tán đến tế bào lân cận (VD: yếu tố tăng trưởng); **tín hiệu synap (synaptic)** – tế bào thần kinh tiết chất dẫn truyền thần kinh vào khe synap, tác động cực nhanh lên tế bào đích liền kề; **tín hiệu nội tiết (endocrine/hormonal)** – tế bào tuyến nội tiết tiết hormone vào máu, hormone di chuyển khắp cơ thể nhưng chỉ tế bào có thụ thể phù hợp mới đáp ứng. Nhìn chung: tín hiệu càng đi xa thì đáp ứng càng chậm nhưng phạm vi ảnh hưởng càng rộng.

4.1.4 Direct contact signaling

Some signaling requires no diffusible messenger at all – cells communicate through direct physical contact.

Gap junctions (animal cells) are protein channels that directly connect the cytoplasm of adjacent cells, allowing ions, second messengers, and other small signaling molecules to pass freely between the two cells without ever entering the extracellular space. **Plasmodesmata** are the plant-cell equivalent: channels through adjoining cell walls that connect the cytoplasm of neighboring plant cells, allowing water, nutrients, and signaling molecules to move directly from cell to cell.

A second form of direct-contact signaling, sometimes called **juxtacrine signaling** or cell-surface recognition, does not require a channel at all: a membrane-bound signal molecule on one cell binds directly to a receptor protein on an adjacent cell's surface. This mechanism is essential for embryonic development (cells recognizing their neighbors to organize tissues) and for immune responses (a T cell recognizing a membrane-bound antigen–MHC complex displayed on another cell).

Signaling type	Mechanism	Example	Range / speed
Paracrine	Local regulator diffuses to nearby cells	Growth factors in wound repair	Short / moderate
Synaptic	Neurotransmitter released into synapse	Acetylcholine at a neuromuscular junction	Very short / very fast
Endocrine	Hormone travels through the bloodstream	Insulin, epinephrine, thyroid hormone	Long / slow
Direct contact	Gap junctions, plasmodesmata, or membrane-bound ligand–receptor binding	Cardiac muscle gap junctions; T-cell antigen recognition	Contact only / immediate

VN **GIẢI THÍCH TIẾNG VIỆT**

Gap junction (ở tế bào động vật) và **plasmodesmata** (ở tế bào thực vật) là các kênh nối trực tiếp tế bào chất của hai tế bào liền kề, cho phép ion và phân tử tín hiệu nhỏ đi thẳng từ tế bào này sang tế bào kia mà không cần đi qua dịch ngoại bào. Đây là cơ chế truyền tín hiệu nhanh

nhất vì không có bước khuếch tán qua khoảng ngoại bào – ví dụ điển hình là gap junction giữa các tế bào cơ tim, giúp tín hiệu điện lan truyền đồng bộ để tim co bóp nhịp nhàng.

4.2 The Signal Transduction Pathway

Regardless of the type of signal or distance traveled, once a ligand reaches a target cell, the target cell processes the signal in three conceptually distinct stages: **reception**, **transduction**, and **response**.

4.2.1 Reception: ligand–receptor specificity

Reception occurs when a signal molecule (ligand) binds to a receptor protein, causing the receptor to change shape (undergo a conformational change) or aggregate with other receptors – this is the event that activates the receptor. Binding is highly specific: a receptor's shape matches only one ligand or a small family of closely related ligands, just as an enzyme's active site matches only its substrate.

Which type of receptor a ligand uses depends on the ligand's chemistry:

- **Hydrophilic, large, or charged ligands** (most peptide hormones such as insulin and glucagon, and neurotransmitters and local regulators) cannot cross the hydrophobic interior of the plasma membrane. They bind to **membrane receptors** embedded in the plasma membrane, with an extracellular ligand-binding domain and an intracellular domain that triggers the next stage of the pathway.
- **Hydrophobic, small, lipid-soluble ligands** (steroid hormones such as estrogen, testosterone, and cortisol, as well as thyroid hormone and vitamin D) diffuse directly across the phospholipid bilayer. They bind to **intracellular receptors** located in the cytoplasm or nucleus. The resulting hormone–receptor complex often acts directly as a **transcription factor**, binding DNA and altering gene expression – collapsing reception and part of the response into a single step.

Reasoning: predicting receptor location

Epinephrine (adrenaline) is a small, charged, water-soluble amine derived from an amino acid; cortisol is a hydrophobic steroid built from a four-ring carbon skeleton. Predict where each hormone's receptor is located, and whether the immediate response is likely to be fast/cytoplasmic or slow/transcriptional.

Epinephrine is hydrophilic and cannot cross the plasma membrane, so its receptor (a GPCR, the β-adrenergic receptor) must be embedded in the **plasma membrane**. Because it acts through a rapid second-messenger cascade on existing cytoplasmic enzymes, the response (e.g., glycogen breakdown) is **fast** (seconds).

Cortisol is lipid-soluble and diffuses freely across the membrane, so its receptor is **intracellular** (cytoplasmic, then translocating to the nucleus). Because the hormone–receptor complex must bind DNA and alter transcription, synthesizing new proteins, the response is **slower** (minutes to hours) but longer-lasting.

VN GIẢI THÍCH TIẾNG VIỆT

Có hai loại thụ thể phân theo tính chất hoá học của ligand: **thụ thể màng** dành cho ligand ưa nước/phân tử lớn (không qua được màng, VD hormone peptide như insulin, epinephrine) – phần ngoại bào của thụ thể gắn ligand, phần nội bào kích hoạt tầng truyền tin bên trong tế bào chất. **Thụ thể nội bào** dành cho ligand kỵ nước/phân tử nhỏ (khuếch tán trực tiếp qua màng, VD hormone steroid như estrogen, testosterone, cortisol) – phức hợp hormone–thụ thể thường đóng vai trò trực tiếp như một yếu tố phiên mã (transcription factor), gắn vào ADN và thay đổi biểu hiện gen.

4.2.2 Transduction: relay, second messengers, and amplification

Transduction converts the signal received at the cell surface (or in the cytoplasm) into a form that can bring about a specific cellular response. Rarely does the activated receptor act on the final target directly; instead, the signal passes through a chain of **relay molecules** – a **signal transduction pathway**.

Two mechanisms dominate transduction pathways:

- **Phosphorylation cascades**: many relay molecules are **protein kinases**, enzymes that transfer a phosphate group from ATP onto a target protein, changing its shape and activity (usually activating it). One kinase can phosphorylate and activate the next kinase in the chain, producing a cascade. **Protein phosphatases** remove these phosphate groups, switching the pathway back off – phosphorylation is a reversible molecular switch.
- **Second messengers**: small, nonprotein, water-soluble molecules or ions (cyclic AMP, Ca^{2+}, IP_3, diacylglycerol) that diffuse rapidly through the cytosol, broadcasting the signal from the plasma membrane to targets throughout the cell far faster than any protein could diffuse.

Critically, transduction pathways do not just relay a signal – they typically **amplify** it. Because each activated enzyme in the cascade can act on many copies of the next-step molecule (rather than one-to-one), a single bound ligand at the cell surface can ultimately generate a very large intracellular response.

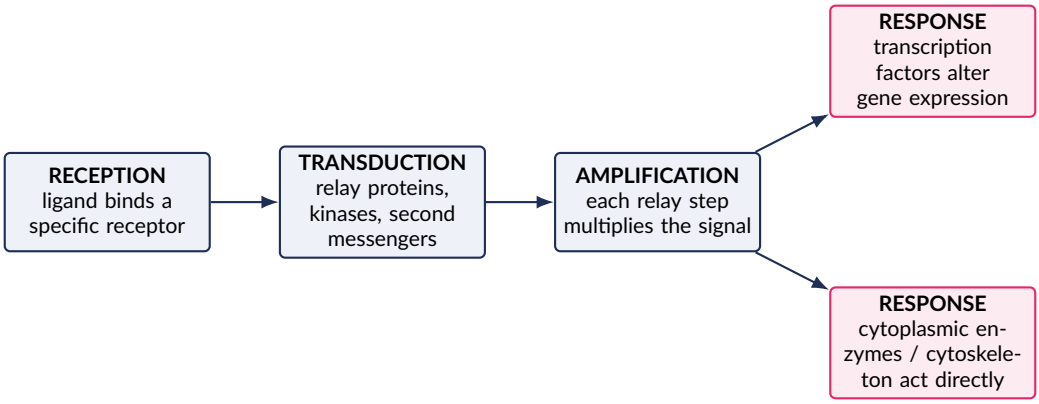
> **The three stages of signal transduction:** (1) **Reception** – a receptor binds its specific ligand and is activated; (2) **Transduction** – a chain of relay molecules (kinases, second messengers) carries and amplifies the signal through the cell; (3) **Response** – the pathway alters transcription (gene expression) or acts directly on existing cytoplasmic machinery.

4.2.3 Response: transcriptional and cytoplasmic outcomes

The final stage, **response**, is the specific cellular activity triggered by the pathway. Responses fall into two broad categories:

- **Transcriptional (nuclear) responses**: the pathway activates or represses transcription factors, which bind regulatory DNA sequences and switch specific genes on or off, changing which proteins the cell produces. These responses are slower (they require new mRNA and protein synthesis) but can permanently change cell identity or behavior (e.g., growth-factor pathways that switch on cyclin genes to trigger cell division).
- **Cytoplasmic responses**: the pathway acts directly on existing proteins already present in the cell – opening an ion channel, activating a metabolic enzyme, or rearranging the cytoskeleton. These responses are fast (seconds) because no new protein synthesis is required (e.g., epinephrine triggering glycogen breakdown within seconds).

Whichever kind of response results, cell signaling pathways are almost always followed by mechanisms that shut the pathway back off (ligand is degraded or dissociates, receptors are internalized, second messengers are broken down, phosphatases remove phosphate groups) – without deactivation, a transient signal would produce a permanent response.



The three stages of a signal transduction pathway. Reception activates a single receptor; transduction relays and amplifies the signal through several steps; the response is either a transcriptional change or a direct cytoplasmic effect.

(!) Lỗi thường gặp: Do not treat signal transduction as a simple one-to-one relay ("one ligand in, one response molecule out"). Because relay enzymes act catalytically on many copies of the next molecule, the pathway typically **amplifies** the original signal by several orders of magnitude. A single hormone molecule can ultimately alter the activity of hundreds of thousands of molecules inside the target cell (Section on signal amplification, below).

VN **GIẢI THÍCH TIẾNG VIỆT**

Đừng nhầm truyền tin tế bào là một chuỗi "1 tín hiệu vào – 1 đáp ứng ra". Vì mỗi enzyme trong chuỗi truyền tin có thể xúc tác nhiều phân tử ở bước tiếp theo (hoạt động như enzyme, không phải chỉ chuyển tiếp 1–1), tín hiệu được **khuếch đại** rất mạnh qua từng bước. Đây chính là lý do một lượng cực nhỏ hormone trong máu (nồng độ nanomol/lít) vẫn có thể gây ra đáp ứng rõ rệt và nhanh chóng bên trong tế bào đích.

4.3 Membrane Receptors and Signaling Pathways

Membrane receptors fall into a few major structural families. AP Biology focuses on three: G-protein-coupled receptors, receptor tyrosine kinases, and ligand-gated ion channels.

4.3.1 G-protein-coupled receptors (GPCRs) and second messengers

A **G-protein-coupled receptor (GPCR)** is a membrane protein that threads back and forth across the plasma membrane seven times (seven transmembrane α-helices). On the cytoplasmic side, an inactive GPCR is loosely associated with a **G protein**, a relay protein that binds the nucleotide GDP when inactive. GPCRs are the largest family of membrane receptors in humans and mediate an enormous range of processes – vision, smell, taste, heart rate, mood, and many hormone responses – which is why a large fraction of modern pharmaceutical drugs target GPCRs.

Mechanism: (1) a ligand binds the extracellular side of the GPCR, changing its shape; (2) the activated GPCR binds the associated G protein and acts as a guanine-nucleotide exchange factor, causing the G protein to release GDP and bind GTP instead; (3) the GTP-bound G protein is now active and dissociates from the receptor to diffuse along the membrane, activating an **effector enzyme**; (4) the G protein eventually hydrolyzes its own bound GTP back to GDP, deactivating itself – an intrinsic "timer" that shuts the pathway off.

Two classic GPCR-triggered second-messenger systems:

- **cAMP pathway**: the effector enzyme **adenylyl cyclase** converts ATP into **cyclic AMP (cAMP)**. cAMP diffuses through the cytosol and activates **protein kinase A (PKA)**, which phosphorylates a range of target proteins, altering their activity (e.g., triggering glycogen breakdown in liver and muscle cells in response to epinephrine).

- **IP_3/Ca^{2+} pathway**: the effector enzyme **phospholipase C** cleaves a membrane phospholipid (PIP_2) into two second messengers: **IP_3** (inositol trisphosphate), which diffuses through the cytosol and opens Ca^{2+} channels on the endoplasmic reticulum, releasing stored Ca^{2+} into the cytosol; and **diacylglycerol (DAG)**, which stays in the membrane and helps activate protein kinase C. The released Ca^{2+} itself acts as a second messenger, regulating numerous cytoplasmic enzymes and (in muscle) triggering contraction.

VN **GIẢI THÍCH TIẾNG VIỆT**

GPCR là thụ thể xuyên màng 7 lần, khi gắn ligand sẽ kích hoạt một **protein G** gắn kèm ở mặt trong màng (đổi GDP thành GTP để "bật"). Protein G hoạt hoá tiếp một enzyme hiệu ứng: hoặc **adenylyl cyclase** (tạo ra **cAMP** – chất truyền tin thứ cấp hoạt hoá PKA), hoặc **phospholipase C** (tạo ra IP_3 và DAG, trong đó IP_3 mở kênh giải phóng Ca^{2+} từ lưới nội chất). Cả hai con đường đều dùng **chất truyền tin thứ cấp** để khuếch tán tín hiệu nhanh khắp tế bào chất, thay vì phải chờ một protein lớn di chuyển.

4.3.2 Receptor tyrosine kinases (RTKs) and phosphorylation cascades

A **receptor tyrosine kinase (RTK)** is a single-pass membrane protein with an extracellular ligand-binding domain and an intracellular domain that itself is an enzyme – a **tyrosine kinase**, which phosphorylates tyrosine residues on target proteins. RTKs typically respond to growth factors (e.g., epidermal growth factor, insulin).

Mechanism: (1) ligand binding causes two RTK monomers to come together and **dimerize**; (2) within the dimer, each monomer's kinase domain phosphorylates tyrosine residues on the *other* monomer's cytoplasmic tail (**trans-autophosphorylation**); (3) the resulting phosphotyrosines act as docking sites that recruit multiple different relay proteins simultaneously, each triggering its own downstream signal transduction pathway. Because a single activated RTK dimer can dock several different relay proteins at once, one receptor can trigger **several distinct pathways in parallel** – coordinating complex responses such as cell growth, division, survival, and changes in shape all from a single growth-factor signal.

VN **GIẢI THÍCH TIẾNG VIỆT**

RTK là thụ thể xuyên màng 1 lần với phần nội bào có hoạt tính enzyme kinase. Khi ligand (thường là yếu tố tăng trưởng) gắn vào, hai đơn phân RTK ghép đôi lại (**dimer hoá**) và tự phosphoryl hoá lẫn nhau trên các gốc tyrosine. Các vị trí phosphotyrosine này là "bến đỗ" cho nhiều protein tiếp sức khác nhau cùng lúc – vì vậy MỘT thụ thể RTK có thể khởi động ĐỒNG THỜI nhiều con đường truyền tin khác nhau, khác với GPCR (thường theo một con đường chính tại một thời điểm).

4.3.3 Ligand-gated ion channels

A **ligand-gated ion channel** is a membrane protein that acts simultaneously as receptor and channel. In the closed (resting) state, the channel blocks the passage of specific ions. When the correct ligand binds, the channel protein changes shape, opening (or in some cases closing) a pore that allows specific ions ($Na+$, $K+$, Ca^{2+}, or $Cl-$) to flow across the membrane down their electrochemical gradients. This ion flow changes the electrical potential across the membrane, forming the molecular basis of fast synaptic signaling in neurons – for example, acetylcholine binding the nicotinic acetylcholine receptor at a neuromuscular junction opens a channel that admits $Na+$, depolarizing the muscle cell membrane and triggering contraction. Because the response is a direct conformational change rather than a multi-step enzymatic cascade, ligand-gated ion channels act on a millisecond timescale – the fastest of the three receptor types.

4.3.4 Comparing GPCR and RTK pathways

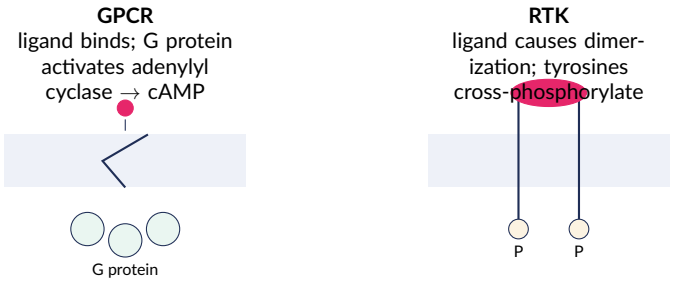
Feature	GPCR pathway	RTK pathway
Structure	Single polypeptide, 7 transmembrane helices	Single-pass polypeptide; functions as a dimer when active
Activation	Ligand binding activates an associated G protein	Ligand binding triggers dimerization and trans-autophosphorylation
Enzymatic activity	None in the receptor itself; effector enzyme (e.g., adenylyl cyclase) is a separate downstream protein	Receptor itself is the enzyme (tyrosine kinase)
Typical second step	Second messenger (cAMP, Ca^{2+}) diffuses signal through cytosol	Phosphotyrosine docking sites recruit multiple relay proteins directly
Pathways triggered	Usually one dominant cascade per receptor type	Often several parallel cascades from one activated receptor
Example ligands	Epinephrine, glucagon, many neurotransmitters, odorants	Insulin, epidermal growth factor, platelet-derived growth factor

Reasoning: GPCR or RTK?

A researcher studies two receptors. Receptor X: a single polypeptide crosses the membrane seven times; blocking its associated G protein completely abolishes the cell's response. Receptor Y: adding the ligand causes two copies of the receptor to associate at the cell surface, and mass spectrometry shows new phosphate groups appear on tyrosine residues of the receptor's cytoplasmic tail within seconds. Identify each receptor type and justify your answer.

Receptor X is a **GPCR**: the seven-transmembrane topology is diagnostic, and the fact that blocking the associated G protein abolishes signaling shows the receptor itself has no catalytic activity – it must relay through a separate G protein.

Receptor Y is an **RTK**: ligand-induced *dimerization* and appearance of *phosphotyrosine* on the receptor's own cytoplasmic tail are the signature of trans-autophosphorylation by the receptor's intrinsic tyrosine kinase activity.



Simplified receptor mechanisms. Left: a GPCR (wavy line) activates an associated G protein (three circles) upon ligand binding. Right: ligand binding dimerizes two RTK monomers, which phosphorylate (P) each other's cytoplasmic tyrosines.

4.3.5 Signal amplification

Because relay molecules in a transduction pathway are frequently enzymes acting catalytically – not simply passing the message on one-to-one – the number of activated molecules can multiply dramatically at each step. A single active enzyme molecule, while active, can convert thousands of substrate molecules; if several such catalytic steps occur in sequence, the multipliers compound.

Ví dụ mẫu · Signal amplification calculation

Consider a hypothetical GPCR cascade. One hormone molecule binds one receptor. The activated receptor activates 10 G-protein/adenylyl-cyclase complexes; each complex synthesizes 100 molecules of cAMP before being switched off. Each cAMP molecule activates one PKA molecule (1:1). Each active PKA molecule phosphorylates and activates 20 molecules of a downstream enzyme. Each of those enzyme molecules catalyzes the release of 50 molecules of the final product before the pathway is deactivated. How many product molecules ultimately result from the single original hormone molecule, and what is the overall amplification factor?

Multiply the amplification factor at each successive step:

$$1 \text{ hormone} \xrightarrow{\times 10} 10 \text{ G-protein/AC complexes} \xrightarrow{\times 100} 1{,}000 \text{ cAMP} \xrightarrow{\times 1} 1{,}000 \text{ PKA}$$

$$\xrightarrow{\times 20} 20{,}000 \text{ active enzyme} \xrightarrow{\times 50} 1{,}000{,}000 \text{ product molecules.}$$

A single hormone molecule ultimately generates 1×10^6 product molecules – an overall amplification of about **one million-fold** ($10 \times 100 \times 1 \times 20 \times 50 = 1{,}000{,}000$). This is why hormone concentrations in blood can be extraordinarily low (nanomolar) and still produce a fast, large, measurable cellular response.

VN **GIẢI THÍCH TIẾNG VIỆT**

Vì mỗi bước trong tầng truyền tin thường là một enzyme hoạt động xúc tác (chứ không phải chuyển tiếp 1 phân tử – 1 phân tử), số lượng phân tử được hoạt hoá tăng theo cấp số nhân qua từng bước. Nhân các hệ số khuếch đại của từng bước lại với nhau sẽ ra tổng hệ số khuếch đại của cả tầng tín hiệu – thường đạt tới hàng trăm nghìn đến hàng triệu lần chỉ từ MỘT phân tử tín hiệu ban đầu. Đây là nguyên lý toán học đằng sau độ nhạy cực cao của hệ thống nội tiết.

4.4 Altered Signal Transduction and Disease

Because signal transduction pathways depend on a precise sequence of protein–protein and protein–ligand interactions, a mutation affecting any single component can change the cellular response – sometimes with serious medical consequences.

- A **receptor mutation** can make a receptor unable to bind its ligand (loss of sensitivity to the signal) or can lock a receptor in its active shape even without the ligand present (constitutive, ligand-independent activation).
- A mutation in a **relay protein** (a kinase, a G protein, or a second-messenger-generating enzyme) can make that step **overactive** (permanently "on," continuously signaling) or **underactive** (unable to relay the signal even when the receptor is correctly activated).
- Because growth-factor pathways (often RTK → relay cascade → transcription factors that switch on cell-division genes) normally require an external growth-factor signal to proceed, mutations that make any step of this pathway constitutively active can cause a cell to behave as though it is permanently being told to divide – even with no growth factor present. This is a central mechanism in many cancers.

Reasoning: an overactive relay protein and cancer

The *RAS* gene encodes a G protein that relays signals from activated RTKs to downstream kinase cascades promoting cell division. Normal Ras protein is active only briefly: it binds GTP

when triggered by an upstream RTK, then quickly hydrolyzes the GTP to GDP and switches itself back off. A point mutation in *RAS*, found in a substantial share of human tumors, produces a Ras protein that binds GTP normally but has lost the ability to hydrolyze it efficiently. Predict the consequence for the cell.

If mutant Ras cannot hydrolyze its bound GTP, it remains permanently in the **active, GTP-bound** state, continuously transmitting a "divide" signal to the downstream kinase cascade regardless of whether a growth factor has bound the upstream RTK. The cell effectively receives a constant, ligand-independent proliferation signal – one of the ways a signal transduction mutation converts a normal proto-oncogene into a cancer-promoting oncogene (discussed further below).

VN **GIẢI THÍCH TIẾNG VIỆT**

Đột biến trong con đường truyền tín hiệu có thể làm một thành phần trở nên **hoạt động quá mức (overactive)** – luôn "bật" dù không có tín hiệu – hoặc **kém hoạt động (underactive)** – không truyền được tín hiệu dù thụ thể đã được kích hoạt đúng cách. Gen *RAS* là ví dụ kinh điển: protein Ras bình thường chỉ "bật" tạm thời (gắn GTP rồi tự thuỷ phân về GDP), nhưng đột biến làm mất khả năng tự tắt khiến Ras luôn ở trạng thái hoạt động, liên tục ra lệnh cho tế bào phân chia dù không có yếu tố tăng trưởng – góp phần hình thành khối u.

4.5 Feedback Mechanisms

Signal transduction pathways rarely act in isolation – they are embedded in larger **feedback loops**, in which the output of a pathway influences the strength of the original stimulus. Biological feedback loops fall into two categories with opposite purposes.

4.5.1 Negative feedback

In **negative feedback**, the response reduces or reverses the original stimulus, driving a physiological variable back toward a stable **set point**. Negative feedback is the primary mechanism of **homeostasis** – the maintenance of a relatively stable internal environment despite changes in the external world.

Ví dụ mẫu · Negative feedback: blood glucose regulation

After a meal, a person's blood glucose rises from a fasting level of about 90 mg/dL to 150 mg/dL. Trace the negative feedback loop that returns blood glucose to the set point, and predict what happens if the pancreatic β cells that secrete insulin are destroyed.

Stimulus: blood glucose rises above the set point (≈ 90 mg/dL).
Sensor/control center: β cells of the pancreas detect the elevated glucose and secrete **insulin** into the blood.
Response: insulin binds receptors (RTKs) on liver, muscle, and fat cells, stimulating glucose uptake from the blood and glycogen synthesis in the liver.
Return to set point: blood glucose falls back toward 90 mg/dL; as glucose falls, insulin secretion decreases – the falling variable itself shuts off the stimulus that triggered the response. (If glucose instead falls too low, pancreatic α cells secrete **glucagon**, which stimulates the liver to break down glycogen and release glucose, raising blood glucose back up – the mirror-image negative feedback loop.)

If β cells are destroyed (as in Type 1 diabetes), insulin can no longer be secreted; the negative feedback loop is broken at the sensor/response step, so blood glucose remains chronically elevated after meals instead of returning to the set point.

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Phản hồi âm (negative feedback) là cơ chế chủ đạo duy trì cân bằng nội môi: khi một biến số (VD đường huyết, thân nhiệt) lệch khỏi điểm chuẩn (set point), cơ thể tạo ra đáp ứng **ngược chiều** với sự lệch đó để kéo biến số trở lại điểm chuẩn. Ví dụ đường huyết: đường huyết tăng → tụy tiết insulin → tế bào hấp thu glucose → đường huyết giảm về bình thường → insulin giảm tiết. Điều hoà thân nhiệt hoạt động tương tự: thân nhiệt tăng → giãn mạch, đổ mồ hôi → mất nhiệt → thân nhiệt giảm về điểm chuẩn.

4.5.2 Positive feedback

In **positive feedback**, the response **reinforces** or amplifies the original stimulus, driving the variable further in the same direction. Positive feedback does not maintain a steady state; instead, it drives a process rapidly and decisively toward completion, after which the loop is broken by the completion of the process itself (not by a return to the starting condition).

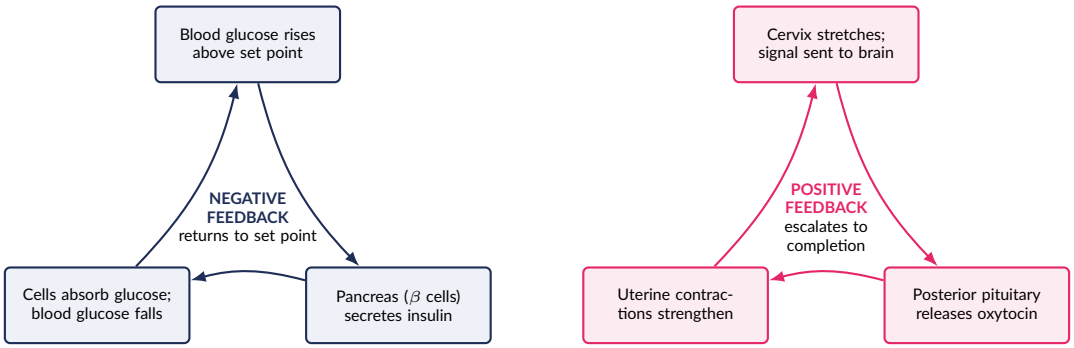
Ví dụ mẫu · Positive feedback: childbirth, contrasted with negative feedback

Describe the positive feedback loop that drives labor contractions during childbirth, and explain why this mechanism – unlike negative feedback – would be inappropriate for maintaining a stable condition such as body temperature.

Stimulus: the baby's head presses against and stretches the cervix.
Response: stretch receptors signal the hypothalamus, which triggers the posterior pituitary to release **oxytocin** into the blood.
Reinforcement: oxytocin stimulates the uterine smooth muscle to contract more strongly, pushing the baby further against the cervix – **increasing**, not decreasing, the original stimulus (cervical stretch).
Escalation and completion: this cycle (stretch → oxytocin → stronger contractions → more stretch) repeats and intensifies until the baby is delivered, at which point cervical stretch stops and the loop is broken – not by returning to the pre-labor state, but by completing the process.

This is the opposite logic of negative feedback: in blood glucose regulation, the response *opposes* the stimulus and the system settles at a set point; in childbirth, the response *reinforces* the stimulus and the system escalates until a distinct endpoint is reached. A positive feedback loop controlling body temperature would be catastrophic: a small rise in temperature would trigger responses that raise it further, with no mechanism to stop the runaway increase.

Other classic examples of positive feedback include the **blood clotting cascade** (activated clotting factors catalyze the activation of additional clotting factors, rapidly amplifying clot formation until the wound is sealed and anticoagulant mechanisms halt the cascade) and the **depolarization phase of an action potential** (initial depolarization opens voltage-gated Na+ channels; Na+ influx depolarizes the membrane further, opening still more Na+ channels, until the channels inactivate near the peak of the spike).

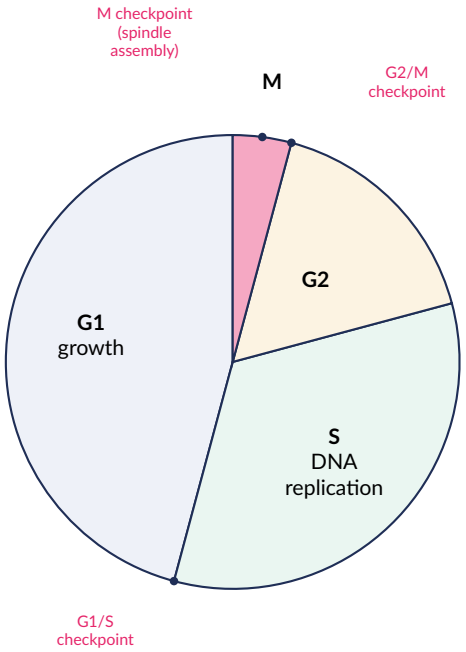


Left: negative feedback (blood glucose regulation) drives a variable back toward a set point, damping the original stimulus. Right: positive feedback (labor contractions) drives a variable further from the starting condition, reinforcing the stimulus until the process is complete.

(!) Lỗi thường gặp: Do not assume "feedback" always means "negative feedback," and do not assume positive feedback is somehow abnormal or harmful. **Negative feedback** maintains stability by *opposing* the direction of change (used for homeostatic variables like blood glucose, body temperature, blood pressure). **Positive feedback** drives a variable *further* in the same direction, on purpose, to rapidly complete a process that needs a decisive endpoint (childbirth, blood clotting, action potentials). When asked to classify a loop, check whether the response opposes the stimulus (negative) or reinforces/amplifies it (positive) – not whether the outcome sounds "good" or "bad."

4.6 The Cell Cycle

Cell division underlies growth, tissue repair, and reproduction in all organisms. The **cell cycle** is the ordered sequence of events, from the birth of a cell to the point it divides into two daughter cells. It has two major phases: a long **interphase** of growth and preparation, and a short **mitotic (M) phase** of nuclear and cytoplasmic division.



The cell cycle as a continuous loop through G1, S, and G2 (interphase) and M (mitosis plus cytokinesis). Dots mark the three major checkpoints: G1/S, G2/M, and the M (spindle assembly) checkpoint.

4.6.1 Interphase: G1, S, and G2

Interphase occupies roughly 90% of a typical dividing cell's cycle and consists of three sub-phases:

- **G1 (Gap 1) phase**: the cell grows in size, synthesizes proteins and organelles, and carries out its normal metabolic roles. Near the end of G1, the cell "decides," at the G1 checkpoint, whether conditions favor continuing through the cycle.
- **S (Synthesis) phase**: the cell replicates its entire genome – each chromosome is copied, producing two identical **sister chromatids** joined at the **centromere**. The centrosome (in animal cells) also duplicates during this phase.

- **G2 (Gap 2) phase**: the cell continues to grow, synthesizes proteins needed for division (e.g., tubulin for the mitotic spindle), and prepares its organelles and cytoskeleton for mitosis.

Some cells exit the cycle altogether into **G0 phase**, a non-dividing, quiescent state. Many highly differentiated cells (mature neurons, cardiac muscle cells) remain in G0 permanently; other cells (e.g., liver cells) can re-enter the cycle from G0 if appropriately stimulated (such as after injury).

(!) Lỗi thường gặp: Interphase is not a "resting" phase. It is the longest part of the cell cycle and the period of greatest metabolic activity – the cell grows, synthesizes proteins, replicates its entire genome (S phase), and manufactures the machinery needed for division (G2). The only genuinely non-dividing, low-activity state is **G0**, which is a distinct exit from the cycle, not a normal part of every interphase.

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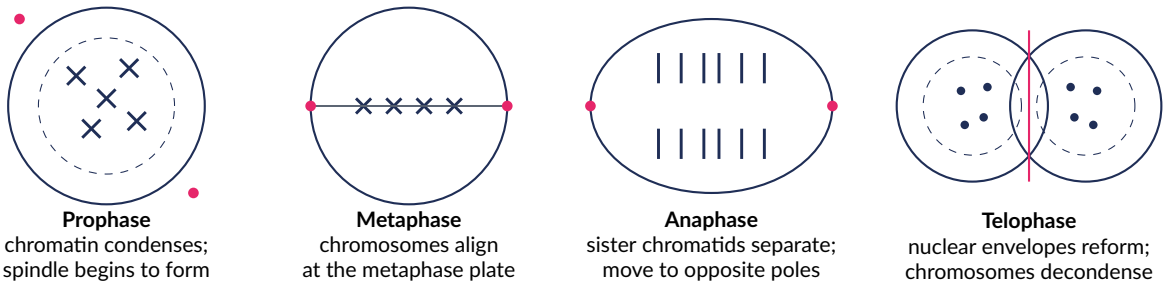
Kỳ trung gian (interphase) KHÔNG phải là giai đoạn "nghỉ ngơi" – đây là giai đoạn tế bào hoạt động trao đổi chất mạnh nhất và chiếm khoảng 90% thời gian chu kỳ tế bào, gồm ba pha: **G1** (tăng trưởng, tổng hợp protein), **S** (nhân đôi ADN, tạo ra hai nhiễm sắc tử chị em dính nhau tại tâm động), và **G2** (tiếp tục tăng trưởng, chuẩn bị bộ máy phân chia). Một số tế bào biệt hoá cao (VD nơ-ron, tế bào cơ tim) rời khỏi chu kỳ vĩnh viễn vào pha **G0** – đây mới thực sự là trạng thái không phân chia.

4.6.2 Mitosis

Mitosis is nuclear division: one nucleus containing duplicated chromosomes divides into two genetically identical daughter nuclei. Mitosis is conventionally divided into five stages, distinguished by the behavior of the chromosomes and the mitotic spindle.

- **Prophase**: chromatin condenses into discrete, visible chromosomes, each consisting of two sister chromatids joined at the centromere. Outside the nucleus, the mitotic spindle begins to form as centrosomes move toward opposite poles of the cell. The nucleolus disappears.
- **Prometaphase**: the nuclear envelope fragments, allowing spindle microtubules to enter the nuclear region. Microtubules attach to **kinetochores**, protein structures assembled at each chromosome's centromere, and begin moving the chromosomes.
- **Metaphase**: all chromosomes align at the **metaphase plate**, an imaginary plane equidistant from the two spindle poles. Each sister chromatid's kinetochore is attached to spindle fibers from opposite poles, so every chromosome is under tension from both directions – a state the spindle assembly checkpoint verifies before allowing the cell to proceed.
- **Anaphase**: the proteins holding the two sister chromatids together at the centromere are cleaved; the sister chromatids separate and become independent chromosomes, pulled toward opposite poles as the kinetochore microtubules shorten. Simultaneously, the cell itself elongates as nonkinetochore microtubules push the two poles further apart.
- **Telophase**: two full sets of chromosomes arrive at opposite poles. Nuclear envelopes re-form around each set, the chromosomes decondense back into loosely packed chromatin, the spindle disassembles, and nucleoli reappear – producing two genetically identical daughter nuclei.



Schematic chromosome behavior through the four principal stages of mitosis. Sister chromatids (joined X shapes) align at the metaphase plate, separate at anaphase, and each daughter cell receives a full chromosome set by telophase.

VN **GIẢI THÍCH TIẾNG VIỆT**

Trình tự nguyên phân (mitosis) và hành vi nhiễm sắc thể: **kỳ đầu (prophase)** – nhiễm sắc chất co xoắn thành nhiễm sắc thể (2 nhiễm sắc tử chị em dính nhau), thoi phân bào bắt đầu hình thành; **kỳ đầu muộn/trước giữa (prometaphase)** – màng nhân biến mất, thoi phân bào gắn vào tâm động; **kỳ giữa (metaphase)** – nhiễm sắc thể xếp thành hàng ở mặt phẳng xích đạo; **kỳ sau (anaphase)** – nhiễm sắc tử chị em tách rời, di chuyển về hai cực; **kỳ cuối (telophase)** – màng nhân tái lập quanh mỗi bộ nhiễm sắc thể, nhiễm sắc thể duỗi xoắn trở lại thành nhiễm sắc chất.

4.6.3 Cytokinesis

Cytokinesis, division of the cytoplasm into two separate daughter cells, typically begins during telophase and completes shortly after mitosis ends. The mechanism differs between animal and plant cells because plant cells are enclosed by a rigid cell wall:

- **Animal cells**: a contractile ring of actin microfilaments assembles just beneath the plasma membrane at the former metaphase plate and progressively contracts, pulling the membrane inward to form a **cleavage furrow** that pinches the cell in two.
- **Plant cells**: because the rigid cell wall prevents the membrane from being pinched inward, Golgi-derived vesicles carrying cell-wall material migrate to the center of the cell and fuse, building outward from the middle to form a **cell plate**, which grows until it fuses with the existing lateral cell wall, creating two separate daughter cells each with its own new wall.

Ví dụ mẫu · Cell-cycle timing and mitotic index

A population of cultured mammalian cells has a total cell cycle length of 24 hours, divided as follows: G1 $= 11$ h, S $= 8$ h, G2 $= 4$ h, M $= 1$ h. (a) What percentage of the cycle is spent in each phase? (b) If the population is asynchronous and at steady state, what mitotic index (fraction of cells seen undergoing mitosis at a random instant) would you expect? (c) In a microscope field of 300 cells, how many would you expect to see in mitosis?

(a) Percentage of time in each phase $= \dfrac{\text{phase duration}}{24\text{ h}} \times 100\%$:

$$\text{G1} = \frac{11}{24} = 45.8\%, \quad \text{S} = \frac{8}{24} = 33.3\%, \quad \text{G2} = \frac{4}{24} = 16.7\%, \quad \text{M} = \frac{1}{24} = 4.2\%.$$

(b) In an asynchronous, steady-state population, the fraction of cells observed in any phase at a random moment equals the fraction of the total cycle time spent in that phase. So the expected **mitotic index** $\approx 4.2\%$ (roughly 1 in every 24 cells).

(c) Expected number in mitosis $= 300 \times 0.042 \approx 12.5$, so about 12–13 cells of the 300 should be seen undergoing mitosis at any instant.

VN GIẢI THÍCH TIẾNG VIỆT

Chỉ số phân bào (mitotic index) là tỉ lệ số tế bào đang trong quá trình nguyên phân so với tổng số tế bào quan sát được tại một thời điểm. Với một quần thể tế bào không đồng bộ (asynchronous) ở trạng thái ổn định, chỉ số phân bào xấp xỉ bằng tỉ lệ thời gian pha M chiếm trong tổng thời gian chu kỳ tế bào – vì xác suất "bắt gặp" một tế bào ở pha nào tỉ lệ thuận với thời lượng của pha đó. Đây là nguyên lý dùng để ước lượng tốc độ phân chia của mô (VD mô khối u thường có chỉ số phân bào cao hơn hẳn mô bình thường).

4.7 Regulation of the Cell Cycle

Progression through the cell cycle is not automatic – it is tightly controlled by an internal **cell cycle control system** that responds to internal signals (Is DNA damaged? Is replication complete? Are chromosomes correctly attached to the spindle?) and external signals (Are nutrients and growth factors available?).

4.7.1 Checkpoints

A **checkpoint** is a control point in the cell cycle where stop and go-ahead signals regulate progression. Three checkpoints are central to AP Biology:

- **G1 checkpoint** (the "restriction point" in mammalian cells): the primary decision point. The cell checks its size, nutrient availability, and whether growth-factor signals are present. If conditions are unfavorable, the cell may exit into G0 instead of continuing toward S phase.
- **G2/M checkpoint**: verifies that DNA replication is complete and that any DNA damage has been repaired before the cell commits to mitosis. This prevents a cell from attempting to segregate incompletely replicated or damaged chromosomes.
- **M checkpoint (spindle assembly checkpoint)**: operates during metaphase, verifying that every chromosome's kinetochore is correctly attached to spindle microtubules from both poles. Anaphase does not begin until all chromosomes are properly attached under tension, preventing chromosomes from being distributed unevenly to the daughter cells (aneuploidy).

(!) **Lỗi thường gặp:** Each checkpoint verifies a *different* thing, and mixing them up is a common error. **G1 checkpoint**: are conditions (size, nutrients, growth factors) favorable to start the cycle at all? **G2/M checkpoint**: is DNA replication complete and undamaged, ready for mitosis? **M (spindle assembly) checkpoint**: are all chromosomes correctly attached to spindle fibers from both poles, ready for anaphase? Do not describe the G2/M checkpoint as checking spindle attachment, or the M checkpoint as checking DNA replication – each gate inspects a different stage-specific condition.

VN GIẢI THÍCH TIẾNG VIỆT

Ba điểm kiểm soát (checkpoint) chính của chu kỳ tế bào: **điểm kiểm soát G1** – quyết định tế bào có đủ điều kiện (kích thước, dinh dưỡng, tín hiệu tăng trưởng) để bước vào chu kỳ hay không (nếu không đạt sẽ rút vào G0); **điểm kiểm soát G2/M** – kiểm tra ADN đã nhân đôi đầy đủ và không bị hư hại trước khi bước vào nguyên phân; **điểm kiểm soát thoi phân bào (M/spindle assembly checkpoint)** – kiểm tra mọi nhiễm sắc thể đã gắn đúng vào thoi phân bào từ cả hai cực trước khi cho phép kỳ sau (anaphase) bắt đầu, tránh phân chia nhiễm sắc thể không đều.

4.7.2 Cyclins and cyclin-dependent kinases (CDKs)

The molecular "engine" driving the cell cycle forward through its checkpoints is a family of protein kinases called **cyclin-dependent kinases (CDKs)**. A CDK by itself is catalytically inactive; it becomes active only when bound to a regulatory partner protein called a **cyclin**. The resulting **cyclin–CDK**

complex phosphorylates specific target proteins that trigger the events of that stage of the cycle (e.g., nuclear envelope breakdown, chromosome condensation).

The key to the system's timing is that **cyclin concentration rises and falls** cyclically across the cell cycle (synthesized steadily, then abruptly degraded via the ubiquitin–proteasome pathway at a specific point), while total CDK concentration stays roughly constant throughout. Because an active complex requires both a CDK and its matching cyclin, the cell cycle advances only when the right cyclin accumulates to a sufficient level. The complex that triggers entry into mitosis – cyclin B bound to CDK1 – was historically discovered and named **MPF** (maturation-promoting factor, also called M-phase-promoting factor); MPF activity rises sharply just before the G2/M transition and then collapses as cyclin B is degraded during mitosis.

Reasoning: cyclin oscillation and a non-degradable cyclin

Explain why cyclin concentration must fall again after triggering mitosis, and predict what would happen to a cell if its cyclin B protein were experimentally mutated so that it could never be degraded by the ubiquitin–proteasome pathway.

The cyclin–CDK complex is a molecular switch: it must turn *off* as well as on. If cyclin B were never degraded, CDK1 would remain permanently active. Because active cyclin B–CDK1 (MPF) drives cells *into* mitosis but its degradation is required for cells to exit mitosis (nuclear envelope reassembly, chromosome decondensation, cytokinesis completion), a cell with non-degradable cyclin B would be predicted to **arrest in a mitotic state** – unable to complete telophase and cytokinesis and re-enter a normal G1, because the "go" signal for exiting mitosis never turns off.

VN **GIẢI THÍCH TIẾNG VIỆT**

Chu kỳ tế bào được vận hành bởi các phức hợp **cyclin–CDK**: CDK (kinase phụ thuộc cyclin) chỉ có hoạt tính khi gắn với cyclin tương ứng. Nồng độ cyclin dao động lên xuống theo chu kỳ (tổng hợp liên tục rồi bị phân giải đột ngột), trong khi nồng độ CDK gần như không đổi – chính sự dao động của cyclin quyết định "thời điểm" chu kỳ tiến triển. Phức hợp cyclin B–CDK1 (còn gọi là MPF – yếu tố thúc đẩy pha M) là "công tắc" đưa tế bào vào nguyên phân; khi cyclin B bị phân giải, tế bào mới có thể thoát khỏi nguyên phân.

4.7.3 Growth factors

Growth factors are proteins secreted by certain cells that stimulate other cells to divide. Most growth factors bind RTKs on the target cell's surface, triggering signal transduction pathways that ultimately promote the cell's advancement through the G1 checkpoint – for example, by stimulating synthesis of the cyclins needed to activate CDKs. Cells growing in a laboratory dish normally exhibit **density-dependent inhibition** (they stop dividing once they contact neighboring cells on all sides, forming a single layer) and **anchorage dependence** (they must be attached to a surface to divide). Cancer cells characteristically lose both constraints, dividing even without added growth factors, without surface attachment, and without regard for crowding by neighboring cells.

4.7.4 p53 and the DNA-damage response

p53 is a transcription factor and tumor suppressor protein sometimes called "the guardian of the genome." DNA damage (from radiation, chemical mutagens, or replication errors) activates p53, which halts the cell cycle – primarily by inducing production of a CDK inhibitor protein (p21) that blocks cyclin–CDK activity – giving the cell time to repair the damage before proceeding through the G1/S or G2/M checkpoint. If the damage is too severe to repair, p53 can instead trigger **apoptosis** (programmed cell death), eliminating the damaged cell entirely rather than allowing it to divide. Loss-of-function mutations in the *TP53* gene are found in roughly half of all human cancers, reflecting how central this single checkpoint gatekeeper is to preventing damaged cells from proliferating.

Ví dụ mẫu · Checkpoint failure: loss of p53 function

A cell sustains DNA damage from UV radiation. In a normal cell, explain how p53 responds. Then explain what happens if both copies of the *TP53* gene in this cell carry loss-of-function mutations.

Normal cell: DNA damage activates p53, which halts the cell cycle at the G1 (or G2/M) checkpoint (via induction of p21, which inhibits cyclin–CDK activity) so that DNA-repair enzymes can fix the damage before replication or division proceeds. If the damage is irreparable, p53 instead triggers apoptosis, removing the damaged cell.

Cell with both *TP53* alleles nonfunctional: the checkpoint gate is effectively disabled. The cell cycle is not halted despite the DNA damage, and the damaged DNA is replicated and passed on to daughter cells rather than being repaired or the cell being eliminated. Because these daughter cells also lack functional p53, they can continue accumulating further mutations – including mutations that activate proto-oncogenes or disable other tumor suppressor genes – across successive divisions with no checkpoint able to intervene. This progressive, unchecked accumulation of mutations is a key step toward cancer.

VN **GIẢI THÍCH TIẾNG VIỆT**

p53 là protein ức chế khối u, được ví như "người bảo vệ bộ gen" – khi ADN bị tổn thương, p53 tạm dừng chu kỳ tế bào (qua việc cảm ứng p21, chất ức chế phức hợp cyclin–CDK) để tế bào có thời gian sửa chữa, hoặc kích hoạt quá trình **apoptosis** (chết tế bào theo chương trình) nếu tổn thương quá nặng. Khi cả hai alen *TP53* đều mất chức năng, "trạm gác" này bị vô hiệu hoá: ADN hư hại không được sửa chữa mà vẫn được nhân đôi và truyền cho tế bào con, khiến đột biến tích luỹ dần qua nhiều thế hệ tế bào – một bước quan trọng dẫn đến ung thư. Đột biến mất chức năng *TP53* có mặt trong khoảng một nửa số ca ung thư ở người.

4.8 Cancer: Loss of Cell-Cycle Control

Cancer arises when cells accumulate mutations that disable the normal controls on cell division, allowing uncontrolled proliferation. Two broad classes of genes are involved.

4.8.1 Proto-oncogenes and oncogenes

Proto-oncogenes are normal genes whose products promote cell division under appropriate conditions – for example, genes encoding growth factors, growth-factor receptors (such as RTKs), intracellular relay proteins (such as Ras), and transcription factors that switch on cell-division genes (such as Myc). A **gain-of-function** mutation (or gene amplification, or chromosomal rearrangement that places the gene under an overactive promoter) can convert a proto-oncogene into an **oncogene**, whose product is overactive or produced in excess, driving cell division even without an appropriate external signal. Because only one mutated copy is generally sufficient to produce an overactive product, oncogene mutations typically behave as **dominant** at the cellular level.

4.8.2 Tumor suppressor genes

Tumor suppressor genes are normal genes whose products restrain cell division or promote apoptosis – for example, *TP53* (p53) and *RB* (the retinoblastoma protein, which normally holds the cell cycle at the G1 checkpoint until released by appropriate signals). A **loss-of-function** mutation removes this braking function. Because a cell generally has two copies (alleles) of each tumor suppressor gene and one functional copy is often sufficient to maintain control, tumor suppressor loss typically requires both copies to be inactivated (the "two-hit hypothesis") – behaving as **recessive** at the cellular level, in contrast to the dominant behavior of oncogenes.

(!) Lỗi thường gặp: Proto-oncogenes and tumor suppressor genes fail toward cancer by *opposite* molecular logic – do not describe both the same way. An oncogene arises from a **gain-of-function** mutation (the gene product becomes overactive; typically **dominant**, one mutated allele is enough). A disabled tumor suppressor arises from a **loss-of-function** mutation (the gene product's normal braking or repair function is lost; typically **recessive**, both alleles usually need to be inactivated). Both routes remove a control on cell division, but by inverse mechanisms.

VN **GIẢI THÍCH TIẾNG VIỆT**

Hai nhóm gen liên quan đến ung thư có cơ chế NGƯỢC NHAU: **tiền gen ung thư (proto-oncogene)** là gen bình thường thúc đẩy phân chia tế bào; đột biến **được chức năng (gain-of-function)** biến nó thành **gen ung thư (oncogene)** hoạt động quá mức – chỉ cần 1 alen đột biến là đủ gây hại (trội). **Gen ức chế khối u (tumor suppressor gene)** là gen bình thường kìm hãm phân chia hoặc thúc đẩy chết tế bào theo chương trình; đột biến **mất chức năng (loss-of-function)** làm mất "phanh hãm" này – thường cần MẤT CẢ HAI alen mới gây hại (lặn, theo "giả thuyết hai cú đánh" – two-hit hypothesis).

4.8.3 Unchecked proliferation, angiogenesis, and metastasis

Accumulating oncogene activations together with tumor suppressor losses in a single cell lineage progressively erodes cell-cycle control, producing a clone of cells that proliferates without regard to normal growth signals, density-dependent inhibition, or anchorage dependence, forming a mass called a **tumor**. A **benign tumor** remains confined to its original location and does not invade surrounding tissue; a **malignant tumor** (cancer) invades neighboring tissue and can spread.

Sustained tumor growth requires two further capabilities beyond simple uncontrolled division:

- **Angiogenesis**: tumor cells secrete signaling molecules (such as vascular endothelial growth factor, VEGF) that stimulate the growth of new blood vessels into the tumor, supplying the oxygen and nutrients needed to support continued growth beyond the small size that can be sustained by diffusion alone.
- **Metastasis**: malignant cells often lose normal cell-adhesion mechanisms (such as reduced expression of the adhesion protein E-cadherin), allowing them to detach from the primary tumor, invade through surrounding tissue and into blood or lymphatic vessels, and travel to distant sites in the body, where they can establish new secondary tumors.

Biologists commonly summarize this set of acquired traits – proliferative signaling independent of normal growth-factor control, evasion of growth-suppressing checkpoints, resistance to apoptosis, sustained angiogenesis, and invasion/metastasis – as the shared hallmarks that distinguish cancer cells from their normal counterparts.

Reasoning: interpreting mitotic index in tumor tissue

A pathologist compares two tissue samples under the microscope. In normal tissue, 2% of cells are seen undergoing mitosis at any instant. In a biopsy of tumor tissue from the same organ, 18% of cells are seen undergoing mitosis. Explain what this difference suggests about cell-cycle control in the tumor tissue, and connect it to checkpoint function.

Because mitotic index approximates the fraction of total cycle time spent in M phase, a mitotic index nine times higher in the tumor tissue (18% vs. 2%) indicates that a much larger fraction of tumor cells are actively dividing at any given moment – consistent with a shorter effective cell cycle and/or a much larger fraction of cells that have not exited into G0. This pattern is consistent with **loss of checkpoint control**: normal restraints such as the G1 checkpoint's dependence on growth factors, density-dependent inhibition, and p53-mediated arrest in re-

sponse to DNA damage are compromised in the tumor cells, so a much greater proportion of the cell population proceeds continuously through the cycle rather than pausing in G1 or exiting to G0.

VN **GIẢI THÍCH TIẾNG VIỆT**

Ung thư là hậu quả tích luỹ của việc MẤT KIỂM SOÁT chu kỳ tế bào: gen ung thư hoạt động quá mức + gen ức chế khối u mất chức năng → tế bào phân chia không kiểm soát → hình thành khối u. Khối u ác tính cần thêm hai khả năng để phát triển và lan rộng: **tạo mạch máu mới (angiogenesis)** – tiết tín hiệu (VD VEGF) kích thích mạch máu mới mọc vào khối u để cung cấp oxy/dinh dưỡng; và **di căn (metastasis)** – tế bào ung thư mất khả năng bám dính, tách khỏi khối u gốc, xâm nhập mạch máu/bạch huyết và di chuyển đến hình thành khối u thứ phát ở cơ quan khác.

4.9 Practice Problems

Bài tập luyện tập

A cytokine secreted by an immune cell diffuses through the extracellular fluid and alters the behavior of several nearby cells in the same tissue, but has no effect on cells elsewhere in the body. This is best classified as:

(A) Endocrine signaling
(B) Paracrine signaling
(C) Synaptic signaling
(D) Direct contact signaling

Lời giải chi tiết

The signal (a local regulator) diffuses only a short distance through the extracellular fluid and affects nearby cells, with no involvement of the bloodstream, a synapse, or direct contact – the definition of paracrine signaling. **(B)**.

Bài tập luyện tập

Which structure allows ions and small signaling molecules to pass directly from the cytoplasm of one plant cell into the cytoplasm of an adjacent plant cell?

(A) Gap junction
(B) Plasmodesma
(C) Tight junction
(D) Desmosome

Lời giải chi tiết

Plasmodesmata are channels through the cell walls of adjacent plant cells that directly connect their cytoplasms. Gap junctions are the animal-cell equivalent; tight junctions and desmosomes are animal cell-cell attachment structures that do not create cytoplasmic continuity. **(B)**.

Bài tập luyện tập

Cortisol, a steroid hormone, is hydrophobic and lipid-soluble. Its receptor is most likely located:

(A) Embedded in the plasma membrane, with an extracellular ligand-binding domain

(B) Embedded in the plasma membrane, with an intracellular ligand-binding domain

(C) Free in the cytoplasm or nucleus

(D) Secreted into the extracellular fluid

Lời giải chi tiết

Because cortisol is small and hydrophobic, it diffuses directly across the phospholipid bilayer rather than requiring a membrane receptor. Its receptor is therefore intracellular (cytoplasmic, later moving to the nucleus), where the hormone–receptor complex can act as a transcription factor. **(C)**.

Bài tập luyện tập

Which structural feature is diagnostic of a G-protein-coupled receptor (GPCR)?

(A) A single membrane-spanning tyrosine kinase domain

(B) Seven transmembrane α-helices

(C) A ligand-gated pore permeable to ions

(D) An intracellular-only structure with no membrane component

Lời giải chi tiết

GPCRs are defined by a polypeptide that crosses the plasma membrane seven times as α-helices, with an associated G protein on the cytoplasmic side. Option (A) describes an RTK, and (C) describes a ligand-gated ion channel. **(B)**.

Bài tập luyện tập

Adenylyl cyclase, activated by a G protein, converts ATP into:

(A) cAMP

(B) IP_3

(C) Diacylglycerol (DAG)

(D) GTP

Lời giải chi tiết

Adenylyl cyclase catalyzes the conversion of ATP into cyclic AMP (cAMP), the second messenger of the classic GPCR/cAMP pathway. IP_3 and DAG instead arise from phospholipase C cleaving PIP_2 in the alternative GPCR pathway. **(A)**.

Bài tập luyện tập

List, in order, the molecular events that occur after a ligand binds a GPCR that is coupled to phospholipase C, up to the point where cytosolic Ca^{2+} concentration rises.

Lời giải chi tiết

(1) The ligand binds the GPCR, changing its shape. (2) The activated GPCR causes its associated G protein to exchange GDP for GTP, activating the G protein. (3) The active G protein activates the effector enzyme **phospholipase C**. (4) Phospholipase C cleaves the membrane phospholipid PIP_2 into two second messengers: IP_3 and diacylglycerol (DAG). (5) IP_3 diffuses through the cytosol and binds IP_3-gated channels on the endoplasmic reticulum membrane.

(6) These channels open, releasing stored Ca^{2+} from the ER into the cytosol, raising cytosolic Ca^{2+} concentration, which itself then acts as a further second messenger.

Bài tập luyện tập

Binding of a growth factor to a receptor tyrosine kinase (RTK) most directly causes:

(A) Opening of an ion channel

(B) Hydrolysis of GTP bound to an associated G protein

(C) Dimerization of two receptor monomers and trans-autophosphorylation of tyrosine residues

(D) Direct binding of the receptor to DNA

Lời giải chi tiết

Ligand binding causes two RTK monomers to dimerize; each monomer's intracellular kinase domain then phosphorylates tyrosine residues on the other monomer's cytoplasmic tail (trans-autophosphorylation), creating docking sites for relay proteins. **(C)**.

Bài tập luyện tập

The nicotinic acetylcholine receptor at a neuromuscular junction is an example of a:

(A) GPCR

(B) Receptor tyrosine kinase

(C) Ligand-gated ion channel

(D) Intracellular steroid receptor

Lời giải chi tiết

Acetylcholine binding this receptor directly opens a pore permeable to Na+, without any second-messenger cascade – the hallmark of a ligand-gated ion channel, which is why synaptic responses of this kind are the fastest of the receptor mechanisms (milliseconds). **(C)**.

Bài tập luyện tập

Consider a signal transduction cascade activated by a single hormone molecule. The activated receptor activates 5 G-protein/adenylyl-cyclase complexes; each complex synthesizes 200 molecules of cAMP; each cAMP activates one PKA molecule (1:1); each active PKA phosphorylates and activates 8 molecules of a downstream target enzyme; each of those enzyme molecules catalyzes the formation of 25 molecules of the final product. (a) How many product molecules ultimately result from the one hormone molecule? (b) Express the overall amplification as a power of ten.

Lời giải chi tiết

Multiply the amplification factor at each step:

$$1 \xrightarrow{\times 5} 5 \text{ complexes} \xrightarrow{\times 200} 1{,}000 \text{ cAMP} \xrightarrow{\times 1} 1{,}000 \text{ PKA} \xrightarrow{\times 8} 8{,}000 \text{ enzyme} \xrightarrow{\times 25} 200{,}000 \text{ product}.$$

(a) $200{,}000$ product molecules. **(b)** $200{,}000 = 2 \times 10^5$, so the amplification is on the order of 10^5 (roughly a $200{,}000$-fold amplification from a single hormone molecule).

Bài tập luyện tập

In a hypothetical three-step amplifying signal cascade, one signal molecule ultimately produces $64{,}000$ molecules of final product. The first two steps each amplify the signal by a factor of 20. What is the amplification factor of the third step?

Lời giải chi tiết

The total amplification is the product of the three step-factors: $20 \times 20 \times x = 64{,}000$, where x is the unknown third-step factor. $20 \times 20 = 400$, so $x = \dfrac{64{,}000}{400} = 160$. The third step amplifies the signal 160-fold.

Bài tập luyện tập

A point mutation locks the Ras protein in its GTP-bound (active) form because it can no longer hydrolyze GTP efficiently. The most likely consequence for the cell is:

(A) The cell can no longer receive growth-factor signals at all

(B) The downstream kinase cascade is continuously active, promoting cell division even without a growth-factor signal

(C) The cell permanently arrests in G0

(D) DNA replication becomes impossible

Lời giải chi tiết

Normal Ras is active only transiently (GTP-bound), then inactivates itself by hydrolyzing GTP to GDP. A mutant Ras that cannot hydrolyze GTP remains permanently active, continuously signaling the downstream cascade to promote division regardless of whether a growth factor has activated the upstream receptor. **(B)**.

Bài tập luyện tập

A patient has a mutation in the insulin receptor gene that prevents the receptor's extracellular domain from binding insulin at all, though the receptor is otherwise structurally normal. Explain the expected effect on this patient's blood glucose regulation after a meal, and name the general category of disorder this resembles.

Lời giải chi tiết

The insulin receptor is an RTK; if it cannot bind insulin, then even though the pancreas secretes insulin normally in response to rising blood glucose, target cells (liver, muscle, fat) cannot detect it and therefore cannot increase glucose uptake or glycogen synthesis. Blood glucose would remain abnormally elevated after meals despite normal or even elevated circulating insulin levels, because the negative feedback loop is broken at the receptor step, not the hormone-secretion step. This resembles **insulin resistance** (the pattern seen in Type 2 diabetes), as distinct from Type 1 diabetes, where insulin itself is not produced.

Bài tập luyện tập

Which of the following is the best example of a negative feedback loop?

(A) Rising oxytocin during labor further intensifying uterine contractions

(B) A drop in body temperature triggering shivering, which generates heat and raises body temperature back toward the set point

(C) The rising phase of an action potential, where depolarization opens more Na+ channels, causing further depolarization

(D) Amplifying activation of clotting factors during a clotting cascade

Lời giải chi tiết

In (B), the response (heat generation) opposes and reverses the original stimulus (falling temperature), returning the variable to its set point – the defining pattern of negative feedback. The other three options all describe responses that reinforce and amplify the original stimulus (positive feedback). **(B)**.

Bài tập luyện tập

Before a meal, a patient's blood glucose is 85 mg/dL. After a large meal it rises to 165 mg/dL. (a) Describe the negative feedback loop, including the roles of the pancreas, insulin, and target tissues, that returns glucose toward 85 mg/dL. (b) A different patient's pancreatic β cells are completely destroyed by autoimmune attack. Predict this patient's post-meal blood glucose pattern.

Lời giải chi tiết

(a) Rising blood glucose ($85 \rightarrow 165$ mg/dL) is detected by pancreatic β cells, which secrete insulin into the blood. Insulin binds RTK insulin receptors on liver, muscle, and fat cells, stimulating glucose uptake from the blood and glycogen synthesis in the liver. As blood glucose falls back toward 85 mg/dL, less insulin is secreted – the falling variable shuts off the stimulus that triggered the response, completing the negative feedback loop.

(b) Without functional β cells, no insulin can be secreted regardless of how high blood glucose rises. The negative feedback loop is broken at the response step: blood glucose after a meal would rise sharply and remain chronically elevated instead of returning to 85 mg/dL (the pattern seen in Type 1 diabetes).

Bài tập luyện tập

Which scenario best illustrates positive, rather than negative, feedback?

(A) Falling blood glucose stimulating glucagon release, which raises blood glucose back toward the set point

(B) Rising blood pressure triggering vasodilation that lowers blood pressure back toward normal

(C) Cervical stretching during labor stimulating oxytocin release, which increases contraction strength and further cervical stretching

(D) Elevated blood CO2 triggering faster breathing that lowers blood CO2 back toward normal

Lời giải chi tiết

In (C), the response (stronger contractions, more cervical stretch) reinforces and increases the original stimulus rather than reversing it, escalating the process toward a definite endpoint

(birth) – the defining pattern of positive feedback. The other three options all describe the variable being returned toward a set point (negative feedback). **(C)**.

Bài tập luyện tập

Describe how the blood clotting cascade functions as a positive feedback loop, and explain what ultimately stops the cascade from clotting the entire circulatory system rather than just the wound site.

Lời giải chi tiết

When a blood vessel is damaged, exposed tissue factors trigger activation of a small number of clotting factor molecules. Each activated clotting factor is itself an enzyme that activates many additional downstream clotting factor molecules, which in turn activate still more – each step reinforcing and amplifying clot formation, driving the process rapidly toward completion (a stable fibrin clot) rather than toward a steady state. This is stopped from spreading uncontrolled through the whole circulatory system because: the reaction is confined near the site of vessel damage (activated factors are diluted and swept away by normal blood flow once they move away from the local injury site); circulating anticoagulant proteins (e.g., antithrombin) inactivate stray activated clotting factors; and once the wound is physically sealed, no further tissue factor is exposed to sustain the cascade.

Bài tập luyện tập

During which phase of the cell cycle does DNA replication occur?

(A) G1
(B) S
(C) G2
(D) M

Lời giải chi tiết

The S (synthesis) phase of interphase is when the entire genome is replicated, producing sister chromatids joined at the centromere. G1 and G2 are growth/preparation phases; M is mitosis (nuclear division, after replication is complete). **(B)**.

Bài tập luyện tập

A population of cultured cells has a total cell cycle length of 20 hours, divided as: G1 $= 8$ h, S $= 7$ h, G2 $= 4$ h, M $= 1$ h. (a) Calculate the percentage of the cycle spent in each phase. (b) In a microscope field containing 400 asynchronously growing cells at steady state, how many would you expect to observe undergoing mitosis at any instant?

Lời giải chi tiết

(a) Percentage $= \dfrac{\text{phase duration}}{20\text{ h}} \times 100\%$:

$$\text{G1} = \frac{8}{20} = 40\%, \quad \text{S} = \frac{7}{20} = 35\%, \quad \text{G2} = \frac{4}{20} = 20\%, \quad \text{M} = \frac{1}{20} = 5\%.$$

(b) In an asynchronous, steady-state population, the fraction of cells seen in a given phase equals the fraction of total cycle time spent in that phase, so the expected number in mitosis is $400 \times 0.05 = 20$ cells.

Bài tập luyện tập

A student examines an onion root tip under a microscope and counts 600 cells total in the field of view. Of these, 522 are in interphase, 45 are in prophase, 18 are in metaphase, 10 are in anaphase, and 5 are in telophase. (a) Calculate the mitotic index for this sample. (b) If the total cell cycle length for these root-tip cells is 22 hours, estimate the duration of M phase.

Lời giải chi tiết

(a) Cells in mitosis $= 45 + 18 + 10 + 5 = 78$. Mitotic index $= \dfrac{78}{600} = 0.13 = 13\%$.

(b) Assuming the mitotic index approximates the fraction of total cycle time spent in M phase: duration of M $\approx 0.13 \times 22$ h $= 2.86$ h ≈ 2 hours 52 minutes.

Bài tập luyện tập

A cell is observed with all of its chromosomes aligned along a single plane equidistant from the two spindle poles, each chromosome attached to spindle fibers from both poles. This cell is in:

(A) Prophase
(B) Metaphase
(C) Anaphase
(D) Telophase

Lời giải chi tiết

Alignment of all chromosomes at the metaphase plate, with kinetochores attached to spindle fibers from both poles, is the defining feature of metaphase – verified by the spindle assembly checkpoint before anaphase can begin. **(B)**.

Bài tập luyện tập

Cytokinesis in a plant cell is accomplished by the formation of a:

(A) Cleavage furrow
(B) Cell plate
(C) Contractile ring of myosin only
(D) Spindle assembly checkpoint

Lời giải chi tiết

Because the rigid cell wall prevents an animal-style pinching furrow, Golgi-derived vesicles carrying cell-wall material fuse at the cell's midline, growing outward to form a cell plate that becomes the new wall separating the two daughter cells. **(B)**.

Bài tập luyện tập

In two or three sentences each, describe what happens to the chromosomes during prophase, anaphase, and telophase of mitosis.

Lời giải chi tiết

Prophase: chromatin condenses into visible chromosomes, each made of two sister chromatids joined at the centromere; the mitotic spindle begins forming outside the (still intact, then fragmenting) nucleus.

Anaphase: the proteins joining sister chromatids at the centromere are cleaved; each pair of sister chromatids separates into two independent chromosomes, which are pulled toward opposite spindle poles as kinetochore microtubules shorten.

Telophase: the two separated chromosome sets arrive at opposite poles, decondense back into loosely packed chromatin, and a nuclear envelope re-forms around each set, producing two genetically identical daughter nuclei.

Bài tập luyện tập

The spindle assembly checkpoint specifically verifies that:

(A) DNA has been completely and accurately replicated

(B) The cell has grown to a sufficient size

(C) Every chromosome's kinetochore is properly attached to spindle fibers from both poles

(D) Growth factors are present in the extracellular environment

Lời giải chi tiết

The spindle assembly (M) checkpoint operates during metaphase and blocks the onset of anaphase until every chromosome is correctly attached to spindle microtubules from both poles under tension, preventing unequal chromosome distribution to daughter cells. **(C)**.

Bài tập luyện tập

A cyclin-dependent kinase (CDK) is best described as:

(A) An enzyme that is constitutively active regardless of cyclin levels

(B) A protein kinase that becomes catalytically active only when bound to its regulatory cyclin partner

(C) A second messenger that diffuses through the cytosol

(D) A structural protein that forms the mitotic spindle

Lời giải chi tiết

A CDK alone is catalytically inactive; only when bound to the appropriate cyclin does the cyclin–CDK complex gain kinase activity and phosphorylate target proteins that drive cell-cycle events. **(B)**.

Bài tập luyện tập

A cell line is engineered so that its CDK1 protein can never bind cyclin B, even when cyclin B is abundant. Predict the effect on this cell's ability to enter mitosis, and justify your answer in terms of the cyclin–CDK system.

Lời giải chi tiết

Because a CDK is catalytically inactive unless bound to its partner cyclin, and cyclin B–CDK1 (MPF) is the specific active complex required to trigger entry into mitosis (nuclear envelope breakdown, chromosome condensation, spindle assembly), a CDK1 that cannot bind cyclin B can never form active MPF no matter how much cyclin B accumulates. The cell would be unable to trigger the events of mitosis and would be predicted to **arrest in G2**, unable to

proceed to M phase.

Bài tập luyện tập

The primary role of the tumor suppressor protein p53 in response to DNA damage is to:

(A) Directly repair damaged DNA using its own enzymatic activity

(B) Halt the cell cycle (or trigger apoptosis) to prevent a cell with damaged DNA from dividing

(C) Synthesize new cyclin proteins to accelerate the cell cycle

(D) Stimulate angiogenesis

Lời giải chi tiết

p53 does not repair DNA itself; as a transcription factor it induces genes (such as the CDK inhibitor p21) that halt the cell cycle to allow repair enzymes time to work, or triggers apoptosis if the damage is irreparable – preventing a damaged cell from dividing. **(B)**.

Bài tập luyện tập

A key distinction between how oncogenes and inactivated tumor suppressor genes contribute to cancer is that:

(A) Oncogenes typically arise from loss-of-function mutations and act recessively, while inactivated tumor suppressors arise from gain-of-function mutations and act dominantly

(B) Oncogenes typically arise from gain-of-function mutations and act dominantly (one mutant allele is enough), while inactivated tumor suppressors typically require loss-of-function mutation of both alleles and act recessively

(C) Both arise from identical gain-of-function mutations

(D) Neither type of mutation can be inherited

Lời giải chi tiết

Oncogenes arise from gain-of-function mutations (or overexpression) of a proto-oncogene, and one mutated/overactive allele is generally sufficient to drive excess signaling (dominant). Tumor suppressor genes normally restrain division; disabling that brake generally requires loss-of-function mutation of both alleles (recessive at the cellular level), consistent with the two-hit hypothesis. **(B)**.

Bài tập luyện tập

Which of the following is classified as a tumor suppressor gene rather than a proto-oncogene?

(A) *RAS*

(B) *MYC*

(C) *TP53* (p53)

(D) A gene encoding a growth-factor receptor

Lời giải chi tiết

TP53 encodes p53, which normally restrains the cell cycle and promotes apoptosis in response to DNA damage – a braking function whose *loss* contributes to cancer, the signature of a tumor

suppressor gene. *RAS*, *MYC*, and growth-factor receptor genes are proto-oncogenes, whose *gain*-of-function conversion to oncogenes promotes cancer. **(C)**.

Bài tập luyện tập

State the two-hit hypothesis for tumor suppressor genes. Then, using *TP53* as an example, explain why a person born with one already-nonfunctional *TP53* allele in every cell has a substantially higher lifetime cancer risk than a person born with two normal alleles, even though every one of that person's cells still has one working copy of *TP53* at birth.

Lời giải chi tiết

Two-hit hypothesis: because most tumor suppressor genes act recessively at the cellular level (one functional copy is normally sufficient to maintain control), a given cell generally must lose function of *both* alleles – two independent inactivating "hits" – before that particular brake on the cell cycle is disabled.

A person born with one already-nonfunctional *TP53* allele in every cell needs only **one further somatic mutation** (a single additional hit) in the last working copy, in any one of the trillions of cells in their body, to fully disable p53 in that cell. A person born with two normal alleles needs **two independent somatic mutations to occur in that same single cell**, which is far less statistically likely to happen anywhere in the body over a lifetime. This explains the sharply elevated cancer risk (and typically much earlier onset) seen in individuals who inherit one nonfunctional *TP53* allele.

Bài tập luyện tập

Tumor-secreted VEGF (vascular endothelial growth factor) contributes to cancer progression primarily by:

(A) Directly mutating tumor-suppressor genes

(B) Stimulating the growth of new blood vessels into the tumor, supplying oxygen and nutrients

(C) Repairing DNA damage in tumor cells

(D) Inhibiting the cell cycle in tumor cells

Lời giải chi tiết

VEGF drives angiogenesis, the growth of new blood vessels into the tumor. Without an adequate blood supply, a tumor cannot grow beyond the small size that diffusion alone can support with oxygen and nutrients. **(B)**.

Bài tập luyện tập

Explain the process of metastasis, and explain specifically why reduced expression of the cell-adhesion protein E-cadherin is significant for this process.

Lời giải chi tiết

Metastasis is the spread of cancer cells from a primary tumor to establish new, secondary tumors at distant sites in the body. Malignant cells first detach from the primary tumor mass, invade through surrounding tissue, penetrate into blood or lymphatic vessels, travel through the circulation, exit at a distant site, and proliferate there to form a new tumor. E-cadherin

is a membrane protein that normally holds epithelial cells firmly attached to their neighbors; reduced E-cadherin expression weakens these normal cell-cell adhesions, which is what allows individual malignant cells to detach from the primary tumor and become invasive in the first place – making it a key step enabling metastasis.

Bài tập luyện tập

A pathologist measures mitotic index in three tissue samples from the same organ:

Sample	Mitotic index
Normal tissue	1.5%
Untreated tumor tissue	16%
Tumor tissue treated with an RTK-blocking drug	4%

(a) What does the difference between normal tissue and untreated tumor tissue suggest about cell-cycle control in the tumor? (b) Propose a mechanism by which a drug that blocks RTK signaling could produce the observed drop in mitotic index in the treated tumor tissue.

Lời giải chi tiết

(a) Because mitotic index approximates the fraction of total cycle time spent in M phase, a mitotic index roughly ten times higher in untreated tumor tissue (16% vs. 1.5%) indicates that a much larger fraction of tumor cells are actively dividing at any given moment. This is consistent with **loss of normal cell-cycle control** – reduced dependence on the G1 checkpoint's requirement for growth factors, loss of density-dependent inhibition, and/or defective p53-mediated arrest – allowing far more cells to continuously cycle rather than pausing in G1 or exiting to G0.

(b) If the tumor's excessive proliferation is driven substantially by an overactive RTK (e.g., a receptor that is overexpressed or dimerizes without needing ligand) continuously signaling through a kinase cascade to promote passage through the G1 checkpoint, a drug that blocks RTK activity would reduce this downstream proliferative signal. More cells would then remain arrested at the G1 checkpoint (or exit into G0) instead of continuously cycling, lowering the fraction of cells caught in mitosis at any instant – consistent with the observed drop in mitotic index from 16% to 4%.

Heredity

Mục tiêu Unit: Giảm phân (meiosis) và nguồn gốc biến dị di truyền; các quy luật Mendel (phân ly, phân ly độc lập) với lai một tính và lai hai tính; di truyền ngoài Mendel (trội không hoàn toàn, đồng trội, đa alen, tương tác gen, di truyền đa gen, đa hiệu, gen liên kết và tần số tái tổ hợp); ảnh hưởng môi trường lên kiểu hình (norm of reaction); và cơ sở nhiễm sắc thể của di truyền (di truyền liên kết giới tính, không phân ly, đột biến cấu trúc nhiễm sắc thể).

5.1 Meiosis: Producing Haploid Gametes

Sexually reproducing organisms alternate between a diploid state ($2n$, two full sets of chromosomes) and a haploid state (n, one set). **Meiosis** is the specialized nuclear division that converts a diploid germ-line cell into four haploid cells — gametes in animals, spores in plants — so that fertilization (the fusion of two haploid gametes) restores the diploid number in the next generation. Meiosis is preceded by a single round of DNA replication (S phase) and then proceeds through *two* sequential divisions, Meiosis I and Meiosis II, with no further replication in between.

Why two divisions?

One replication followed by two divisions halves the chromosome number exactly once. **Meiosis I** is the **reductional division**: homologous chromosomes separate, halving the chromosome number. **Meiosis II** is the **equational division**: sister chromatids separate, mechanically similar to mitosis but starting from an already-haploid cell. Net result: one diploid cell ($2n$, replicated) $\rightarrow$ four haploid cells (n, unreplicated).

5.1.1 Meiosis I: pairing, crossing over, and reductional division

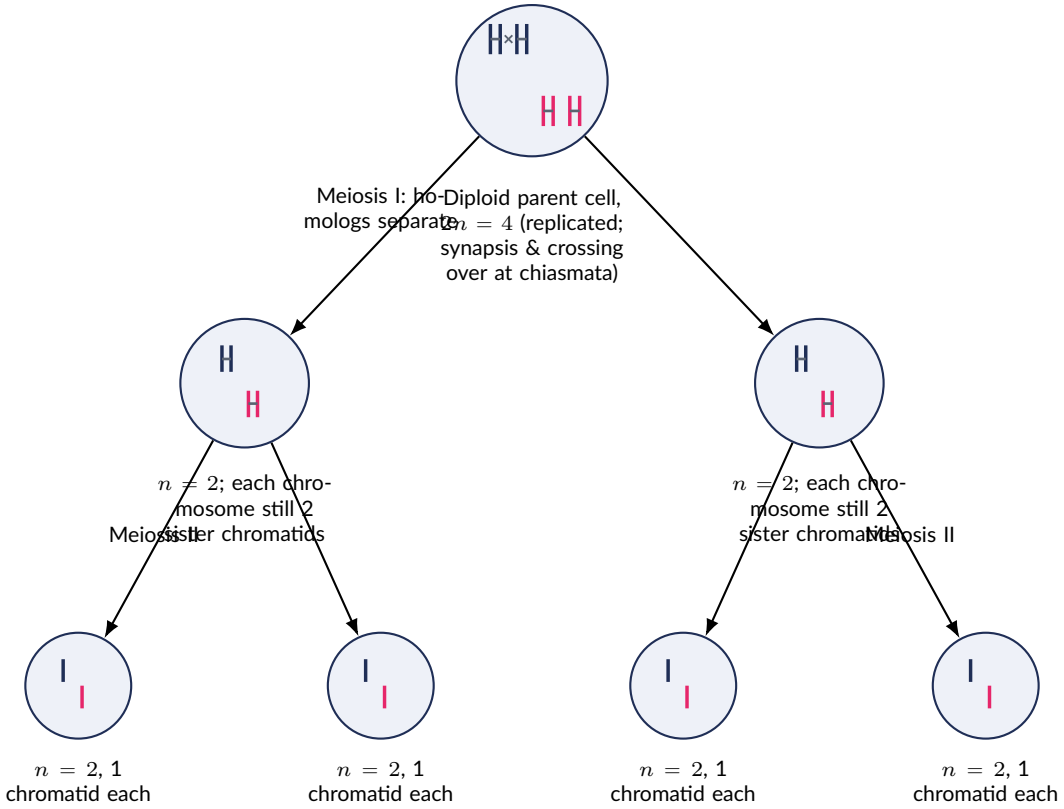
During **prophase I**, each replicated chromosome (already two sister chromatids joined at a centromere) finds and pairs with its homologous partner in a process called **synapsis**, forming a four-chromatid structure called a **tetrad** (bivalent). While paired, non-sister chromatids can exchange segments of DNA at contact points called **chiasmata** — this exchange is **crossing over**, the physical basis of genetic recombination within a chromosome. At **metaphase I**, tetrads align at the metaphase plate, with each homologous pair oriented randomly with respect to the two poles (the cellular basis of independent assortment, Section 5.2). At **anaphase I**, homologous chromosomes separate and move to opposite poles; sister chromatids remain joined and travel together. By **telophase I**, two haploid cells have formed — each has n chromosomes, but every chromosome still consists of two sister chromatids.

Meiosis I is reductional: chromosome number is cut in half ($2n \rightarrow n$) because homologous *chromosomes* — not sister chromatids — separate. Each resulting cell is haploid, but each chromosome within it remains duplicated (two sister chromatids joined at one centromere).

5.1.2 Meiosis II: equational division

The two haploid cells produced by Meiosis I proceed directly into Meiosis II, with *no* intervening S phase. Meiosis II mechanically resembles mitosis: at **metaphase II**, individual chromosomes (each still

a pair of sister chromatids) align singly at the metaphase plate; at **anaphase II**, the **sister chromatids** finally separate and move to opposite poles. The outcome of Meiosis II is four haploid cells, each with n unreplicated (single-chromatid) chromosomes.



Meiosis in a cell with $2n = 4$ (two homologous pairs). Meiosis I separates homologous chromosomes (reductional division); crossing over at chiasmata during prophase I recombines maternal and paternal alleles. Meiosis II separates sister chromatids (equational division), yielding four haploid ($n = 2$) gametes.

VN **GIẢI THÍCH TIẾNG VIỆT**

Giảm phân gồm **hai lần phân bào** nhưng chỉ **một lần** nhân đôi DNA (pha S), nên số lượng nhiễm sắc thể (NST) giảm đi một nửa. Giảm phân I là **phân bào giảm nhiễm**: các NST tương đồng (homologous chromosomes) tách nhau ra — bước này làm giảm bộ NST từ $2n$ xuống n; trước đó, trong kỳ đầu I, các NST tương đồng bắt cặp (synapsis) và trao đổi chéo (crossing over) tại các điểm tiếp hợp (chiasmata). Giảm phân II là **phân bào cân bằng**, cơ chế giống nguyên phân: các nhiễm sắc tử chị em (sister chromatids) mới tách nhau ra. Ghi nhớ: "tương đồng tách ở GP I, chị em tách ở GP II."

5.1.3 Mitosis versus meiosis

Both processes begin with one round of DNA replication, but they differ fundamentally in mechanism, product, and biological role.

Feature	Mitosis	Meiosis
Number of divisions	One	Two (Meiosis I, then Meiosis II)
Homologous pairing	Does not occur	Occurs (synapsis) in prophase I
Crossing over	Does not occur	Occurs between non-sister chromatids in prophase I
Daughter cells produced	2	4
Ploidy of products	Diploid ($2n$), same as parent	Haploid (n), half the parent
Genetic identity to parent	Genetically identical (clones)	Genetically distinct (crossing over + independent assortment)
Biological role	Growth, tissue repair, asexual reproduction	Gamete/spore formation for sexual reproduction

VN **GIẢI THÍCH TIẾNG VIỆT**

Nguyên phân (mitosis) tạo ra tế bào con giống hệt tế bào mẹ về mặt di truyền (dùng cho sinh trưởng, thay thế mô) — chỉ MỘT lần phân bào, không có bắt cặp NST tương đồng. Giảm phân (meiosis) tạo giao tử đơn bội có biến dị di truyền so với tế bào mẹ và giữa các giao tử với nhau (dùng cho sinh sản hữu tính) — gồm HAI lần phân bào liên tiếp sau một lần nhân đôi DNA duy nhất.

5.2 Meiosis and Genetic Diversity

Sexual reproduction generates far more genetic variation among offspring than would arise from mutation alone, because meiosis and fertilization combine and reshuffle existing alleles in new ways every generation. Three independent mechanisms contribute:

Three sources of variation

(1) Crossing over (recombination): exchange of DNA segments between non-sister chromatids of homologous chromosomes at chiasmata in prophase I creates chromosomes with new combinations of maternal and paternal alleles. **(2) Independent assortment:** each homologous pair orients randomly at metaphase I, independent of how other pairs orient, so the maternal/paternal origin of each chromosome in a gamete is essentially a coin flip. **(3) Random fertilization:** which of the many possible sperm fuses with which of the many possible eggs is essentially random, multiplying the variation from the two parents together.

For an organism with haploid number n (i.e., n homologous pairs), independent assortment alone can produce 2^n chromosomally distinct gamete types, since each of the n pairs independently contributes one of 2 possible orientations to a given gamete.

Ví dụ mẫu · Independent assortment in human gametes

Humans have a haploid number of $n = 23$. Ignoring crossing over entirely, how many chromosomally distinct types of gametes can one person produce through independent assortment alone?

Each of the 23 homologous pairs independently contributes either its maternal or paternal member to a gamete, so the number of combinations is

$$2^n = 2^{23} = 8{,}388{,}608.$$

Because both parents independently generate this many gamete types, and fertilization pairs any egg with any sperm, the number of possible chromosome combinations in a zygote from independent assortment alone is $2^{23} \times 2^{23} = 2^{46} \approx 7 \times 10^{13}$ — and crossing over multiplies this further, since it creates entirely new (non-parental) chromosomes that were never counted among the 2^{23}.

VN **GIẢI THÍCH TIẾNG VIỆT**

Ba cơ chế làm tăng biến dị di truyền ở loài sinh sản hữu tính: (1) **trao đổi chéo** (crossing over) — hoán đổi đoạn DNA giữa các nhiễm sắc tử không chị em của cặp NST tương đồng; (2) **phân ly độc lập** (independent assortment) — mỗi cặp NST tương đồng xếp hàng ngẫu nhiên độc lập với các cặp khác ở kỳ giữa I, cho 2^n tổ hợp giao tử khác nhau (với n là số cặp NST tương đồng, tức bộ NST đơn bội); (3) **thụ tinh ngẫu nhiên** — bất kỳ tinh trùng nào cũng có thể kết hợp với bất kỳ trứng nào. Ba cơ chế này nhân với nhau, tạo ra số lượng tổ hợp gen khổng lồ ở đời con, gần như không có hai cá thể nào (trừ sinh đôi cùng trứng) giống hệt nhau về mặt di truyền.

5.3 Mendelian Genetics

5.3.1 Core vocabulary

Gregor Mendel's pea-plant experiments established that heritable traits are controlled by discrete factors (now called **genes**), which exist in alternative forms called **alleles**. In a diploid organism, each gene is present in two copies (one from each parent), located at the same position (**locus**) on a pair of homologous chromosomes.

Key definitions

Genotype — the allelic makeup of an individual (e.g., Tt). **Phenotype** — the observable trait produced by that genotype (e.g., tall). **Homozygous** — two identical alleles at a locus (TT or tt). **Heterozygous** — two different alleles at a locus (Tt). **Dominant allele** (capital letter) — produces its phenotype whenever present, masking a recessive allele in a heterozygote. **Recessive allele** (lowercase letter) — produces its phenotype only when homozygous.

VN **GIẢI THÍCH TIẾNG VIỆT**

Kiểu gen (genotype) là tổ hợp alen (Tt); **kiểu hình** (phenotype) là biểu hiện ra bên ngoài (thân cao). **Đồng hợp** (homozygous) = hai alen giống nhau (TT hoặc tt); **dị hợp** (heterozygous) = hai alen khác nhau (Tt). Alen **trội** (dominant, chữ hoa) luôn biểu hiện kiểu hình khi có mặt (kể cả ở dạng dị hợp); alen **lặn** (recessive, chữ thường) chỉ biểu hiện khi ở trạng thái đồng hợp lặn.

5.3.2 The law of segregation and the monohybrid cross

Mendel's **law of segregation**: the two alleles of a gene separate (segregate) from each other during gamete formation, so each gamete receives only one allele per gene. The physical basis is the separation of homologous chromosomes at anaphase I (and ultimately of sister chromatids at anaphase II), which guarantees each gamete gets exactly one copy of each chromosome — and therefore one allele of each gene.

A **monohybrid cross** tracks a single gene. A **Punnett square** lists the possible gametes of one parent along the top and of the other along the side, filling in each cell with the resulting offspring genotype.

Ví dụ mẫu · Monohybrid cross

In pea plants, tall (T) is dominant to short (t). Cross two heterozygous plants, $Tt \times Tt$. Find the genotypic and phenotypic ratios of the offspring.
Each parent produces gametes T or t (probability $\frac{1}{2}$ each). The Punnett square gives genotypes $TT : Tt : Tt : tt$, i.e. a genotypic ratio $1\,TT : 2\,Tt : 1\,tt$. Since T is dominant, both TT and Tt are tall: phenotypic ratio 3 tall : 1 short.

VN **GIẢI THÍCH TIẾNG VIỆT**
Quy luật phân ly: hai alen của một gen tách nhau ra khi hình thành giao tử, mỗi giao tử chỉ nhận MỘT alen. Cơ sở tế bào học: sự phân ly của cặp NST tương đồng ở kỳ sau I (và sự phân ly nhiễm sắc tử chị em ở kỳ sau II) đảm bảo mỗi giao tử chỉ có một bản sao của mỗi gen. Lai một tính trạng dị hợp $Tt \times Tt$ luôn cho tỉ lệ kiểu gen $1 : 2 : 1$ và tỉ lệ kiểu hình $3 : 1$ (nếu trội hoàn toàn).

5.3.3 The law of independent assortment and the dihybrid cross

Mendel's **law of independent assortment**: alleles of genes located on different (non-homologous) chromosome pairs segregate into gametes independently of one another. The physical basis is the random orientation of different homologous pairs at metaphase I — how pair 1 orients does not influence how pair 2 orients. This law applies to genes on *different* chromosomes (or far apart on the same chromosome); it does *not* hold for tightly linked genes on the same chromosome (Section 5.4.6).

A **dihybrid cross** tracks two genes simultaneously. Crossing two double heterozygotes for unlinked genes, e.g. $RrYy \times RrYy$ (round R/wrinkled r seed shape; yellow Y/green y seed color), produces the classic $9 : 3 : 3 : 1$ phenotypic ratio.

$\times$	RY	Ry	rY	ry
RY	$RRYY$	$RRYy$	$RrYY$	$RrYy$
Ry	$RRYy$	$RRyy$	$RrYy$	$Rryy$
rY	$RrYY$	$RrYy$	$rrYY$	$rrYy$
ry	$RrYy$	$Rryy$	$rrYy$	$rryy$

Dihybrid Punnett square for $RrYy \times RrYy$ (seed shape $\times$ seed color, unlinked genes). Reading the 16 cells: 9 round-yellow ($R\_Y\_$) : 3 round-green (R_yy) : 3 wrinkled-yellow ($rrY\_$) : 1 wrinkled-green ($rryy$).

Because the two genes assort independently, the dihybrid ratio is simply the *product* of the two monohybrid ratios: $(3 : 1) \times (3 : 1) = 9 : 3 : 3 : 1$. This same logic (the **product rule** of probability) lets us skip the full 16-box grid entirely for probability questions.

Product rule vs. addition rule. For *independent* events (e.g., the outcome at one gene locus and the outcome at an unlinked locus), the probability that *both* occur is the *product* of their individual probabilities: $P(A \text{ and } B) = P(A) \times P(B)$. For *mutually exclusive* outcomes (e.g., an offspring is either $AABB$ *or* $aabb$, not both), the probability that *either* occurs is the *sum*: $P(A \text{ or } B) = P(A) + P(B)$.

Ví dụ mẫu · Dihybrid probability by the product rule

Cross $AaBb \times AaBb$ (two unlinked genes). Find (a) the probability an offspring has genotype $AaBb$, and (b) the probability an offspring shows the dominant phenotype for *both* traits.
(a) At the A locus, $Aa \times Aa$ gives Aa with probability $\frac{1}{2}$. At the B locus, $Bb \times Bb$ gives Bb with

probability $\frac{1}{2}$. Since the two loci assort independently,

$$P(AaBb) = P(Aa) \times P(Bb) = \tfrac{1}{2} \times \tfrac{1}{2} = \tfrac{1}{4}.$$

(b) $P(A\_) = \frac{3}{4}$ (dominant phenotype at locus A: AA or Aa) and $P(B\_) = \frac{3}{4}$ similarly, so

$$P(A\_B\_) = \tfrac{3}{4} \times \tfrac{3}{4} = \tfrac{9}{16}.$$

Ví dụ mẫu · Complement rule: at least one recessive trait

From the same cross $AaBb \times AaBb$, three offspring are produced. What is the probability that *at least one* of the three shows the fully recessive phenotype ($aabb$)?

First find the probability a single offspring is $aabb$: $P(aabb) = P(aa) \times P(bb) = \frac{1}{4} \times \frac{1}{4} = \frac{1}{16}$. So $P(\text{not } aabb) = 1 - \frac{1}{16} = \frac{15}{16}$ for each offspring. Since the three births are independent,

$$P(\text{none of 3 are } aabb) = \left(\tfrac{15}{16}\right)^3 = \frac{3375}{4096} \approx 0.824.$$

By the **complement rule**, $P(\text{at least one } aabb) = 1 - 0.824 = 0.176$, or about 17.6%.

(!) Lỗi thường gặp: Do not confuse the **product rule** (AND, independent events — multiply) with the **addition rule** (OR, mutually exclusive outcomes — add). A common error is adding probabilities of a joint genotype/phenotype instead of multiplying (e.g., writing $P(AaBb) = \frac{1}{2} + \frac{1}{2}$ instead of $\frac{1}{2} \times \frac{1}{2}$), or multiplying when the question actually asks for one outcome *or* another mutually exclusive one.

VN **GIẢI THÍCH TIẾNG VIỆT**

Quy luật phân ly độc lập: các gen nằm trên các cặp NST khác nhau (không liên kết) phân ly vào giao tử một cách độc lập với nhau — cơ sở tế bào học là sự sắp xếp ngẫu nhiên của mỗi cặp NST tương đồng ở kỳ giữa I. Nhờ đó, xác suất của một kiểu gen/kiểu hình đồng thời ở hai gen KHÔNG liên kết bằng **tích** xác suất riêng của từng gen (quy tắc nhân — "và"). Quy tắc cộng ("hoặc") chỉ dùng cho các biến cố loại trừ lẫn nhau (không thể xảy ra đồng thời).

5.3.4 Test crosses: determining an unknown genotype

An individual showing the dominant phenotype could be homozygous dominant or heterozygous — the phenotype alone cannot distinguish them. A **test cross** resolves this ambiguity by crossing the unknown individual with a homozygous recessive individual and examining the offspring ratio.

Ví dụ mẫu · Test cross

A pea plant with purple flowers (dominant, P) has an unknown genotype: either PP or Pp. It is crossed with a white-flowered plant (pp), producing 48 offspring: 24 purple and 24 white. What is the genotype of the purple parent?

If the purple parent were PP: $PP \times pp \rightarrow$ all offspring Pp (100% purple, 0% white). If the purple parent were Pp: $Pp \times pp \rightarrow \frac{1}{2}\,Pp$ (purple) : $\frac{1}{2}\,pp$ (white), a $1:1$ ratio. The observed $24:24$ ($1:1$) ratio matches the heterozygous prediction, so the purple parent's genotype is Pp.

5.3.5 Testing ratios: the chi-square goodness-of-fit test

Real crosses never match expected Mendelian ratios exactly, due to chance sampling. The **chi-square (χ^2) goodness-of-fit test** asks whether the deviation between observed and expected counts is small enough to be explained by chance, or large enough to reject the hypothesized ratio.

$$\chi^2 = \sum \frac{(O-E)^2}{E}, \qquad \text{degrees of freedom } df = (\text{number of categories}) - 1.$$

Compare the computed χ^2 to a critical value from a chi-square table at a chosen significance level (typically $\alpha = 0.05$). If $\chi^2 \leq$ critical value, **fail to reject** the null hypothesis (the data are consistent with the expected ratio). If $\chi^2 >$ critical value, **reject** the null hypothesis (the data deviate significantly from the expected ratio).

Ví dụ mẫu · Chi-square goodness-of-fit test

The dihybrid cross $RrYy \times RrYy$ predicts a $9:3:3:1$ ratio of round-yellow : round-green : wrinkled-yellow : wrinkled-green. Of 160 offspring, the observed counts are 98, 32, 24, and 6. Test the fit to the $9:3:3:1$ hypothesis at $\alpha = 0.05$.

Step 1 — expected counts (from $160 \times \frac{9}{16}, \frac{3}{16}, \frac{3}{16}, \frac{1}{16}$): 90, 30, 30, 10.

Step 2 — χ^2 terms:

$$\frac{(98-90)^2}{90} = 0.711, \quad \frac{(32-30)^2}{30} = 0.133, \quad \frac{(24-30)^2}{30} = 1.200, \quad \frac{(6-10)^2}{10} = 1.600.$$

$$\chi^2 = 0.711 + 0.133 + 1.200 + 1.600 = 3.644.$$

Step 3 — degrees of freedom: $df = 4 - 1 = 3$. The critical value at $\alpha = 0.05$, $df = 3$ is 7.815.

Step 4 — conclusion: since $3.644 < 7.815$, we **fail to reject** the null hypothesis: the observed data are consistent with the expected $9:3:3:1$ ratio (the small deviation is attributable to chance).

VN **GIẢI THÍCH TIẾNG VIỆT**

Kiểm định chi bình phương (χ^2) dùng để kiểm tra xem số liệu quan sát được (observed, O) có phù hợp với tỉ lệ kỳ vọng (expected, E) theo lý thuyết Mendel hay không. Công thức: $\chi^2 = \sum \frac{(O-E)^2}{E}$; bậc tự do $df =$ số loại kiểu hình -1. So sánh χ^2 tính được với giá trị tới hạn (critical value) tra bảng ở mức ý nghĩa $\alpha = 0.05$: nếu χ^2 NHỎ HƠN giá trị tới hạn $\Rightarrow$ chưa đủ bằng chứng bác bỏ giả thuyết (số liệu phù hợp với tỉ lệ kỳ vọng); nếu χ^2 LỚN HƠN $\Rightarrow$ bác bỏ giả thuyết (số liệu lệch có ý nghĩa thống kê so với tỉ lệ kỳ vọng).

5.4 Beyond Simple Dominance: Non-Mendelian Inheritance

Many real traits do not follow the simple dominant/recessive pattern of Mendel's peas. The underlying chromosomal mechanics (meiosis, segregation, independent assortment) are unchanged — only the relationship between genotype and phenotype becomes more elaborate.

5.4.1 Incomplete dominance

In **incomplete dominance**, the heterozygote's phenotype is an intermediate **blend** of the two homozygous phenotypes — neither allele fully dominates.

Ví dụ mẫu · Incomplete dominance

In snapdragons, red flower color (C^RC^R) and white flower color (C^WC^W) blend to give pink (C^RC^W) in heterozygotes. Cross two pink plants, $C^RC^W \times C^RC^W$. Find the phenotypic ratio of the offspring.

Gametes from each parent: C^R or C^W ($\frac{1}{2}$ each). Offspring genotypes: $\frac{1}{4}\,C^RC^R$ (red), $\frac{1}{2}\,C^RC^W$ (pink), $\frac{1}{4}\,C^WC^W$ (white) — a $1:2:1$ ratio. Unlike simple dominance, the genotypic and phenotypic ratios are identical here, because the heterozygote has its own distinct, intermediate phenotype rather than resembling one homozygote.

5.4.2 Codominance

In **codominance**, the heterozygote expresses *both* parental phenotypes simultaneously and *distinctly* (not blended). Classic examples: the AB blood type (I^AI^B individuals express both A and B surface antigens on their red blood cells); roan cattle or horses (red and white hairs both present, interspersed, rather than blended pink); the human MN blood group (heterozygotes express both M and N antigens).

(!) Lỗi thường gặp: Incomplete dominance and codominance are easy to confuse. In **incomplete dominance**, the heterozygote shows a single *blended*, *intermediate* phenotype (pink flower — a genuinely new, third phenotype). In **codominance**, the heterozygote shows *both* original phenotypes *fully and distinctly* at the same time (both A and B antigens present, not a hypothetical "AB-blend" antigen). Ask: is the heterozygote phenotype an intermediate blend, or a simultaneous display of both traits?

VN **GIẢI THÍCH TIẾNG VIỆT**

Trội không hoàn toàn (incomplete dominance): thể dị hợp cho ra kiểu hình **trung gian, pha trộn** giữa hai kiểu hình bố mẹ (VD: hoa hồng phấn = đỏ + trắng trộn lẫn). Đồng trội (codominance): thể dị hợp biểu hiện **đồng thời và đầy đủ** CẢ HAI kiểu hình bố mẹ, không pha trộn (VD: nhóm máu AB có cả kháng nguyên A và kháng nguyên B trên bề mặt hồng cầu, không phải một kháng nguyên "lai" nào khác).

5.4.3 Multiple alleles: the ABO blood group

A gene can have more than two allelic forms circulating in a population, even though any single diploid individual carries at most two. The human **ABO blood group** is controlled by three alleles at one locus: I^A and I^B (codominant with each other), and i (recessive to both).

Genotype(s)	Phenotype (blood type)
I^AI^A or I^Ai	A
I^BI^B or I^Bi	B
I^AI^B	AB
ii	O

Ví dụ mẫu · ABO multiple-alleles cross

A man with blood type AB (I^AI^B) and a woman with blood type A, heterozygous (I^Ai), have children. Find the possible genotypes and phenotypes of the offspring, with proportions.

Father's gametes: I^A or I^B ($\frac{1}{2}$ each). Mother's gametes: I^A or i ($\frac{1}{2}$ each). Combining:

$$\tfrac{1}{4}\, I^A I^A \text{ (A)}, \quad \tfrac{1}{4}\, I^A i \text{ (A)}, \quad \tfrac{1}{4}\, I^A I^B \text{ (AB)}, \quad \tfrac{1}{4}\, I^B i \text{ (B)}.$$

Phenotype proportions: type A $= \frac{1}{2}$, type AB $= \frac{1}{4}$, type B $= \frac{1}{4}$, type O $= 0$ (impossible, since the father contributes no i allele).

VN **GIẢI THÍCH TIẾNG VIỆT**

Hệ nhóm máu ABO có **ba alen** (I^A, I^B, i) cùng tồn tại trong quần thể, nhưng mỗi người chỉ mang tối đa hai trong ba alen đó. I^A và I^B **đồng trội** với nhau (tạo nhóm máu AB khi cùng có mặt); cả hai đều trội hoàn toàn so với i. Đây là ví dụ kết hợp giữa **đa alen** (nhiều hơn 2 alen ở mức quần thể) và **đồng trội** (ở mức cá thể dị hợp $I^A I^B$).

5.4.4 Epistasis

Epistasis occurs when the alleles of one gene mask or modify the phenotypic expression of a different, non-allelic gene. A classic example is coat color in Labrador retrievers, controlled by two genes: gene B (pigment *type*: B = black, b = brown/chocolate) and gene E (pigment *deposition*: E = pigment is deposited in the coat, e = no pigment is deposited, so the coat appears yellow *regardless* of the B genotype). The ee genotype is epistatic to the B locus.

VN **GIẢI THÍCH TIẾNG VIỆT**

Tương tác gen át chế (epistasis): alen của một gen che lấp/làm thay đổi sự biểu hiện kiểu hình của một gen KHÁC (không alen với nó) — khác với trội/lặn (chỉ xảy ra giữa hai alen của CÙNG một gen). Ví dụ kinh điển: ở chó Labrador, kiểu gen ee (gen E quy định lắng đọng sắc tố) át chế hoàn toàn gen B (quy định loại sắc tố đen/nâu), khiến lông có màu vàng bất kể kiểu gen B là gì.

5.4.5 Polygenic inheritance

Polygenic inheritance occurs when a single phenotypic trait is influenced by *multiple* genes, each contributing a small, typically additive effect. Because there are many possible combinations of alleles across all the contributing loci (often further modified by environment), the resulting phenotype varies **continuously** (a bell-shaped distribution) rather than falling into a few discrete categories. Human height and skin color are classic polygenic traits.

5.4.6 Pleiotropy

Pleiotropy occurs when a single gene influences multiple, seemingly unrelated phenotypic traits. The sickle-cell allele (in the HBB gene) is a classic example: it alters red blood cell shape, reduces oxygen-carrying efficiency, confers some resistance to malaria in heterozygotes, and can cause circulatory blockages and organ damage. Marfan syndrome (a mutation in the $FBN1$ gene, which encodes a connective-tissue protein) similarly affects the skeletal system (tall stature, long limbs), the cardiovascular system (risk of aortic aneurysm), and the eyes (lens dislocation) — all from a single gene.

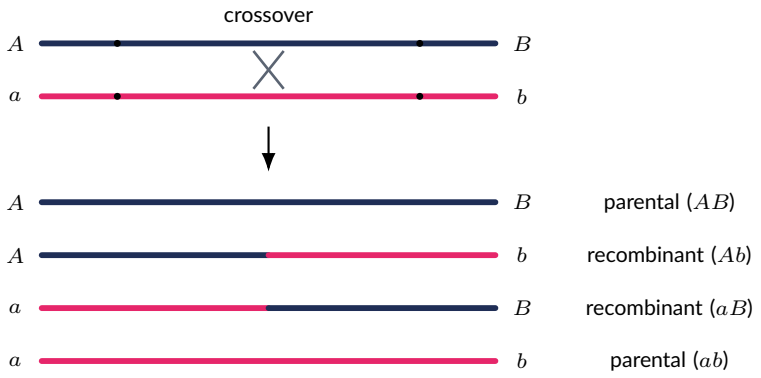
VN **GIẢI THÍCH TIẾNG VIỆT**

Di truyền đa gen (polygenic inheritance): MỘT tính trạng chịu ảnh hưởng của NHIỀU gen khác nhau, mỗi gen đóng góp một phần nhỏ (cộng gộp) ⇒ kiểu hình biến thiên liên tục (VD: chiều cao, màu da người), không chia thành vài loại rõ rệt như tính trạng Mendel đơn giản. Di truyền đa hiệu (pleiotropy): NGƯỢC LẠI về hướng tác động — MỘT gen duy nhất ảnh hưởng đến

NHIỀU tính trạng khác nhau cùng lúc (VD: alen hồng cầu hình liềm ảnh hưởng đến hình dạng hồng cầu, khả năng vận chuyển oxy, và khả năng kháng sốt rét).

5.4.7 Linked genes and recombination frequency

Genes located close together on the *same* chromosome are physically **linked**: they tend to be inherited together and do not obey independent assortment, because their fate depends on whether a crossover happens to occur between them. The only way to separate (recombine) linked alleles is crossing over during prophase I.



A single crossover between linked loci A/a and B/b produces two unchanged (parental) chromatids and two recombinant chromatids. Recombination frequency $= \dfrac{\text{recombinant offspring}}{\text{total offspring}} \times 100\%$ estimates the map distance between the loci.

The **recombination frequency (RF)** between two linked genes is measured from testcross data:

$$\text{RF} = \frac{\text{number of recombinant offspring}}{\text{total offspring}} \times 100.$$

Genes farther apart on a chromosome are more likely to have a crossover occur somewhere between them, so RF increases with physical distance — this lets geneticists build a **linkage map**, where 1 map unit (centimorgan, cM) $\approx 1\%$ recombination frequency.

Ví dụ mẫu · Recombination frequency and map distance

In fruit flies, body color (gray G/black g) and wing shape (normal W/vestigial w) are linked. A testcross ($GgWw \times ggww$) produces 1000 offspring: 465 gray-normal, 470 black-vestigial (parental types), 38 gray-vestigial, and 27 black-normal (recombinant types). Find the recombination frequency and the map distance.

Recombinants: $38 + 27 = 65$. Total offspring: $465 + 470 + 38 + 27 = 1000$.

$$\text{RF} = \frac{65}{1000} \times 100 = 6.5.$$

The two genes are approximately 6.5 map units (cM) apart on the chromosome.

(!) Lỗi thường gặp: A recombination frequency near 50% does *not* necessarily mean the genes are on different chromosomes — it can also mean they are so far apart on the *same* chromosome that a crossover occurs between them almost every meiosis, making them assort as if independent. RF of 50% is the *ceiling*: values cannot exceed 50%, since that is what unlinked (or maximally distant) genes already produce.

VN **GIẢI THÍCH TIẾNG VIỆT**

Gen liên kết (linked genes) nằm gần nhau trên CÙNG một NST, có xu hướng di truyền cùng nhau, KHÔNG tuân theo quy luật phân ly độc lập — trừ khi có trao đổi chéo xảy ra giữa chúng. **Tần số tái tổ hợp** $= \dfrac{\text{số cá thể tái tổ hợp}}{\text{tổng số cá thể}} \times 100\%$ tỉ lệ thuận với khoảng cách vật lý giữa hai gen trên NST — đây là cơ sở để lập bản đồ di truyền (1 đơn vị bản đồ $\approx 1\%$ tần số tái tổ hợp). Tần số tái tổ hợp tối đa là 50% (khi hai gen phân ly độc lập, dù trên cùng NST rất xa nhau hay trên hai NST khác nhau).

5.5 Environmental Effects on Phenotype: Norm of Reaction

Genotype does not always fully determine phenotype: the environment can modify how a genotype is expressed. The **norm of reaction** is the range of phenotypes that a single genotype can produce across a range of environmental conditions.

Two classic examples

Temperature-sensitive coat color (Himalayan rabbits, Siamese cats): these animals carry a temperature-sensitive allele of the enzyme *tyrosinase*, which catalyzes melanin (pigment) production. The enzyme is only active at *cooler* temperatures, so pigment develops at the cooler extremities (ears, nose, paws, tail), while the warmer body core stays pale. The same genotype thus produces different fur colors at different body locations, purely because of local temperature. **Hydrangea flower color**: the same genotype can produce blue flowers in acidic soil (where aluminum ions are more soluble and available to roots) or pink flowers in alkaline soil (where aluminum is less available) — a striking example of a single genotype's phenotype shifting with an environmental variable (soil chemistry) rather than any change in the plant's alleles.

VN **GIẢI THÍCH TIẾNG VIỆT**

Norm of reaction (mức phản ứng) là khoảng biến thiên kiểu hình mà MỘT kiểu gen có thể tạo ra trong các môi trường khác nhau — kiểu gen không đổi, nhưng kiểu hình thay đổi theo môi trường. Ví dụ: thỏ Himalaya/mèo Xiêm có enzyme tổng hợp sắc tố (tyrosinase) chỉ hoạt động ở nhiệt độ THẤP, nên lông chỉ sẫm màu ở các vùng lạnh hơn của cơ thể (tai, mũi, chân, đuôi), còn phần thân ấm hơn thì lông nhạt màu — dù đó là CÙNG một kiểu gen. Tương tự, hoa cẩm tú cầu (hydrangea) cùng kiểu gen nhưng ra hoa xanh ở đất chua (nhiều nhôm hòa tan) và hoa hồng ở đất kiềm.

5.6 Chromosomal Basis of Inheritance

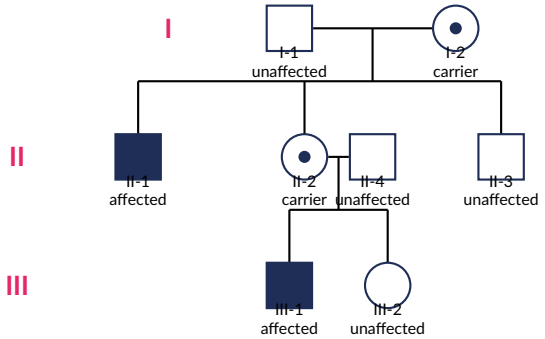
5.6.1 Sex determination and sex-linked traits

In humans, sex is determined by the sex chromosomes: females are XX, males are XY. The **SRY** gene on the Y chromosome triggers male development. Because males have only one X chromosome, they are **hemizygous** for X-linked genes — they express whatever allele is on their single X, with no second copy to mask it. This produces distinctive inheritance patterns for **X-linked recessive** traits such as red-green color blindness and hemophilia:

X-linked recessive inheritance patterns

Affected males are more common than affected females (a male needs only one copy of the recessive allele; a female needs two). An affected father cannot pass the trait to his sons (they receive his Y, not his X) but passes the recessive allele to *all* his daughters, making them at

least carriers. A heterozygous (**carrier**) mother is phenotypically unaffected but can pass the allele to sons, who will be affected — this is why the trait often appears to "skip" a generation, resurfacing in a grandson through a carrier daughter.



Pedigree for an X-linked recessive trait (e.g., color blindness). Squares = males, circles = females; filled = affected; open with a central dot = carrier; open = unaffected, non-carrier. The carrier mother I-2 has an affected son II-1; her daughter II-2, though unaffected herself, must also be a carrier because *her* son III-1 is affected — the classic skip-generation, male-biased pattern of X-linked recessive inheritance.

Ví dụ mẫu · X-linked recessive cross

Color blindness is X-linked recessive. A carrier mother (X^HX^h) and an unaffected father (X^HY) have children. Find the genotypes/phenotypes of the offspring and their proportions.
Mother's gametes: X^H or X^h ($\frac{1}{2}$ each). Father's gametes: X^H or Y ($\frac{1}{2}$ each). Offspring:

$$\tfrac{1}{4}\,X^HX^H\ (\text{unaffected daughter}), \qquad \tfrac{1}{4}\,X^HX^h\ (\text{carrier daughter}),$$

$$\tfrac{1}{4}\,X^HY\ (\text{unaffected son}), \qquad \tfrac{1}{4}\,X^hY\ (\text{affected son}).$$

All daughters are phenotypically unaffected (though half are carriers); of the sons, half are affected. This is the classic X-linked recessive signature: the trait affects sons more often than daughters, even though neither parent is affected in this cross.

(!) Lỗi thường gặp: Do not assume an unaffected female is free of the recessive allele. Heterozygous **carrier** females are phenotypically normal (the dominant allele masks the recessive one) yet can pass the recessive allele to roughly half their offspring. In pedigree analysis, an unaffected woman with an affected son, an affected brother, or an affected father must be treated as an obligate carrier.

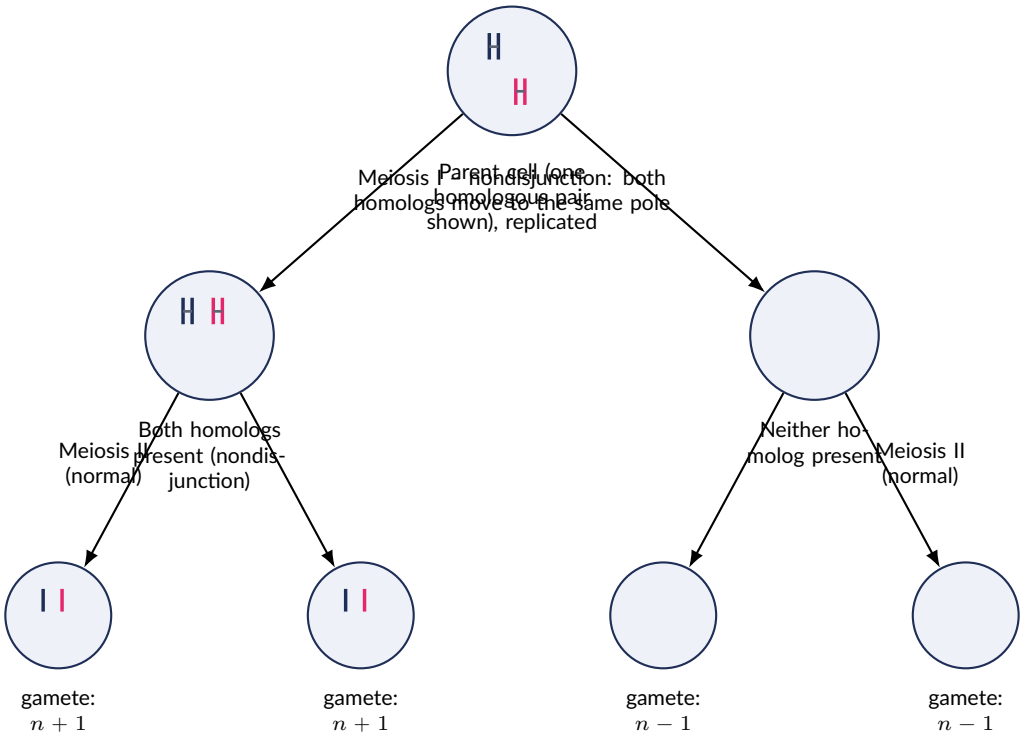
VN **GIẢI THÍCH TIẾNG VIỆT**

Ở người, giới tính được xác định bởi cặp NST giới tính (XX = nữ, XY = nam); gen SRY trên NST Y khởi động phát triển nam. Vì nam chỉ có MỘT NST X, họ ở trạng thái **bán hợp tử** (hemizygous) — bất kỳ alen lặn nào trên X đều biểu hiện ra kiểu hình (không có alen thứ hai để che lấp). Do đó, các bệnh liên kết X lặn (mù màu, máu khó đông) gặp ở NAM nhiều hơn NỮ; người mẹ dị hợp (**người mang gen** — carrier) có kiểu hình bình thường nhưng có thể truyền alen lặn cho con trai, khiến bệnh dường như "bỏ qua" một thế hệ rồi xuất hiện lại ở cháu trai.

5.6.2 Nondisjunction and aneuploidy

Nondisjunction is the failure of chromosomes to separate properly during meiosis (at anaphase I or anaphase II), producing gametes with an abnormal chromosome number — **aneuploidy** ($n+1$ or

$n-1$ for the affected chromosome). Fertilizing an abnormal ($n \pm 1$) gamete with a normal (n) gamete produces a **trisomy** ($2n+1$: three copies of one chromosome) or **monosomy** ($2n-1$: one copy).



Nondisjunction at anaphase I: a homologous pair fails to separate, so both homologs travel to the same pole. Meiosis II then proceeds normally (sister chromatids separate), producing four abnormal gametes: two with an extra copy of the chromosome ($n+1$) and two missing it entirely ($n-1$).

Ví dụ mẫu · Nondisjunction and trisomy 21

A germ cell undergoes nondisjunction of chromosome 21 at anaphase I; meiosis II proceeds normally. (a) State the chromosome-21 content of each of the four resulting gametes. (b) If one such gamete is fertilized by a normal gamete, what condition results, and how many total chromosomes does the zygote have (human $2n = 46$)?

(a) Nondisjunction at anaphase I sends both homologs of chromosome 21 to the same pole; meiosis II then separates sister chromatids normally, so *all four* gametes are abnormal: two gametes carry 2 copies of chromosome 21 ($n+1 = 24$ chromosomes total), and two carry 0 copies ($n-1 = 22$ chromosomes total).

(b) An $n+1$ gamete (24 chromosomes) fertilized by a normal $n = 23$ gamete gives a zygote with $24 + 23 = 47$ chromosomes, with three copies of chromosome 21 — **trisomy 21 (Down syndrome)**. (An $n-1$ gamete fertilized normally would instead give 45 chromosomes with only one copy of chromosome 21 — monosomy 21.)

Common human aneuploidies

Trisomy 21 (Down syndrome): 47 chromosomes, three copies of chromosome 21. **Klinefelter syndrome**: karyotype $47, XXY$ — an extra X chromosome in a male. **Turner syndrome**: karyotype $45, X$ — only one sex chromosome (a single X, no second X or Y) in a female — a monosomy. All three arise from nondisjunction during gamete formation in a parent.

(!) Lỗi thường gặp: Nondisjunction can occur at *either* anaphase I *or* anaphase II, and the resulting gametes differ. **Nondisjunction at anaphase I** (homologs fail to separate): *all four* resulting gametes are abnormal — two are $n+1$, two are $n-1$. **Nondisjunction at anaphase II** (sister chromatids fail to separate, in only one of the two secondary cells): the *other* secondary cell still divides normally, giving two normal (n) gametes, while the affected cell gives one $n+1$ and one $n-1$ gamete — so the net result is 2 normal, 1 trisomic-forming, 1 monosomic-forming.

VN **GIẢI THÍCH TIẾNG VIỆT**

Không phân ly (nondisjunction) là hiện tượng NST không tách đúng cách trong giảm phân, tạo giao tử thừa hoặc thiếu NST (dị bội — aneuploidy). Nếu xảy ra ở kỳ sau I (cặp NST tương đồng không tách): CẢ 4 giao tử đều bất thường (2 giao tử $n+1$, 2 giao tử $n-1$). Nếu xảy ra ở kỳ sau II (nhiễm sắc tử chị em không tách, chỉ ở MỘT trong hai tế bào thứ cấp): có 2 giao tử bình thường (n), 1 giao tử $n+1$, 1 giao tử $n-1$. Ví dụ ở người: hội chứng Down (ba nhiễm sắc thể 21 — trisomy 21), hội chứng Klinefelter ($47, XXY$), hội chứng Turner ($45, X$).

5.6.3 Chromosomal structural mutations

Beyond changes in chromosome *number*, chromosomes can undergo structural rearrangements that alter gene dosage or gene order.

Mutation	Description	Example / consequence
Deletion	Loss of a chromosome segment	Cri-du-chat syndrome (deletion on the short arm of chromosome 5)
Duplication	A segment is repeated, present in extra copy	Increases gene dosage; provides raw material for new gene functions over evolutionary time
Inversion	A segment is excised, flipped $180°$, and reinserted (same material, reversed order)	Can disrupt genes at the breakpoints; suppresses normal crossing over within the inverted region in heterozygotes
Translocation	A segment relocates to a nonhomologous chromosome; a *reciprocal* translocation exchanges segments between two nonhomologous chromosomes	Philadelphia chromosome (translocation between chromosomes 9 and 22), associated with chronic myelogenous leukemia (CML)

VN **GIẢI THÍCH TIẾNG VIỆT**

Bốn loại đột biến cấu trúc NST: **mất đoạn** (deletion) — mất hẳn một đoạn NST; **lặp đoạn** (duplication) — một đoạn được nhân thêm bản sao; **đảo đoạn** (inversion) — một đoạn bị cắt ra, xoay ngược $180°$ rồi gắn lại (vẫn đủ vật chất di truyền nhưng đảo trật tự gen); **chuyển đoạn** (translocation) — một đoạn NST gắn sang một NST khác không tương đồng (chuyển đoạn tương hỗ = trao đổi đoạn giữa hai NST khác nhau). Ví dụ: hội chứng "tiếng mèo kêu" (cri-du-chat) do mất đoạn NST số 5; NST Philadelphia (chuyển đoạn giữa NST 9 và 22) liên quan đến bệnh bạch cầu dòng tủy mạn tính.

5.7 Practice Problems

Bài tập luyện tập

Which statement best describes the primary purpose of meiosis in sexually reproducing organisms?

(A) To repair damaged tissue by producing identical diploid cells

(B) To produce four genetically diverse haploid gametes from a diploid germ cell

(C) To increase the total number of chromosomes in somatic cells

(D) To convert haploid spores into diploid zygotes without fertilization

Lời giải chi tiết

Meiosis reduces a diploid germ cell to four haploid gametes, and crossing over plus independent assortment make those gametes genetically diverse. **(B)**.

Bài tập luyện tập

Crossing over between non-sister chromatids of homologous chromosomes occurs during:

(A) Prophase of mitosis

(B) Prophase I of meiosis

(C) Anaphase II of meiosis

(D) Interphase, before DNA replication

Lời giải chi tiết

Homologous chromosomes synapse and exchange segments at chiasmata during prophase I; mitosis has no synapsis or crossing over at all. **(B)**.

Bài tập luyện tập

A diploid cell has $2n = 6$. State the chromosome number and chromatid status of a cell (a) immediately after telophase I, and (b) immediately after telophase II.

Lời giải chi tiết

(a) After telophase I: $n = 3$ chromosomes, each still composed of 2 sister chromatids (homologs separated in Meiosis I; sister chromatids have not yet separated). (b) After telophase II: $n = 3$ chromosomes, each now a single chromatid (sister chromatids separated in Meiosis II).

Bài tập luyện tập

Which of the following is true of mitosis but NOT of meiosis?

(A) DNA replicates once before division

(B) Homologous chromosomes pair up (synapsis)

(C) Daughter cells are genetically identical to the parent cell

(D) The process produces four daughter cells

Lời giải chi tiết

DNA replication once before division happens in both processes; synapsis and four daughter cells are unique to meiosis. Only genetically-identical daughter cells is unique to mitosis. **(C)**.

Bài tập luyện tập

Drosophila melanogaster has a haploid number of $n = 4$. Ignoring crossing over, how many genetically distinct gamete types can an individual fly produce through independent assortment alone?

Lời giải chi tiết

Each of the 4 homologous pairs independently contributes one of 2 orientations to a gamete: $2^n = 2^4 = 16$ distinct combinations.

Bài tập luyện tập

The law of independent assortment is best explained at the cellular level by:

(A) Random alignment of homologous chromosome pairs at metaphase I

(B) Random separation of sister chromatids at anaphase II

(C) Random crossing over between sister chromatids

(D) Random fusion of two haploid gametes at fertilization

Lời giải chi tiết

Each homologous pair orients randomly and independently of other pairs at metaphase I, which is the cellular basis of independent assortment. **(A)**.

Bài tập luyện tập

In pea plants, tall (T) is dominant to short (t). A tall plant of unknown genotype is crossed with a short plant (tt); the offspring are 42 tall and 39 short. What is the genotype of the tall parent?

Lời giải chi tiết

A $TT \times tt$ cross gives 100% tall offspring; a $Tt \times tt$ testcross gives a $1:1$ tall:short ratio. The observed $42:39$ is close to $1:1$, so the tall parent's genotype is Tt.

Bài tập luyện tập

Cross $AABb \times AaBb$. Find the probability that an offspring has genotype $AaBb$.

Lời giải chi tiết

At the A locus, $AA \times Aa$ gives Aa with probability $\frac{1}{2}$. At the B locus, $Bb \times Bb$ gives Bb with probability $\frac{1}{2}$. By the product rule (independent loci): $P(AaBb) = \frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$.

Bài tập luyện tập

Two pea plants have genotypes Tt and TT (tall dominant). Which statement is correct?

(A) They have different genotypes but the same phenotype (both tall)

(B) They have the same genotype and the same phenotype

(C) They have different phenotypes because Tt is short

(D) They cannot be compared without a Punnett square

Lời giải chi tiết

Tt and TT are different genotypes, but since T is dominant, both are phenotypically tall. **(A)**.

Bài tập luyện tập

A researcher crosses two heterozygous purple-flowered pea plants ($Pp \times Pp$), expecting a $3:1$ (purple:white) ratio among 1000 offspring. She observes 720 purple and 280 white. Conduct a chi-square goodness-of-fit test at $\alpha = 0.05$.

Lời giải chi tiết

Expected: purple $= 0.75 \times 1000 = 750$; white $= 0.25 \times 1000 = 250$.

$$\chi^2 = \frac{(720-750)^2}{750} + \frac{(280-250)^2}{250} = \frac{900}{750} + \frac{900}{250} = 1.2 + 3.6 = 4.8.$$

$df = 2 - 1 = 1$; critical value at $\alpha = 0.05$ is 3.841. Since $4.8 > 3.841$, we **reject** the null hypothesis: the observed data deviate significantly from the expected $3:1$ ratio.

Bài tập luyện tập

In four-o'clock plants, red-flowered (C^RC^R) crossed with white-flowered (C^WC^W) produces all pink-flowered offspring (C^RC^W). This is an example of:

(A) Codominance
(B) Incomplete dominance
(C) Epistasis
(D) Polygenic inheritance

Lời giải chi tiết

The heterozygote shows a single blended, intermediate phenotype (pink), the hallmark of incomplete dominance. **(B)**.

Bài tập luyện tập

A person with blood type AB expresses both A and B antigens simultaneously and distinctly on their red blood cells, rather than a blended intermediate antigen. This pattern of allele expression is:

(A) Incomplete dominance
(B) Codominance
(C) Pleiotropy
(D) Epistasis

Lời giải chi tiết

Both alleles are fully and simultaneously expressed, not blended — this is codominance. **(B)**.

Bài tập luyện tập

Epistasis occurs when:

(A) Two genes on the same chromosome are inherited together

(B) The alleles of one gene mask or modify the phenotypic expression of a different gene

(C) A single gene influences multiple unrelated traits

(D) Heterozygotes show a blended phenotype

Lời giải chi tiết

This is the definition of epistasis (an interaction between two different, non-allelic genes). **(B)**.

Bài tập luyện tập

In Labrador retrievers, gene B (B=black, b=chocolate) determines pigment type, and gene E (E=pigment deposited, e=no pigment deposited, giving yellow fur regardless of B genotype) is epistatic to gene B. A cross of two double heterozygotes ($BbEe \times BbEe$) produces 320 puppies. Predict the expected number of black, chocolate, and yellow puppies.

Lời giải chi tiết

Standard dihybrid genotype fractions: $\frac{9}{16}\ B\_E\_$, $\frac{3}{16}\ bbE\_$, $\frac{3}{16}\ B\_ee$, $\frac{1}{16}\ bbee$. Since ee is epistatic (always yellow, regardless of B), yellow $= \frac{3}{16} + \frac{1}{16} = \frac{4}{16}$. Phenotypic ratio: 9 black : 3 chocolate : 4 yellow (of 16). Expected counts of 320: black $= \frac{9}{16} \times 320 = 180$; chocolate $= \frac{3}{16} \times 320 = 60$; yellow $= \frac{4}{16} \times 320 = 80$ (check: $180 + 60 + 80 = 320$).

Bài tập luyện tập

Human skin color and height are examples of polygenic traits because:

(A) They are controlled by a single gene with many alleles

(B) They are influenced by multiple genes, each contributing a small additive effect, producing continuous phenotypic variation

(C) They show a blended phenotype only in heterozygotes

(D) They are located exclusively on the X chromosome

Lời giải chi tiết

Polygenic traits are shaped by many genes acting additively, producing a continuous (bell-curve) range of phenotypes. **(B)**.

Bài tập luyện tập

The allele responsible for sickle-cell disease affects red blood cell shape, oxygen transport, and malaria resistance simultaneously. This is an example of:

(A) Polygenic inheritance

(B) Pleiotropy

(C) Epistasis

(D) Codominance

Lời giải chi tiết

One gene affecting multiple, seemingly unrelated traits is the definition of pleiotropy. **(B)**.

Bài tập luyện tập

In corn, the genes for seed color (C/c) and seed shape (S/s) are linked. A testcross ($CcSs \times ccss$) produces 1000 offspring: 447 colored-full, 439 colorless-shrunken (parental types), 61 colored-shrunken, and 53 colorless-full (recombinant types). Calculate the recombination frequency and the map distance.

Lời giải chi tiết

Recombinants $= 61 + 53 = 114$. Total $= 447 + 439 + 61 + 53 = 1000$.

$$\text{RF} = \frac{114}{1000} \times 100 = 11.4.$$

The two genes are approximately 11.4 map units (cM) apart.

Bài tập luyện tập

Two genes on the same chromosome show a recombination frequency of 50%. The most likely explanation is:

(A) The genes are extremely close together

(B) The genes are so far apart on the chromosome that crossovers between them are as frequent as independent assortment

(C) No crossing over ever occurs between them

(D) The genes are alleles of one another

Lời giải chi tiết

An RF of 50% is the ceiling reached when genes are far enough apart (or unlinked) that they assort as if independent. **(B)**.

Bài tập luyện tập

A Himalayan rabbit is genetically identical at all body regions. A patch of white fur on its warm back is shaved, and an ice pack is taped over the area while it regrows. Predict the color of the regrown fur and explain why, referencing the norm of reaction.

Lời giải chi tiết

The regrown fur will be **dark**, not white. The temperature-sensitive tyrosinase enzyme is active only at cooler temperatures; the ice pack cools the shaved patch enough for the enzyme to function there and produce pigment, even though that skin region is normally warm (and normally pigment-free). This is a norm of reaction: the same genotype produces different phenotypes depending on the local environmental temperature.

Bài tập luyện tập

Two genetically identical hydrangea clones are grown in different soils: one in acidic soil (blue flowers), one in alkaline soil (pink flowers). This illustrates:

(A) Incomplete dominance

(B) A norm of reaction – the same genotype expressed differently across environments

(C) A new mutation in the alkaline-soil plant

(D) Codominance

Lời giải chi tiết

Same genotype, different phenotype driven by an environmental variable (soil pH/aluminum availability) — a norm of reaction. **(B)**.

Bài tập luyện tập

In humans, an individual's sex is determined by:

(A) The number of autosomes inherited

(B) The presence of the SRY gene on the Y chromosome, which triggers male development in an XY individual

(C) Maternal hormone levels during pregnancy

(D) The number of Barr bodies present at fertilization

Lời giải chi tiết

The Y-linked SRY gene triggers the developmental pathway toward male anatomy. **(B)**.

Bài tập luyện tập

Hemophilia is X-linked recessive. A woman has a hemophiliac father and an unaffected, non-carrier mother; she marries an unaffected man. (a) What is the woman's genotype? (b) Give the probability that a son of this couple is affected, and that a daughter is affected.

Lời giải chi tiết

(a) Her father (X^hY) passed his only X (X^h) to all daughters; her mother (X^HX^H) passed X^H. Woman's genotype: X^HX^h (unaffected carrier). (b) Husband is X^HY. Cross $X^HX^h \times X^HY$: offspring $\frac{1}{4}\,X^HX^H$, $\frac{1}{4}\,X^HX^h$, $\frac{1}{4}\,X^HY$, $\frac{1}{4}\,X^hY$. Probability a **son** is affected $= \frac{1}{2}$ (of sons, half are X^hY). Probability a **daughter** is affected $= 0$ (no daughter can receive two X^h alleles, since the father contributes only X^H to daughters).

Bài tập luyện tập

A phenotypically unaffected woman who carries one recessive allele for an X-linked disorder on one of her two X chromosomes is called a:

(A) Homozygous recessive

(B) Hemizygous individual

(C) Carrier

(D) Mosaic

Lời giải chi tiết

An unaffected heterozygote for a recessive allele is a carrier. **(C)**.

Bài tập luyện tập

If nondisjunction of a single homologous pair occurs at anaphase I (and meiosis II proceeds normally), the four resulting gametes will be:

(A) All four normal (n)

(B) Two normal (n), one $(n+1)$, one $(n-1)$

(C) Two gametes $(n+1)$ and two gametes $(n-1)$ – no normal gametes

(D) All four $(n+1)$

Lời giải chi tiết

Anaphase I nondisjunction sends both homologs to one pole; meiosis II separates sister chromatids normally in both resulting cells, so all four gametes are abnormal: two $n+1$, two $n-1$. **(C)**.

Bài tập luyện tập

A germ cell undergoes nondisjunction of chromosome 21 at anaphase I; meiosis II proceeds normally. (a) State the chromosome-21 content of each of the four resulting gametes. (b) If one such gamete is fertilized by a normal gamete, what condition results, and how many total chromosomes does the zygote have?

Lời giải chi tiết

(a) All four gametes are abnormal for chromosome 21: two carry 2 copies ($n+1=24$ chromosomes total), two carry 0 copies ($n-1=22$ chromosomes total). (b) Fertilizing an $n+1$ gamete (24 chromosomes) with a normal $n=23$ gamete gives $24+23=47$ chromosomes with three copies of chromosome 21 — **trisomy 21 (Down syndrome)**.

Bài tập luyện tập

A male individual has karyotype $47, XXY$, is typically taller than average, and often has reduced fertility. This condition is:

(A) Turner syndrome

(B) Klinefelter syndrome

(C) Down syndrome

(D) Trisomy 18

Lời giải chi tiết

$47, XXY$ (an extra X chromosome in a male) is Klinefelter syndrome. **(B)**.

Bài tập luyện tập

An individual with karyotype $45, X$ (a single X chromosome and no Y) has:

(A) Klinefelter syndrome

(B) Turner syndrome

(C) An extra autosome

(D) XYY syndrome

Lời giải chi tiết

$45, X$ (monosomy of the sex chromosome, in a female) is Turner syndrome. **(B)**.

Bài tập luyện tập

A chromosomal mutation in which a segment is excised, flipped $180°$, and reinserted at the same location (same genetic material, reversed order) is a(n):

(A) Deletion
(B) Duplication
(C) Inversion
(D) Translocation

Lời giải chi tiết

Excision, $180°$ flip, and reinsertion of the same material describes an inversion. **(C)**.

Bài tập luyện tập

A patient's karyotype shows a segment of chromosome 22 exchanged with a segment of chromosome 9, producing the "Philadelphia chromosome" associated with chronic myelogenous leukemia. (a) Name this type of chromosomal structural mutation. (b) Explain how it differs from a deletion.

Lời giải chi tiết

(a) This is a (reciprocal) **translocation** — segments exchanged between two nonhomologous chromosomes (9 and 22). (b) A deletion is an outright *loss* of a chromosome segment with no compensating gain; a translocation *relocates* a segment to a different chromosome (in a reciprocal translocation, material is exchanged rather than lost), though genes disrupted at the breakpoints can still cause disease (here, a fusion gene linked to CML).

Bài tập luyện tập

A cross between two $AaBb$ individuals produces 5 offspring. What is the probability that *none* of the 5 offspring shows the fully recessive ($aabb$) phenotype? What is the probability that *at least one* does?

Lời giải chi tiết

$P(aabb) = \frac{1}{4} \times \frac{1}{4} = \frac{1}{16}$, so $P(\text{not } aabb) = \frac{15}{16}$ per offspring. For 5 independent offspring:

$$P(\text{none } aabb) = \left(\tfrac{15}{16}\right)^5 = \frac{759375}{1048576} \approx 0.724 \ (72.4\%).$$

By the complement rule, $P(\text{at least one } aabb) = 1 - 0.724 = 0.276$ (about 27.6%).

Bài tập luyện tập

Which statement correctly relates linkage to Mendel's law of independent assortment?

(A) Linked genes obey independent assortment perfectly because they are on the same chromosome
(B) Genes located close together on the same chromosome tend to be inherited together and violate independent assortment, unless separated by crossing over
(C) Independent assortment only applies to genes on the X chromosome
(D) Linkage always produces a $9:3:3:1$ phenotypic ratio in a dihybrid cross

Lời giải chi tiết

Linked genes are the exception to independent assortment; crossing over is the only way to recombine them. **(B)**.

Bài tập luyện tập

A woman of genotype I^Ai (blood type A) and a man of genotype I^Bi (blood type B) have a child. What is the probability the child has blood type O?

Lời giải chi tiết

Mother's gametes: I^A or i ($\frac{1}{2}$ each). Father's gametes: I^B or i ($\frac{1}{2}$ each). Type O requires genotype ii: $P(ii) = P(i \text{ from mother}) \times P(i \text{ from father}) = \frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$.

Gene Expression and Regulation

Mục tiêu Unit: Cấu trúc DNA/RNA và nguyên tắc bổ sung Chargaff; cơ chế tái bản DNA (bán bảo toàn, mạch dẫn đầu và mạch ra chậm, các enzyme tham gia, telomere); phiên mã và xử lý tiền mRNA ở sinh vật nhân thực (gắn mũ, đuôi poly-A, cắt nối exon/intron, cắt nối luân phiên); dịch mã (ribosome, codon–anticodon, wobble, các giai đoạn khởi đầu–kéo dài–kết thúc); điều hòa biểu hiện gen ở vi khuẩn (operon *lac*, operon *trp*) và ở sinh vật nhân thực (biểu sinh, yếu tố phiên mã, điều hòa sau phiên mã/dịch mã, microRNA); cơ sở phân tử của sự biệt hóa tế bào; các loại đột biến (điểm, dịch khung) và hậu quả của chúng; và công nghệ sinh học (enzyme cắt giới hạn, điện di, PCR, giải trình tự, CRISPR-Cas9).

6.1 DNA and RNA Structure: A Molecular Foundation

Deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) are polymers of **nucleotides**, each built from three parts: a five-carbon sugar (deoxyribose in DNA, ribose in RNA), a phosphate group, and a nitrogenous base. Successive nucleotides are joined by **phosphodiester bonds** linking the 3′ carbon of one sugar to the 5′ phosphate of the next, giving every nucleic acid strand an inherent chemical direction: a free 5′ phosphate end and a free 3′ hydroxyl end. DNA's nitrogenous bases are the purines **adenine (A)** and **guanine (G)**, and the pyrimidines **cytosine (C)** and **thymine (T)**; RNA replaces thymine with the pyrimidine **uracil (U)**.

Double-stranded DNA forms a double helix of two **antiparallel** strands (one runs 5′ $\rightarrow$3′, its partner 3′ $\rightarrow$5′) held together by hydrogen bonds between complementary bases on opposite strands: A pairs with T (two hydrogen bonds) and G pairs with C (three hydrogen bonds). This complementarity is summarized by **Chargaff's rules**: in any double-stranded DNA, %A $=$ %T and %G $=$ %C, so %A $+$ %G $=$ %T $+$ %C $= 50\%$ of all bases.

Chargaff's rules (double-stranded DNA only): $\%A = \%T$ and $\%G = \%C$, so $\%A + \%G = 50\%$. Given any one percentage, all four are determined. RNA is typically single-stranded, so Chargaff's equalities do not apply to a single RNA strand.

Ví dụ mẫu · Applying Chargaff's rules

A double-stranded DNA sample is 28% adenine. Find the percentages of T, G, and C.
Since $\%A = \%T$: $\%T = 28\%$. Since the four percentages sum to 100% and $\%G = \%C$:

$$\%G + \%C = 100 - 28 - 28 = 44\% \;\Rightarrow\; \%G = \%C = 22\%.$$

Check: $\%A + \%G = 28 + 22 = 50\%$, matching $\%T + \%C = 28 + 22 = 50\%$ (✓).

VN **GIẢI THÍCH TIẾNG VIỆT**

Quy tắc Chargaff chỉ áp dụng cho DNA **mạch kép**: vì A luôn bắt cặp bổ sung với T, và G luôn bắt cặp với C, nên số lượng (và do đó phần trăm) của A phải bằng T, và của G phải bằng C. Biết một tỉ lệ phần trăm là suy ra được cả bốn. Quy tắc này KHÔNG áp dụng cho RNA mạch đơn hay cho một mạch DNA đơn lẻ, vì không có mạch bổ sung để "cân bằng" theo tỉ lệ.

	DNA	RNA
Sugar	Deoxyribose (no 2′-OH)	Ribose (has 2′-OH)
Bases	A, T, G, C	A, U, G, C
Strands	Double-stranded (usually)	Single-stranded (usually)
Stability	More chemically stable; suited to long-term storage	Less stable, more reactive
Role	Long-term genetic information storage	mRNA (message), tRNA (adaptor), rRNA (ribosome structure/catalysis)

Structural and functional differences between DNA and RNA.

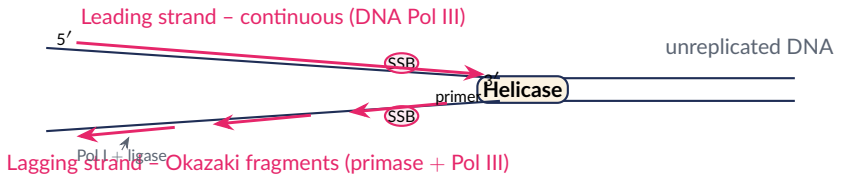
6.2 DNA Replication

DNA replication is **semiconservative**: each of the two resulting double helices contains one original (parental) strand and one newly synthesized strand. This was confirmed by the classic Meselson–Stahl density-gradient experiment, which distinguished semiconservative replication from two rival hypotheses (conservative and dispersive) using ^{15}N/^{14}N-labeled DNA. Replication begins at specific **origins of replication**, where **helicase** unwinds and separates the two parental strands, opening a replication "bubble" with a **replication fork** at each end. **Single-strand binding proteins (SSB)** coat the exposed single strands to keep them from re-annealing or being degraded, while **topoisomerase** relieves the mechanical strain (supercoiling) that builds up ahead of the fork as the helix unwinds.

DNA polymerases cannot start a new strand from scratch; they can only extend an existing 3′ end. **Primase** therefore lays down a short **RNA primer** complementary to the template, providing the free 3′-OH that **DNA polymerase III** (the main replicative polymerase in bacteria) uses to synthesize new DNA, always in the **5′ →3′** direction, while reading the template strand $3' \to 5'$.

Why the two new strands are made differently

Because the two parental strands are antiparallel, and DNA polymerase only synthesizes $5' \to 3'$, the two new strands must be made differently at a single fork that opens in one direction. The **leading strand** is synthesized **continuously** in the same direction the fork is opening, needing only one primer at the origin. The **lagging strand** is synthesized **discontinuously**, in short **Okazaki fragments**, each primed separately by primase and extended by Pol III back toward the previous fragment, because its polymerase must periodically restart as the fork exposes new template behind the direction of its own synthesis.



The replication fork: helicase unwinds the double helix; single-strand binding proteins (SSB) stabilize the exposed single strands. The leading strand is synthesized continuously toward the fork; the lagging strand is synthesized discontinuously as Okazaki fragments (each primed by primase). DNA Pol I later replaces the RNA primers with DNA, and ligase seals the remaining nicks.

After Pol III finishes each Okazaki fragment, **DNA polymerase I** removes the RNA primers (via its $5' \to 3'$ exonuclease activity) and fills the resulting gaps with DNA; **DNA ligase** then seals the remaining nicks in the sugar-phosphate backbone, joining the fragments into one continuous strand.

Replication machinery at a glance: Helicase (unwinds) → SSB proteins (stabilize single strands) → Primase (lays RNA primers) → DNA Pol III (synthesizes new DNA $5' \to 3'$) → DNA Pol I (replaces primers with DNA) → Ligase (seals nicks).

VN **GIẢI THÍCH TIẾNG VIỆT**

Tái bản DNA là **bán bảo toàn** (semiconservative): mỗi phân tử DNA con gồm một mạch cũ (từ DNA mẹ) và một mạch mới tổng hợp. Vì DNA polymerase chỉ tổng hợp theo chiều $5' \to 3'$ và hai mạch khuôn ngược chiều nhau, nên tại một chạc ba tái bản: **mạch dẫn đầu** (leading strand) được tổng hợp liên tục, còn **mạch ra chậm** (lagging strand) được tổng hợp thành từng đoạn ngắn gọi là **đoạn Okazaki**, mỗi đoạn cần một đoạn mồi RNA (primer) riêng do primase tạo ra.

(!) Lỗi thường gặp: It is tempting to think the lagging strand is synthesized "$3' \to 5'$" because it looks backward in diagrams. In fact, *every* DNA polymerase – on both the leading and lagging strand – synthesizes new DNA only in the $5' \to 3'$ direction. What differs is the *overall* direction of synthesis relative to the moving fork: the leading strand's synthesis direction matches the fork's movement (continuous), while the lagging strand's synthesis direction is opposite to the fork's movement, forcing it to restart repeatedly (discontinuous, as Okazaki fragments).

DNA polymerases also proofread as they go: Pol III's $3' \to 5'$ exonuclease activity detects and excises mismatched nucleotides immediately after they are added, dramatically increasing replication fidelity. Combined with post-replication mismatch repair, the overall error rate of DNA replication is roughly 1 in 10^9–10^{10} base pairs.

Ví dụ mẫu · Estimating Okazaki fragment number

In bacteria, Okazaki fragments average about 1000 nucleotides in length. If one round of replication of the 4.6×10^6 bp *E. coli* chromosome proceeds bidirectionally from a single origin, roughly how many Okazaki fragments are synthesized in total (considering only the lagging-strand template of both forks combined)?

Bidirectional replication from one origin creates two forks, each copying about half the chromosome; together, the two lagging-strand templates span approximately the full genome length, 4.6×10^6 nt.

$$\text{Number of fragments} \approx \frac{4.6 \times 10^6 \text{ nt}}{1000 \text{ nt/fragment}} \approx 4{,}600 \text{ fragments.}$$

Each of these ~ 4600 fragments needs its own RNA primer, later removed by DNA Pol I and sealed by ligase – illustrating why the lagging strand is enzymatically far more "expensive" to replicate than the leading strand, which needs only one primer for the whole strand.

6.2.1 Telomeres and the end-replication problem

Linear eukaryotic chromosomes face a special difficulty: on the lagging strand, once the RNA primer at the extreme 5′ end of a chromosome is removed, there is no upstream 3′-OH for any polymerase to extend from, so that short stretch cannot be replaced. Each round of replication therefore leaves the daughter DNA slightly shorter at that end. Repetitive, noncoding **telomere** sequences (in humans, TTAGGG repeats) cap chromosome ends and absorb this progressive shortening, protecting essential genes from being eroded. The enzyme **telomerase**, a ribonucleoprotein carrying its own internal RNA template, can extend the 3′ overhang at chromosome ends by adding telomeric repeats, counteracting shortening; it is active in germ-line cells, stem cells, and (abnormally) many cancer cells, but is largely inactive in most somatic cells, where progressive telomere shortening is linked to cellular aging and replicative senescence.

VN **GIẢI THÍCH TIẾNG VIỆT**

Vì DNA polymerase không thể khởi đầu tổng hợp mà không có mồi, và không còn mạch nào để mồi thêm ở đầu tận cùng $5'$ của mạch ra chậm sau khi đoạn mồi RNA cuối cùng bị loại bỏ, nên đầu mút nhiễm sắc thể (telomere) bị ngắn dần sau mỗi lần tái bản – gọi là **vấn đề tái bản đầu mút** (end-replication problem). Telomerase giải quyết vấn đề này bằng cách kéo dài thêm đoạn lặp telomere, nhưng enzyme này thường chỉ hoạt động mạnh ở tế bào mầm, tế bào gốc, và (bất thường) ở tế bào ung thư.

6.3 Transcription and RNA Processing

Transcription copies a gene's information from DNA into a complementary, single-stranded **RNA** molecule. **RNA polymerase** binds a specific DNA sequence, the **promoter**, which orients the enzyme and determines which of the two DNA strands is read. Only one strand, the **template strand**, is actually read by RNA polymerase, and it is read $3' \to 5'$; the resulting RNA is synthesized $5' \to 3'$ and is complementary to the template (using U in place of T). The other DNA strand, the **coding** (or **sense**) strand, is not read directly, but has the same sequence as the mRNA transcript (substituting T for U) and runs in the same $5' \to 3'$ direction.

(!) Lỗi thường gặp: The **template strand** (read by RNA polymerase, $3' \to 5'$) and the **coding/sense strand** (same sequence as the mRNA, not read directly) are easy to mix up. A quick check: the mRNA should always match the coding strand letter-for-letter (with U replacing T) and run in the *same* $5' \to 3'$ direction as the coding strand – never the template strand.

Ví dụ mẫu · DNA template → mRNA

A gene's template strand reads 3′-TACCGAAAAGCTATT-5′. Write the resulting mRNA transcript, with correct 5′/3′ ends.

RNA polymerase reads the template $3' \to 5'$ (left to right, as written) and builds mRNA $5' \to 3'$ by complementary base pairing (A↔U, T↔A, G↔C, C↔G):

Template ($3' \to 5'$): T A C C G A A A A G C T A T T

mRNA ($5' \to 3'$): 5′-A U G G C U U U U C G A U A A-3′.

Grouped in codons: AUG-GCU-UUU-CGA-UAA.

VN **GIẢI THÍCH TIẾNG VIỆT**

Mạch khuôn (template strand) được RNA polymerase đọc theo chiều $3' \to 5'$, và mRNA được tổng hợp theo chiều $5' \to 3'$, luôn bổ sung và đối song song (antiparallel) với mạch khuôn. Vì vậy trình tự mRNA giống hệt mạch mã hoá (coding/sense strand) – chỉ khác là U thay cho T – đó là lý do mạch mã hoá được gọi là "mạch có ý nghĩa", cùng chiều và cùng trình tự với mRNA.

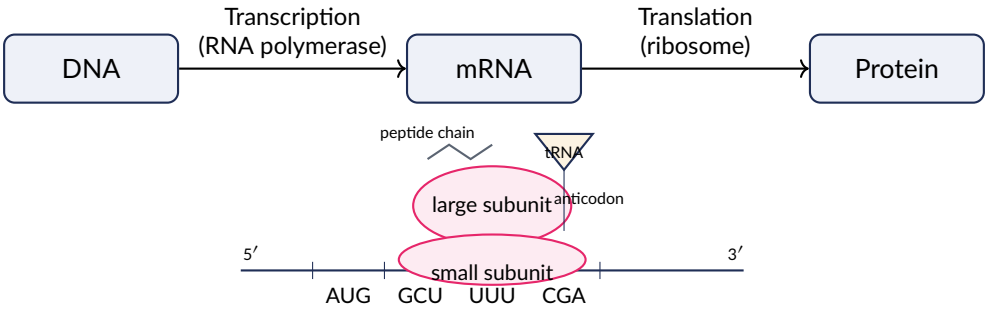
6.3.1 Pre-mRNA processing in eukaryotes

In eukaryotes, the initial RNA polymerase product (**pre-mRNA**) is extensively modified in the nucleus before export to the cytoplasm:

- A modified guanine nucleotide, the **5′ cap**, is added to the 5′ end shortly after transcription begins – protecting the transcript from degradation and helping ribosomes recognize the mRNA during translation initiation.
- A **poly-A tail** (up to ~ 250 adenine nucleotides) is added enzymatically to the 3′ end after cleavage of the primary transcript – also protecting against degradation and assisting nuclear export and

translation.

- **Splicing**: eukaryotic genes typically contain **introns** (noncoding intervening sequences) interspersed among **exons** (coding sequences retained in the mature mRNA). A large ribonucleoprotein complex, the **spliceosome**, recognizes intron boundaries, excises each intron as a loop, and joins the flanking exons together.
- **Alternative splicing**: different subsets of exons can be joined from the same pre-mRNA transcript in different cells or conditions, producing multiple distinct mature mRNAs – and therefore multiple protein **isoforms** – from a single gene. This greatly expands the protein-coding capacity of a genome beyond its raw gene count.



Overview of gene expression (top): DNA → mRNA → protein. Translation snapshot (bottom): the ribosome (large + small subunit) moves along mRNA one codon at a time; a charged tRNA delivers its amino acid to the growing peptide chain by anticodon–codon pairing.

VN **GIẢI THÍCH TIẾNG VIỆT**

Cắt nối luân phiên (alternative splicing) là lý do một gen duy nhất có thể tạo ra nhiều loại protein khác nhau (isoform) tuỳ theo tổ hợp exon nào được giữ lại trong mRNA trưởng thành. Đây là một cơ chế điều hoà biểu hiện gen quan trọng, giúp bộ gen người ($\sim 20{,}000$ gen) mã hoá được số lượng protein lớn hơn nhiều so với số gen.

6.4 Translation

Translation converts the sequence of codons in mRNA into a sequence of amino acids (a polypeptide), carried out by **ribosomes** – complexes of ribosomal RNA (rRNA) and protein, organized into a **large subunit** and a **small subunit**. The small subunit binds mRNA; the large subunit contains the site where peptide bonds form, a reaction catalyzed by rRNA itself (making the ribosome a **ribozyme**).

Each three-nucleotide **codon** in the mRNA specifies one amino acid (or a stop signal). **Transfer RNAs (tRNAs)** are adaptor molecules that physically link codons to amino acids: each tRNA carries a specific amino acid at its 3′ end and has a complementary three-base **anticodon** that base-pairs with an mRNA codon. **Aminoacyl-tRNA synthetases** – one specific enzyme for each of the 20 amino acids – catalyze "charging": attaching the correct amino acid to its corresponding tRNA(s), using ATP.

Wobble base pairing: pairing at the third codon position (which pairs with the first, 5′, position of the anticodon) is less strict than at the first two positions, so a single tRNA can often recognize more than one codon differing only at the third base. This is why only about 40–45 distinct tRNAs are needed to read all 61 sense codons.

Ví dụ mẫu · Anticodon–codon pairing

A tRNA has the anticodon 3′-AAG-5′. Which mRNA codon does it pair with, and which amino acid does it carry?

Anticodon and codon pair antiparallel, base for base: A↔U and G↔C.

$$\text{Anticodon } 3'\text{-A A G-}5' \quad \longleftrightarrow \quad \text{Codon } 5'\text{-U U C-}3'.$$

UUC codes for **Phe** (phenylalanine) – so this tRNA is "charged" with phenylalanine by phenylalanyl-tRNA synthetase.

1st	U	C	A	G	3rd
U	Phe	Ser	Tyr	Cys	U
U	Phe	Ser	Tyr	Cys	C
U	Leu	Ser	Stop	Stop	A
U	Leu	Ser	Stop	Trp	G
C	Leu	Pro	His	Arg	U
C	Leu	Pro	His	Arg	C
C	Leu	Pro	Gln	Arg	A
C	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
A	Ile	Thr	Asn	Ser	C
A	Ile	Thr	Lys	Arg	A
A	Met*	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
G	Val	Ala	Asp	Gly	C
G	Val	Ala	Glu	Gly	A
G	Val	Ala	Glu	Gly	G

Standard genetic code (RNA codons → amino acid). Read: first base (row group) + second base (column) + third base (rightmost column) = codon. *AUG codes for Met and also serves as the start codon.

Properties of the genetic code

Triplet: three nucleotides (a codon) specify one amino acid. **Non-overlapping:** the mRNA is read in successive, non-overlapping triplets from a fixed reading frame set by the start codon. **Redundant (degenerate):** most amino acids are specified by more than one codon (up to six for Leu, Ser, Arg), largely due to wobble at the third position; degeneracy provides some buffering against mutation. **(Nearly) universal:** with a few minor exceptions (e.g., some mitochondrial genomes), essentially all known organisms use the same genetic code – strong evidence of common ancestry.

VN **GIẢI THÍCH TIẾNG VIỆT**

Bốn tính chất của mã di truyền: **bộ ba** (triplet) – 3 nucleotide mã hoá 1 amino acid; **không chồng lấp** (non-overlapping) – đọc liên tiếp từng bộ ba, không dùng lại nucleotide; **thoái hoá / dư thừa** (degenerate/redundant) – một amino acid có thể được mã hoá bởi nhiều codon khác nhau; **phổ biến gần như toàn bộ sinh giới** (nearly universal) – hầu hết sinh vật dùng chung một bảng mã di truyền, minh chứng cho nguồn gốc chung của sự sống.

6.4.1 Initiation, elongation, and termination

Initiation: the small ribosomal subunit binds the mRNA and locates the **start codon**, **AUG**, which also codes for methionine. An initiator tRNA carrying methionine pairs with the start codon in the ribosome's **P site**; the large subunit then joins to complete the functional ribosome.

Elongation: a charged tRNA with an anticodon complementary to the next codon enters the ribosome's **A site** (aminoacyl site). The ribosome (via rRNA-catalyzed peptidyl transfer) forms a **peptide bond** between the amino acid in the A site and the growing polypeptide chain held by the tRNA in the **P site** (peptidyl site). The ribosome then **translocates** one codon along the mRNA: the now-uncharged tRNA moves from the P site to the **E site** (exit site) and leaves, the tRNA bearing the growing chain moves from A to P, and a new codon is exposed in the now-empty A site. This cycle repeats, adding one amino acid per turn.

Termination: when a **stop codon** (UAA, UAG, or UGA) enters the A site, no tRNA recognizes it (there is no corresponding anticodon); instead a **release factor** protein binds, triggering hydrolysis of the bond between the polypeptide and the final tRNA, releasing the completed protein and disassembling the ribosome.

Ví dụ mẫu · Translating an mRNA sequence

Translate the mRNA 5′-AUG-GCU-UUU-CGA-UAA-3′ (from the transcription example above) into its amino acid sequence, using the standard genetic code.

Reading codon by codon: AUG = Met (start); GCU = Ala; UUU = Phe; CGA = Arg; UAA = Stop (no amino acid added; translation terminates here).

Protein: Met — Ala — Phe — Arg.

VN **GIẢI THÍCH TIẾNG VIỆT**

Dịch mã trải qua ba giai đoạn: **khởi đầu** (tiểu đơn vị nhỏ gắn mRNA, tRNA khởi đầu mang Met bắt cặp với codon mở đầu AUG tại vị trí P, tiểu đơn vị lớn gắn vào); **kéo dài** (tRNA mới mang amino acid vào vị trí A, hình thành liên kết peptide, ribosome dịch chuyển một codon: A→P→E); **kết thúc** (codon dừng UAA/UAG/UGA không có tRNA tương ứng, yếu tố giải phóng (release factor) gắn vào, giải phóng chuỗi polypeptide).

6.5 Regulation of Gene Expression in Prokaryotes: Operons

Bacteria conserve energy by producing certain proteins only when needed, largely by controlling transcription. Many bacterial genes for a shared metabolic pathway are organized into an **operon**: a single promoter and operator controlling transcription of several structural genes together as one polycistronic mRNA.

6.5.1 The lac operon: an inducible operon

The *E. coli* ***lac*** **operon** contains three structural genes (*lacZ*, *lacY*, *lacA*) encoding enzymes for lactose metabolism, downstream of a **promoter (P)** and **operator (O)**. A separate regulatory gene, *lacI*, constitutively produces the **lac repressor** protein. By default (no lactose), the repressor binds the operator, physically blocking RNA polymerase from transcribing the structural genes – the operon is **OFF**. When lactose is present, a metabolite of lactose (**allolactose**) binds the repressor, changing its shape so it can no longer bind the operator; RNA polymerase is then free to transcribe *lacZYA* – the operon is **induced (ON)**. Because the regulatory protein here *blocks* transcription by default and is removed by the inducer, the *lac* operon is called **inducible**.

Lactose metabolism is also coupled to the cell's preferred sugar, glucose, through **catabolite repression**. When glucose is scarce, intracellular cyclic AMP (cAMP) rises and binds an activator protein, **CAP** (catabolite activator protein); the cAMP–CAP complex binds a site near the promoter and helps RNA polymerase bind more effectively, boosting transcription. When glucose is abundant, cAMP falls, CAP is inactive, and transcription – even with the repressor removed – stays low. This ensures the cell fully commits to lactose metabolism only when lactose is present *and* glucose (the preferred energy source) is scarce.

The *lac* operon: **left**, no lactose – the active repressor bound at the operator (O) blocks RNA polymerase; **right**, lactose present – allolactose inactivates the repressor, freeing the operator so RNA polymerase can transcribe *lacZYA*.

Ví dụ mẫu · Determining lac operon activity

For each combination of lactose and glucose availability, state whether the *lac* operon is transcribed and explain why.

Lactose	Glucose	Repressor / CAP state	Transcription
Absent	High	Repressor bound to O (blocks); CAP inactive	**Off** (double block)
Absent	Low	Repressor bound to O (blocks); CAP active but irrelevant	**Off** (repressor blocks)
Present	High	Repressor released; CAP inactive (low cAMP)	**Low/basal** (no CAP boost)
Present	Low	Repressor released; CAP active (high cAMP)	**High** (maximal induction)

Maximal transcription requires *both* conditions at once: lactose present (to release the repressor from the operator) *and* glucose scarce (so active CAP helps RNA polymerase bind the promoter efficiently).

(!) Lỗi thường gặp: It is a common error to assume lactose alone maximizes *lac* operon transcription. Removing the repressor (via lactose/allolactose) only takes the "brake" off; without low glucose (and therefore active CAP), RNA polymerase still binds the promoter poorly, giving only a low, basal transcription level. Full induction needs lactose present *and* glucose scarce at the same time.

6.5.2 The trp operon: a repressible operon

The *trp* operon encodes enzymes for **tryptophan biosynthesis** and behaves oppositely to *lac* in one key sense: it is normally **ON** (transcribed), because its repressor is synthesized in an **inactive** form that cannot bind the operator by itself. When tryptophan is abundant in the cell, it acts as a **corepressor**, binding the trp repressor and activating it; the activated repressor then binds the operator and shuts down transcription. This is a classic case of **feedback inhibition** at the level of gene expression: the end product of a pathway (tryptophan) suppresses further synthesis of the enzymes that make it. Because the regulatory protein here becomes active (and blocks transcription) only when bound by a corepressor, the *trp* operon is called **repressible**.

VN **GIẢI THÍCH TIẾNG VIỆT**

Operon *lac* là operon **cảm ứng** (inducible): mặc định TẮT, chỉ được "mở" khi có lactose làm bất hoạt protein ức chế. Operon *trp* là operon **kìm hãm** (repressible): mặc định BẬT (vì protein ức chế mặc định không hoạt động), chỉ bị "tắt" khi tryptophan (sản phẩm cuối) dư thừa gắn vào protein ức chế làm nó hoạt hoá và khoá operator lại – đây là ức chế ngược (feedback inhibition).

VN **GIẢI THÍCH TIẾNG VIỆT**
Kiểm soát dị hoá (catabolite repression) qua CAP/cAMP: khi glucose ít, cAMP tăng, phức hợp cAMP–CAP gắn gần promoter giúp RNA polymerase bám tốt hơn ⇒ tăng phiên mã operon *lac*. Khi glucose nhiều, cAMP giảm, CAP không hoạt động ⇒ dù có lactose, phiên mã vẫn ở mức thấp. Đây là lý do vi khuẩn "ưu tiên" sử dụng glucose hơn lactose.

6.6 Regulation of Gene Expression in Eukaryotes

Eukaryotic gene expression is regulated at many points beyond the simple on/off logic of a bacterial operon, from chromatin structure all the way through to protein degradation.

6.6.1 Chromatin remodeling and epigenetics

DNA in eukaryotic cells is packaged with histone proteins into **chromatin**; how tightly that chromatin is packed strongly affects whether genes in a region can be transcribed. **Histone acetylation** – addition of acetyl groups to positively charged histone tails – neutralizes their charge, loosening histone–DNA contacts and opening chromatin into an accessible, transcriptionally active state (**euchromatin**). Removing these acetyl groups (deacetylation), or certain patterns of histone methylation, re-condenses chromatin into a more closed, transcriptionally silent state (**heterochromatin**). **DNA methylation** – addition of methyl groups directly to cytosine bases, often at CpG-rich regions near promoters – generally **silences** genes, both by hindering transcription factor binding directly and by recruiting proteins that further condense chromatin. These heritable, DNA-sequence-independent chemical marks are studied under **epigenetics**.

> **Loosen → activate, tighten → silence:** histone acetylation and DNA demethylation are generally associated with active transcription; histone deacetylation and DNA methylation are generally associated with gene silencing.

VN **GIẢI THÍCH TIẾNG VIỆT**
Biểu sinh (epigenetics) là những thay đổi có thể di truyền trong biểu hiện gen mà KHÔNG làm thay đổi trình tự DNA. Hai cơ chế chính: **methyl hoá DNA** (gắn nhóm methyl vào cytosine, thường làm im lặng gen) và **biến đổi histone** – ví dụ **acetyl hoá histone** làm lỏng cấu trúc nhiễm sắc chất, thúc đẩy phiên mã; khử acetyl làm chặt lại, ức chế phiên mã.

6.6.2 Transcription factors, enhancers, and promoters

Eukaryotic transcription requires **general transcription factors** to assemble RNA polymerase II at the promoter, but the *level* of transcription is fine-tuned by **specific transcription factors** (activators or repressors) that bind regulatory DNA sequences – **enhancers** (which can lie thousands of base pairs away, brought into contact with the promoter by DNA looping) and **silencers**. Different cell types express different combinations of transcription factors, so the same enhancer/promoter region can be bound very differently in different cells – a **combinatorial control** strategy that lets a limited number of regulatory proteins generate many distinct expression patterns.

6.6.3 Post-transcriptional and post-translational regulation

Regulation continues after an mRNA is made:

- **Alternative splicing** generates multiple mRNAs/protein isoforms from one gene (Section 6.3).
- **mRNA stability/degradation**: sequences in the 3′ untranslated region (UTR) and the length of the poly-A tail influence how long an mRNA persists before being degraded – a longer-lived mRNA is translated more times, producing more protein.
- **MicroRNAs (miRNA)**: short (~ 21–23 nucleotide) noncoding RNAs that base-pair with complementary sequences (often in the 3′ UTR) of target mRNAs, typically as part of the **RISC** complex.

This either blocks translation of the target mRNA or marks it for degradation, silencing gene expression post-transcriptionally.

Finally, **post-translational modification** can regulate an already-made protein: phosphorylation, cleavage of an inactive precursor into an active protein, addition of other chemical groups, and tagging with **ubiquitin** (which marks proteins for destruction by the proteasome) all alter a protein's activity, localization, or lifespan without changing how much mRNA was made.

VN **GIẢI THÍCH TIẾNG VIỆT**

Điều hoà biểu hiện gen ở sinh vật nhân thực diễn ra ở NHIỀU cấp độ, không chỉ giới hạn ở phiên mã: (1) cấu trúc nhiễm sắc chất/biểu sinh; (2) yếu tố phiên mã + enhancer/promoter; (3) sau phiên mã (cắt nối luân phiên, độ bền mRNA, microRNA); (4) sau dịch mã (biến đổi hoá học, phân giải protein qua ubiquitin–proteasome). Đây là lý do tế bào có thể phản ứng rất linh hoạt và chính xác với tín hiệu môi trường/phát triển.

Where regulation can act along the gene-expression pathway: chromatin structure → transcription initiation (TFs, enhancers) → RNA processing (splicing) → mRNA transport/stability (miRNA, UTR elements) → translation initiation → post-translational modification/degradation. A cell can tune protein output at any – or several – of these steps.

6.7 Gene Expression and Cell Specialization

Nearly every somatic cell in a multicellular organism carries the same genome (with rare exceptions, such as mature red blood cells that lose their nucleus, or lymphocytes that rearrange immunoglobulin genes). Yet a neuron, a muscle cell, and a skin cell look and function completely differently. This is possible because cells express only a subset of their genes at any time – **differential gene expression** – so each cell type produces its own characteristic proteome.

During development, cascades of **regulatory proteins** (transcription factors) and extracellular **signaling molecules** progressively restrict which genes a cell can express, committing it to a particular fate. In some cases, a single "master regulatory" transcription factor is sufficient to redirect a cell's identity – for example, forced expression of the transcription factor **MyoD** in cultured non-muscle cells can activate the entire suite of muscle-specific genes, pushing them toward a muscle-like phenotype. Once established, these patterns of gene expression are often reinforced and stably maintained across cell divisions by the epigenetic marks (Section 6.1) laid down during differentiation.

VN **GIẢI THÍCH TIẾNG VIỆT**

Mọi tế bào soma của một cơ thể (từ một hợp tử duy nhất) đều mang bộ gen giống hệt nhau, nhưng biểu hiện các gen KHÁC NHAU – đó gọi là **biểu hiện gen khác biệt** (differential gene expression), và chính điều này tạo ra sự **biệt hoá tế bào** (cell differentiation): tế bào cơ biểu hiện mạnh gen actin/myosin, tế bào thần kinh biểu hiện mạnh gen kênh ion và protein dẫn truyền thần kinh, dù cả hai có cùng DNA.

Same genome, different proteome: cell identity is determined not by which genes a cell *has*, but by which genes it *expresses* – controlled by the regulatory proteins, signaling pathways, and epigenetic state established during development.

6.8 Mutations

A **mutation** is any permanent change in a DNA sequence. Mutations can arise spontaneously from errors during **DNA replication** that escape proofreading and repair, from chemical **mutagens** (e.g., base analogs, intercalating agents that distort the helix), or from **radiation** (UV light causes adja-

cent pyrimidines to form thymine dimers; ionizing radiation, such as X-rays, can break DNA strands outright).

6.8.1 Point mutations

A **point mutation** substitutes a single nucleotide for another. Its effect on the resulting protein depends on the genetic code and the mutation's position:

- **Silent mutation**: the changed codon still specifies the *same* amino acid (thanks to codon degeneracy, especially wobble at the third position). The DNA sequence changes, but the protein sequence does not.
- **Missense mutation**: the changed codon specifies a *different* amino acid. The effect ranges from negligible (a "conservative" substitution to a chemically similar amino acid, often in a non-critical region) to severe (a drastic change at a functionally critical position – e.g., the single missense mutation underlying sickle-cell disease).
- **Nonsense mutation**: the changed codon becomes a premature **stop codon**, truncating the protein. This is usually the most damaging type of point mutation, since the protein loses its entire C-terminal portion and is often nonfunctional.

(!) Lỗi thường gặp: A **silent** mutation still changes the *DNA and mRNA sequence* – it is a real mutation, detectable by sequencing. What makes it "silent" is only that the resulting *codon still specifies the same amino acid*, so the protein's amino acid sequence is unaffected. "Silent" describes the phenotypic/protein-level consequence, not the absence of a DNA-level change.

Ví dụ mẫu · Classifying point mutations

Using the codon table, classify each single-nucleotide substitution below (drawn from the reference gene fragment AUG-GCU-UUU-CGA-UAA used in earlier examples).

(a) Codon 3, UUU → UUC: both UUU and UUC code for **Phe** ⇒ **silent** (no change to the protein).

(b) Codon 3, UUU → UCU: UUU = Phe, but UCU = Ser ⇒ **missense** (Phe → Ser; since Phe is nonpolar/aromatic and Ser is small and polar, this substitution could plausibly disrupt local protein structure).

(c) Codon 4, CGA → UGA: CGA = Arg, but UGA is a **stop** codon ⇒ **nonsense** (the protein is truncated immediately after codon 3, losing the normal C-terminal residue and stop – here, losing Arg).

6.8.2 Frameshift mutations

Insertions or deletions of nucleotides can be far more disruptive than substitutions. If the number of nucleotides inserted or deleted is *not* a multiple of three, every downstream codon is read in a shifted frame from that point onward – a **frameshift mutation**. This typically scrambles the entire downstream amino acid sequence and often introduces a premature stop codon by chance, usually producing a severely truncated, nonfunctional protein. In contrast, an insertion or deletion of exactly **three** nucleotides (or a multiple of three) adds or removes one (or more) whole codon(s) but leaves the reading frame – and therefore all other codons – intact.

Ví dụ mẫu · Frameshift vs. in-frame indel

Starting from mRNA 5′-AUG-GCU-UUU-CGA-UAA-3′ (protein Met-Ala-Phe-Arg-Stop), compare the effect of different insertions placed right after the start codon.

$+1$ **insertion** (insert G): new sequence AUG-GGC-UUU-UCG-AUA-A(...) → codons AUG(Met)

GGC(Gly) UUU(Phe) UCG(Ser) AUA(Ile)...– every codon after the insertion point is shifted; the protein reads Met-Gly-Phe-Ser-Ile-..., completely different from the original, with no stop codon yet in sight (translation continues until a chance stop codon appears downstream).
-1 **deletion** (delete the first G of codon 2): new sequence AUG-CUU-UUC-GAU-AA(...) → codons AUG(Met) CUU(Leu) UUC(Phe) GAU(Asp)...– again shifted and scrambled from that point on.
$+3$ **insertion** (insert a full codon, AAA): new sequence AUG-AAA-GCU-UUU-CGA-UAA → codons AUG(Met) AAA(Lys) GCU(Ala) UUU(Phe) CGA(Arg) UAA(Stop) – the reading frame is preserved; the protein simply gains one extra residue, Met-**Lys**-Ala-Phe-Arg, with the rest of the sequence unchanged.

(!) Lỗi thường gặp: Do not assume "bigger change = worse outcome." A large in-frame insertion/deletion (a multiple of 3 nt) can be relatively mild, simply adding or removing a few amino acids while preserving the rest of the protein. A *single*-nucleotide insertion or deletion, though smaller, is usually far more damaging, because it shifts the reading frame for the entire remainder of the gene.

6.8.3 Location matters

The phenotypic consequence of a mutation depends heavily on *where* it occurs. A mutation in a **coding (exon) region** can alter the protein sequence as described above. A mutation in a **regulatory region** (e.g., a promoter or enhancer) may not change the protein's amino acid sequence at all, but can change *how much*, *when*, or *where* the gene is expressed – sometimes with major phenotypic consequences. A mutation within an **intron** often has no effect, since introns are spliced out of the mature mRNA – unless the mutation disrupts a splice-site sequence recognized by the spliceosome, in which case splicing itself can go wrong (e.g., intron retention or exon skipping).

VN **GIẢI THÍCH TIẾNG VIỆT**
Hậu quả của một đột biến phụ thuộc rất nhiều vào **vị trí**: đột biến trong vùng mã hoá (exon) có thể làm thay đổi protein; đột biến trong vùng điều hoà (promoter/enhancer) có thể không đổi trình tự protein nhưng làm thay đổi MỨC ĐỘ/THỜI ĐIỂM biểu hiện gen; đột biến trong intron thường vô hại (vì bị cắt bỏ khi ghép nối) – TRỪ KHI nó phá vỡ vị trí cắt nối, khi đó chính quá trình ghép nối bị lỗi.

6.9 Biotechnology: Tools for Studying and Manipulating DNA

6.9.1 Restriction enzymes and recombinant DNA

Bacteria defend against invading viral DNA using **restriction enzymes** (restriction endonucleases), each of which recognizes a specific, usually palindromic, DNA sequence (a **recognition site**, typically 4–8 bp) and cuts the DNA there, often leaving short single-stranded overhangs ("sticky ends") that can base-pair with any other DNA cut by the same enzyme. This makes it possible to build **recombinant DNA**: a fragment of DNA from one source (e.g., a gene of interest) is cut with a restriction enzyme and spliced – via complementary sticky ends and **DNA ligase** – into a **plasmid vector** (a small circular DNA molecule) cut with the same enzyme. The recombinant plasmid can then be introduced into bacteria (transformation), which replicate it and can express the inserted gene.

6.9.2 Gel electrophoresis

Gel electrophoresis separates DNA fragments by size. DNA is uniformly negatively charged (from its phosphate backbone), so when a voltage is applied across a porous gel, all fragments migrate toward

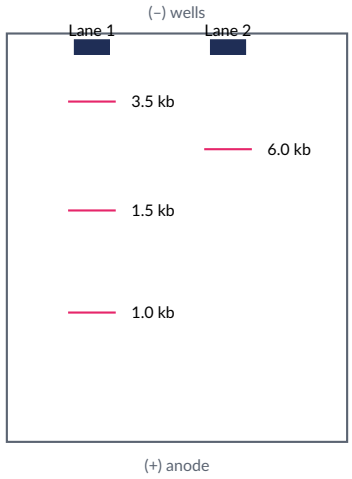
the positive electrode; **smaller fragments move farther** through the gel's pores in a given time than larger ones, which are more impeded. After electrophoresis, fragment sizes can be read from their migration distance (typically compared against a DNA ladder of known sizes).

Ví dụ mẫu · Restriction digestion and gel migration

A 5.0 kb circular plasmid is cut with a restriction enzyme that recognizes 3 sites on the plasmid. (a) How many fragments result? (b) If the resulting fragments are 2.5 kb, 1.5 kb, and 1.0 kb, rank them by migration distance on a gel, from *closest* to the well to *farthest*.

(a) For a *circular* DNA molecule, the number of fragments equals the number of cut sites (the first cut linearizes the circle; each additional cut then adds one more fragment): 3 sites $\Rightarrow$ **3 fragments**. (Check: $2.5 + 1.5 + 1.0 = 5.0$ kb, matching the plasmid's total size.)

(b) Larger fragments migrate the least; smaller fragments migrate the farthest: closest to the well $\rightarrow$ farthest: 2.5 kb $\rightarrow$ 1.5 kb $\rightarrow$ 1.0 kb.



Agarose gel electrophoresis: DNA (negatively charged) migrates from the wells toward the positive electrode; **smaller fragments migrate farther** in a given time because they move more easily through the gel matrix. Lane 1 shows three fragments from a digest (3.5, 1.5, 1.0 kb); Lane 2 shows a single 6.0 kb linearized fragment.

VN **GIẢI THÍCH TIẾNG VIỆT**

Enzyme cắt giới hạn nhận diện một trình tự DNA đặc hiệu (thường đối xứng, palindromic) và cắt tại đó, thường tạo đầu dính (sticky ends) có thể ghép nối bổ sung với bất kỳ đoạn DNA nào khác được cắt bởi cùng enzyme đó – đây là cơ sở để tạo DNA tái tổ hợp. Trên gel điện di, DNA mang điện âm nên di chuyển về cực dương; đoạn CÀNG NHỎ di chuyển CÀNG XA vì len lỏi qua các lỗ gel dễ dàng hơn.

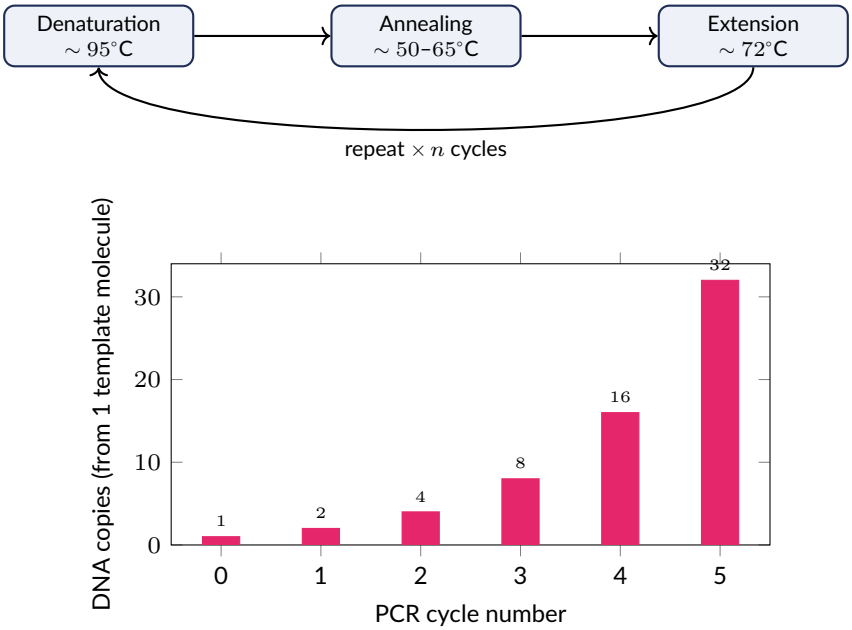
6.9.3 Polymerase chain reaction (PCR)

PCR amplifies a specific DNA sequence exponentially in a test tube, using a heat-stable DNA polymerase (*Taq* polymerase), two short primers flanking the target sequence, and repeated temperature cycles:

1. **Denaturation** ($\sim 95^{\circ}$C): heat separates the double-stranded DNA into single strands.
2. **Annealing** (~ 50–65°C): the reaction is cooled so the two primers can base-pair to their complementary sequences flanking the target region.
3. **Extension** ($\sim 72^{\circ}$C): *Taq* polymerase extends each primer $5' \rightarrow 3'$, synthesizing a new complementary strand.

Each cycle doubles the number of copies of the target sequence, so after n cycles, starting from N_0 template molecules, the copy number grows **exponentially**:

$$N = N_0 \times 2^n.$$



The PCR cycle (top) and exponential doubling of copy number with each cycle (bottom), starting from a single template molecule: $N = 1 \times 2^n$.

Ví dụ mẫu · Exponential PCR amplification

Starting with 10 template DNA molecules, find the number of copies after (a) 15 cycles and (b) 30 cycles.

(a) $N = 10 \times 2^{15} = 10 \times 32{,}768 = 327{,}680$ copies.

(b) $N = 10 \times 2^{30} = 10 \times 1{,}073{,}741{,}824 = 10{,}737{,}418{,}240 \approx 1.07 \times 10^{10}$ copies (about 10.7 billion).

Just 15 additional cycles increase the yield by roughly a further factor of $2^{15} \approx 32{,}768$ – the hallmark of exponential growth, and the reason PCR can amplify a target sequence from a trace sample to an easily detectable quantity within about 30–35 cycles.

VN **GIẢI THÍCH TIẾNG VIỆT**

PCR khuếch đại một đoạn DNA theo cấp số nhân qua 3 bước lặp lại: **biến tính** (denaturation, tách hai mạch DNA ở nhiệt độ cao), **bắt cặp** (annealing, mồi bắt cặp bổ sung với DNA khuôn), **kéo dài** (extension, DNA polymerase chịu nhiệt tổng hợp mạch mới). Sau n chu kỳ, số bản sao $= N_0 \times 2^n$ – tăng theo hàm mũ, không phải tuyến tính.

6.9.4 DNA sequencing and CRISPR-Cas9

DNA sequencing determines the exact order of nucleotides in a DNA fragment. The classic Sanger method uses chain-terminating dideoxynucleotides (ddNTPs) that stop strand synthesis when incorporated, producing fragments of every possible length ending at each position; separating these by size (and identifying which base terminated each fragment) reveals the sequence. Modern high-throughput ("next-generation") sequencing applies similar chemistry in a massively parallel format, sequencing millions of fragments simultaneously.

CRISPR-Cas9 is a gene-editing system adapted from a bacterial adaptive immune mechanism. A synthetic **guide RNA (gRNA)**, designed to be complementary to a specific target DNA sequence, directs the **Cas9** nuclease to that target (adjacent to a short recognition sequence called a PAM). Cas9 then cuts both strands of the DNA at that site. The cell's own repair machinery then acts on the break: error-prone **non-homologous end joining (NHEJ)** often introduces small insertions/deletions that disrupt (knock out) the gene, while, if a template DNA sequence is supplied, **homology-directed repair (HDR)** can introduce a precise, intended edit.

Biotechnology applications: genetic testing/diagnostics (detecting disease-associated alleles via PCR and sequencing), gene therapy (correcting or replacing faulty genes, increasingly via CRISPR-based editing), and genetically modified organisms (GMOs; introducing recombinant genes into crops or other organisms for traits such as pest or herbicide resistance).

VN **GIẢI THÍCH TIẾNG VIỆT**

CRISPR-Cas9: một đoạn RNA dẫn đường (guide RNA) được thiết kế bổ sung với trình tự DNA đích sẽ dẫn enzyme Cas9 đến đúng vị trí đó để cắt đứt cả hai mạch DNA. Tế bào sau đó tự sửa chữa vết cắt: theo cơ chế nối đầu không tương đồng (NHEJ, dễ gây lỗi, thường dùng để "làm hỏng" gen) hoặc theo cơ chế sửa chữa định hướng tương đồng (HDR, cần có mạch khuôn sửa chữa, cho phép chỉnh sửa chính xác).

6.10 Practice Problems

Bài tập luyện tập

A double-stranded DNA sample is found to be 24% guanine. Find the percentages of A, T, and C.

Lời giải chi tiết

Since $\%G = \%C$: $\%C = 24\%$. Since all four sum to 100% and $\%A = \%T$: $\%A + \%T = 100 - 24 - 24 = 52\%$, so $\%A = \%T = 26\%$ each. Check: $\%A + \%G = 26 + 24 = 50\%$ (✓).

Bài tập luyện tập

Which of the following correctly distinguishes RNA from DNA?

(A) RNA uses deoxyribose; DNA uses ribose

(B) RNA contains uracil in place of thymine, and is typically single-stranded

(C) RNA is always double-stranded, like DNA

(D) RNA cannot be transcribed from a DNA template

Lời giải chi tiết

RNA has ribose (not deoxyribose), replaces thymine with uracil, and is typically single-stranded. **(B)**.

Bài tập luyện tập

In the Meselson–Stahl experiment, bacteria grown in heavy (^{15}N) medium were shifted to light (^{14}N) medium. After one round of replication, all DNA had intermediate density; after a second round, two density classes appeared (intermediate and light) in equal amounts. This result supports which model of DNA replication?

(A) Conservative
(B) Semiconservative
(C) Dispersive
(D) None of the models

Lời giải chi tiết

Intermediate density after round 1 rules out conservative replication (which would give one heavy and one light band). Two classes (intermediate + light) after round 2, rather than a continuous smear, rules out dispersive replication. This pattern – consistent, discrete intermediate/light bands – matches **semiconservative** replication: each new helix has one old (heavy) and one new (light) strand. **(B)**.

Bài tập luyện tập

Match each enzyme to its function in DNA replication: (1) Helicase, (2) Single-strand binding protein, (3) Primase, (4) DNA polymerase III, (5) DNA polymerase I, (6) Ligase. Functions: (a) synthesizes new DNA $5' \to 3'$ from a primer; (b) unwinds the double helix at the origin; (c) removes RNA primers and replaces them with DNA; (d) seals remaining nicks in the sugar-phosphate backbone; (e) stabilizes exposed single-stranded template; (f) lays down a short RNA primer.

Lời giải chi tiết

1–(b) Helicase unwinds the helix. 2–(e) SSB proteins stabilize single strands. 3–(f) Primase lays RNA primers. 4–(a) DNA Pol III synthesizes new DNA $5' \to 3'$. 5–(c) DNA Pol I removes primers and fills gaps with DNA. 6–(d) Ligase seals nicks, joining fragments into a continuous strand.

Bài tập luyện tập

Which strand at a replication fork is synthesized discontinuously, as a series of Okazaki fragments?

(A) The leading strand, because it is synthesized toward the fork
(B) The lagging strand, because its polymerase must repeatedly restart as the fork exposes new template
(C) Both strands are synthesized discontinuously
(D) Neither strand is synthesized discontinuously in eukaryotes

Lời giải chi tiết

The lagging strand's polymerase synthesizes in the direction opposite the fork's movement, so it must periodically stop and restart with a new primer as more template becomes available – producing discontinuous Okazaki fragments. **(B)**.

Bài tập luyện tập

Explain why linear eukaryotic chromosomes tend to shorten with each round of replication, how telomerase counteracts this, and in which cell types telomerase is typically most active.

Lời giải chi tiết

On the lagging strand, the RNA primer at the extreme $5'$ end of a linear chromosome cannot be replaced with DNA after removal, because there is no available upstream $3'$-OH for a polymerase to extend from at that terminal position – the end-replication problem. This causes progressive shortening of the telomeric repeat sequences at chromosome ends with each replication cycle. **Telomerase**, a ribonucleoprotein enzyme carrying its own internal RNA template, extends the $3'$ overhang at chromosome ends by adding telomeric repeats, counteracting this shortening. Telomerase is typically most active in **germ-line cells, stem cells, and (abnormally) cancer cells**, which must divide many times without losing essential genetic material; it is largely inactive in most differentiated somatic cells.

Bài tập luyện tập

A gene's template strand reads 3′-TACGTGACCATT-5′. Determine the resulting mRNA transcript (with correct 5′/3′ ends), and identify the start codon and the first two amino acids encoded.

Lời giải chi tiết

Reading the template $3' \to 5'$ and building mRNA $5' \to 3'$ by complementary base pairing (A↔U, T↔A, G↔C, C↔G):

$$\text{Template } 3'\text{-T A C G T G A C C A T T-}5' \;\Rightarrow\; \text{mRNA } 5'\text{-A U G C A C U G G U A A-}3'.$$

Codons: AUG-CAC-UGG-UAA. The start codon is **AUG** (Met); the next two codons are CAC = **His** and UGG = **Trp**; UAA is a stop codon.

Bài tập luyện tập

The 5′ cap and poly-A tail added to eukaryotic pre-mRNA primarily function to:

(A) Encode two extra amino acids at each end of the protein

(B) Protect the transcript from degradation and assist ribosome recognition, nuclear export, and translation

(C) Mark introns for removal by the spliceosome

(D) Convert the pre-mRNA directly into a functional protein

Lời giải chi tiết

Both the cap and poly-A tail protect the mRNA from degradation and help it be recognized and exported/translated efficiently; neither encodes protein sequence nor marks introns. **(B)**.

Bài tập luyện tập

A pre-mRNA transcript contains five exons (1–5). In liver cells, exons 1-2-3-5 are joined into the mature mRNA; in muscle cells, exons 1-2-4-5 are joined instead. Explain how this is possible from a single gene, and name the resulting relationship between the two protein products.

Lời giải chi tiết

Both cell types transcribe the identical pre-mRNA from the same gene, but the spliceosome – guided by cell-type-specific splicing regulatory proteins – selects different combinations of exons to retain (exon 3 in liver, exon 4 in muscle) during **alternative splicing**. This produces two distinct mature mRNAs from one gene, which are translated into two distinct protein **isoforms**.

Bài tập luyện tập

Which of the following is *not* an actual property of the genetic code?

(A) Triplet (three nucleotides specify one amino acid)

(B) Non-overlapping (read in successive, non-repeating triplets)

(C) Redundant/degenerate (most amino acids have more than one codon)

(D) Overlapping (adjacent codons share nucleotides)

Lời giải chi tiết

The genetic code is read in fixed, non-overlapping triplets – adjacent codons do *not* share nucleotides. "Overlapping" is not a true property. **(D)**.

Bài tập luyện tập

Translate the mRNA 5′-AUG-GAA-CGU-UGC-UAG-3′ into its amino acid sequence using the standard genetic code.

Lời giải chi tiết

AUG = Met (start); GAA = Glu; CGU = Arg; UGC = Cys; UAG = Stop.

$$\text{Protein: Met} - \text{Glu} - \text{Arg} - \text{Cys}.$$

Bài tập luyện tập

The wobble hypothesis helps explain why:

(A) Some tRNAs can correctly pair with more than one mRNA codon

(B) DNA replication is semiconservative

(C) Introns are removed before translation

(D) Stop codons require a specific release-factor tRNA

Lời giải chi tiết

Relaxed pairing at the third codon position (paired with the anticodon's first, 5′, position) allows one tRNA to recognize multiple codons differing only at that position, reducing the number of distinct tRNAs needed. **(A)**.

Bài tập luyện tập

Describe, in order, what happens at the ribosome's A, P, and E sites during one cycle of translation elongation.

Lời giải chi tiết

A charged tRNA (carrying the next amino acid) enters the **A site**, its anticodon pairing with the exposed mRNA codon. A peptide bond then forms between this amino acid and the growing polypeptide chain held by the tRNA in the **P site** (catalyzed by the rRNA of the large subunit). The ribosome then **translocates** one codon along the mRNA: the tRNA now holding the growing chain moves from A to P, the previous (now uncharged) P-site tRNA moves to the **E site** and exits the ribosome, and a new codon is exposed in the now-empty A site, ready for the next charged tRNA.

Bài tập luyện tập

In a coding sequence, codon GGA (Gly) is mutated to GGG. This point mutation is best classified as:

(A) Silent
(B) Missense
(C) Nonsense
(D) Frameshift

Lời giải chi tiết

From the codon table, both GGA and GGG code for **Gly**, so the amino acid sequence is unchanged. **(A)**.

Bài tập luyện tập

Starting from mRNA 5′-AUG-CAU-GGC-UAA-3′ (protein Met-His-Gly-Stop), two extra nucleotides, AA, are inserted immediately after the start codon. Determine the new reading frame and the resulting amino acid sequence as far as it can be read, and explain why this is classified as a frameshift mutation.

Lời giải chi tiết

New sequence: AUG-AAC-AUG-GCU-AA(incomplete). New codons: AUG $=$ Met, AAC $=$ Asn, AUG $=$ Met, GCU $=$ Ala, with 2 leftover bases forming no complete codon.

$$\text{New protein (as far as shown): Met} - \text{Asn} - \text{Met} - \text{Ala} - \ldots$$

This is a **frameshift** because 2 nucleotides – not a multiple of 3 – were inserted: every codon boundary downstream of the insertion point shifts, so none of the original His-Gly-Stop sequence is recovered; the total transcript length (14 nt) is also no longer a multiple of 3, confirming the frame has been permanently shifted.

Bài tập luyện tập

A single-nucleotide substitution occurs in three different locations: (a) the middle of an intron, away from any splice site; (b) the promoter region upstream of a gene; (c) the third position of an exon codon, changing UUA to UUG. State the most likely consequence of each.

Lời giải chi tiết

(a) Likely **no effect** on the protein: introns are removed from the mature mRNA regardless of their internal sequence, as long as the splice sites themselves are intact. (b) The protein's amino

acid sequence is unlikely to change, but altering a promoter can change a transcription factor's binding affinity, thereby changing *how much* or *when* the gene is transcribed – potentially major phenotypic effects without any protein sequence change. (c) UUA and UUG both code for **Leu** (codon table), so this is a **silent** mutation – no change to the protein.

Bài tập luyện tập

The *lac* operon is described as "inducible" because:

(A) It is normally on and is shut off by a corepressor

(B) It is normally off and is switched on when an inducer inactivates its repressor

(C) It lacks an operator sequence entirely

(D) It functions identically regardless of lactose or glucose levels

Lời giải chi tiết

"Inducible" means the operon defaults to OFF and is turned ON by an inducer (allolactose) that inactivates the repressor, freeing the operator. **(B)**.

Bài tập luyện tập

Glucose is abundant and lactose is also present in a bacterium's growth medium. Determine the transcriptional state of the *lac* operon and justify your answer, including the roles of both the repressor and CAP.

Lời giải chi tiết

Lactose is present, so allolactose binds and inactivates the *lac* repressor, freeing the operator – the repressor is *not* blocking transcription. However, glucose is abundant, so intracellular cAMP is low, CAP remains inactive, and RNA polymerase binds the promoter only weakly without the cAMP–CAP boost. Net result: the operon is transcribed, but only at a **low, basal level** – not fully off, but far from maximal, because catabolite repression (via inactive CAP) limits transcription while glucose remains available.

Bài tập luyện tập

In the *trp* operon, tryptophan itself acts as a:

(A) Inducer that inactivates the repressor

(B) Corepressor that binds and activates the repressor

(C) Structural gene product

(D) Component of the CAP protein

Lời giải chi tiết

Tryptophan binds the otherwise-inactive *trp* repressor as a corepressor, activating it so it can bind the operator and shut off transcription (feedback inhibition). **(B)**.

Bài tập luyện tập

Contrast the general effect of histone acetylation with that of DNA methylation on gene transcription, and state which chromatin state (euchromatin or heterochromatin) each is generally

associated with.

Lời giải chi tiết

Histone acetylation neutralizes the positive charge on histone tails, loosening histone–DNA packing and opening chromatin into the accessible **euchromatin** state – generally **promoting** transcription. **DNA methylation** (typically at cytosines in CpG-rich regions) generally **silences** genes, both by blocking transcription factor binding directly and by recruiting proteins that condense chromatin into **heterochromatin**. In short: acetylation tends to activate, methylation tends to silence.

Bài tập luyện tập

An enhancer sequence can influence transcription of a gene located tens of thousands of base pairs away because:

(A) RNA polymerase transcribes through the entire intervening DNA before reaching the gene

(B) Activator proteins bound at the enhancer are brought into contact with proteins at the promoter via DNA looping

(C) Enhancers must always be located immediately adjacent to the promoter

(D) Enhancers directly encode part of the mature mRNA

Lời giải chi tiết

DNA looping physically brings a distant enhancer-bound activator complex into contact with the transcription machinery at the promoter, despite the large linear distance separating them on the chromosome. **(B)**.

Bài tập luyện tập

A microRNA (miRNA) is complementary to a sequence in the 3′ UTR of gene X's mRNA. Predict the effect of increased expression of this miRNA on the amount of protein X produced, and explain the molecular mechanism.

Lời giải chi tiết

Increased miRNA expression will **decrease** the amount of protein X produced. Mechanism: the miRNA, loaded into the RISC complex, base-pairs with the complementary sequence in the 3′ UTR of gene X's mRNA; this either blocks the mRNA from being translated or targets it for degradation. This is post-transcriptional silencing – it reduces protein output without necessarily changing how much gene X is transcribed in the first place.

Bài tập luyện tập

Nearly all cells in a person's body contain an identical genome. The primary reason liver cells and skin cells differ so dramatically in structure and function is:

(A) They contain different sets of genes

(B) They express different subsets of their shared genome

(C) Skin cells lack a nucleus

(D) Liver cells contain twice as much DNA as skin cells

Lời giải chi tiết

Differential gene expression – not different gene content – produces distinct cell types from an identical genome. **(B)**.

Bài tập luyện tập

Explain why a restriction enzyme that leaves "sticky ends" allows a foreign DNA fragment to be inserted into a plasmid vector, even though the fragment and the plasmid come from entirely different organisms.

Lời giải chi tiết

The restriction enzyme cuts both the foreign DNA fragment and the plasmid vector at the same specific recognition sequence, leaving the same complementary single-stranded overhangs ("sticky ends") on both pieces of DNA. Because these overhangs are chemically complementary, they can base-pair with each other regardless of which organism the DNA originally came from. DNA ligase then seals the remaining nicks in the sugar-phosphate backbone, producing a stable recombinant plasmid.

Bài tập luyện tập

A linear DNA fragment 6000 bp long is cut by a restriction enzyme at 2 internal sites, producing fragments of 3500 bp, 1500 bp, and 1000 bp. Rank the three fragments by migration distance from the well on an agarose gel, from *least* to *greatest* distance.

Lời giải chi tiết

Check: linear DNA with 2 internal cuts gives $2+1=3$ fragments, and $3500+1500+1000=6000$ bp, matching the original length. Migration distance decreases with fragment size, so the **largest** fragment travels **least** and the **smallest** travels **farthest**:

$$3500 \text{ bp (least distance)} \;<\; 1500 \text{ bp} \;<\; 1000 \text{ bp (greatest distance)}.$$

Bài tập luyện tập

A PCR reaction begins with 8 template DNA molecules. Calculate the number of copies present after (a) 12 cycles and (b) 20 cycles.

Lời giải chi tiết

(a) $N = 8 \times 2^{12} = 8 \times 4096 = 32{,}768$ copies.
(b) $N = 8 \times 2^{20} = 8 \times 1{,}048{,}576 = 8{,}388{,}608$ copies.

Bài tập luyện tập

Which sequence correctly places the three PCR steps in order, with realistic approximate temperatures?

(A) Denaturation ($\sim 95^\circ$C) → Annealing ($\sim 55^\circ$C) → Extension ($\sim 72^\circ$C)

(B) Annealing ($\sim 55^\circ$C) → Extension ($\sim 72^\circ$C) → Denaturation ($\sim 95^\circ$C)

(C) Extension ($\sim 72^\circ$C) → Denaturation ($\sim 95^\circ$C) → Annealing ($\sim 55^\circ$C)

(D) Denaturation ($\sim 72^\circ$C) → Extension ($\sim 95^\circ$C) → Annealing ($\sim 55^\circ$C)

Lời giải chi tiết

Each PCR cycle proceeds: high-temperature denaturation to separate strands, cooler annealing to let primers bind, then intermediate-temperature extension for *Taq* polymerase to synthesize new DNA. **(A)**.

Bài tập luyện tập

Describe the roles of the guide RNA, Cas9, and the PAM sequence in CRISPR-Cas9 gene editing, and explain the difference in outcome between repair via NHEJ and repair via HDR.

Lời giải chi tiết

The **guide RNA (gRNA)** is a synthetic RNA designed to be complementary to a specific target DNA sequence; it directs the **Cas9** nuclease to bind that target, which must lie next to a short **PAM** sequence required for Cas9 to engage the DNA. Once bound, Cas9 cuts both strands of the target DNA. If the cell repairs the break by **NHEJ** (non-homologous end joining), small insertions/deletions are often introduced at the cut site in an error-prone way, typically disrupting (knocking out) the gene. If a repair template is supplied and the cell instead uses **HDR** (homology-directed repair), the break can be repaired using that template, allowing a precise, intended sequence edit rather than a random disruption.

Bài tập luyện tập

Introducing a corrected copy of a gene into a patient's cells to treat a genetic disease is best described as:

(A) Genetic testing

(B) Gene therapy

(C) Genetically modified organism (GMO) production

(D) Gel electrophoresis

Lời giải chi tiết

Delivering a corrected/functional gene copy to treat disease is the definition of gene therapy (as opposed to merely detecting a disease-associated allele, which would be genetic testing). **(B)**.

Bài tập luyện tập

A circular plasmid has 4 recognition sites for restriction enzyme X. (a) How many fragments result from digesting the plasmid with enzyme X alone? (b) If the plasmid is first linearized with a different enzyme (a single cut elsewhere on the plasmid) and then digested with enzyme X, how many fragments result in total?

Lời giải chi tiết

(a) For circular DNA, fragments $=$ number of cuts: 4 sites $\Rightarrow$ **4 fragments**.
(b) Linearizing first adds one more cut, so the DNA now has a total of $1+4=5$ cut sites along its length. For *linear* DNA, fragments $=$ cuts $+1$: $5+1=6$ fragments.

Natural Selection

Mục tiêu Unit: Quan sát và suy luận của Darwin, các kiểu chọn lọc tự nhiên (định hướng, ổn định hoá, phân ly), chọn lọc nhân tạo, di truyền học quần thể và định luật Hardy–Weinberg, các bằng chứng tiến hoá (hoá thạch, địa sinh học, giải phẫu so sánh, phôi học so sánh, sinh học phân tử), cây phát sinh chủng loại, sự hình thành loài, tuyệt chủng, và biến dị trong quần thể (hiệu ứng thắt cổ chai, hiệu ứng người sáng lập).

7.1 Darwin's Observations and the Logic of Natural Selection

Charles Darwin's theory of natural selection rests on a chain of observations and inferences, developed after his voyage on the *HMS Beagle* and later published in *On the Origin of Species* (1859).

Darwin's observations → inferences

Observation 1 — Overproduction: populations produce far more offspring than the environment can support.
Observation 2 — Heritable variation: individuals within a population vary in their traits, and much of this variation can be passed from parent to offspring.
Inference 1 — Struggle for existence: because resources (food, space, mates) are limited, offspring must compete, and not all survive to reproduce.
Inference 2 — Differential survival and reproduction: individuals whose heritable traits make them better suited to the local environment tend to survive longer and leave more offspring than individuals with less favorable traits.
Conclusion — Adaptation: over many generations, this unequal reproductive success causes favorable heritable traits to accumulate in the population, producing populations that are increasingly well suited (**adapted**) to their environment.

Evolution, formally defined: a change in the **allele frequencies** of a population over successive generations. Evolution acts on *populations*, not on individual organisms — a single organism cannot evolve during its lifetime, it can only survive, reproduce, or not.

VN **GIẢI THÍCH TIẾNG VIỆT**

Lập luận của Darwin gồm hai **quan sát** và hai **suy luận**: (1) sinh vật sinh ra nhiều con hơn mức môi trường có thể nuôi dưỡng (sinh sản thừa thãi); (2) các cá thể trong quần thể có biến dị di truyền được. Từ đó suy ra: (3) các cá thể phải cạnh tranh nguồn sống hạn chế (đấu tranh sinh tồn); (4) cá thể có đặc điểm phù hợp hơn với môi trường sẽ sống sót và sinh sản nhiều hơn (sinh sản khác biệt). Kết quả tích luỹ qua nhiều thế hệ là quần thể ngày càng **thích nghi**. Về mặt di truyền học hiện đại, tiến hoá được định nghĩa chính xác là sự **thay đổi tần số alen** của một quần thể qua thời gian — KHÔNG phải sự thay đổi ở một cá thể riêng lẻ.

(!) Lỗi thường gặp: Tiến hoá KHÔNG có "mục tiêu" hay hướng đi tất yếu về phía sự phức tạp hay "hoàn hảo". Chọn lọc tự nhiên chỉ đơn thuần ưu tiên các kiểu hình phù hợp hơn với *môi*

trường hiện tại — môi trường có thể thay đổi, nên một đặc điểm từng có lợi có thể trở nên bất lợi. Vi khuẩn hay sinh vật đơn giản không "kém tiến hoá" hơn sinh vật phức tạp; chúng chỉ đang thích nghi theo một hướng khác. Ngoài ra, các cá thể riêng lẻ không tiến hoá trong đời mình — chỉ **quần thể** mới tiến hoá, qua nhiều thế hệ.

7.2 Patterns of Natural Selection

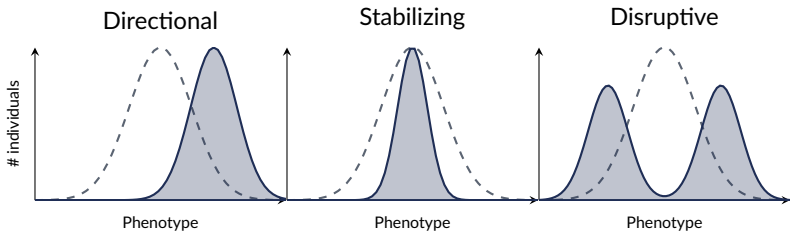
Natural selection acts on the existing distribution of phenotypes in a population. Depending on which phenotypes are favored, selection produces three characteristic patterns.

Three modes of selection

Directional selection favors one phenotypic extreme over the other, shifting the population mean toward that extreme (and often reducing overall variance somewhat). It commonly occurs when the environment changes in a consistent direction or a population colonizes a new environment.

Stabilizing selection favors intermediate phenotypes and selects against both extremes, **reducing variance** around an unchanged mean. It is the most common pattern in stable environments and tends to maintain the status quo.

Disruptive (diversifying) selection favors *both* phenotypic extremes over the intermediate phenotype, **increasing variance** and potentially splitting the population's phenotype distribution into two peaks (**polymorphism**). Over long timescales, disruptive selection can contribute to **sympatric speciation** if the two phenotype classes stop interbreeding.



Effect of each selection mode on a population's phenotype distribution. Dashed grey = distribution before selection; shaded navy = distribution after selection. Directional selection shifts the mean; stabilizing selection narrows the spread; disruptive selection produces two peaks.

Ví dụ mẫu · Directional selection: antibiotic resistance

A bacterial population is exposed to a constant low dose of an antibiotic. A resistance allele R is initially rare. Researchers track the frequency of R over four generations of continuous antibiotic exposure:

Generation	0	1	2	3	4
Frequency of R	2%	9%	28%	61%	85%

Explain the pattern. The antibiotic does not *create* the resistance mutation — R already existed at low frequency in the population before exposure (from ordinary random mutation). The antibiotic acts as a selective agent: bacteria carrying R survive and reproduce, while susceptible bacteria (genotype without R) die before reproducing. Because one phenotypic extreme (resistant) is consistently favored over the other (susceptible), this is **directional selection**, and the population's mean phenotype shifts generation by generation toward resistance.

Ví dụ mẫu · Stabilizing selection: human birth weight

Large surveys of human birth weight and survival (classic data collected by Karn and Penrose) show that infants born near the population average birth weight (≈ 3.3 kg) have the *lowest* mortality, while both smaller (pre-term/low birth weight, higher risk of complications) and larger (difficult delivery) infants have *higher* mortality.

Explain the pattern. Both phenotypic extremes are selected against and the intermediate phenotype is favored $\Rightarrow$ **stabilizing selection**. Over time this reduces the variance in birth weight around the mean without shifting the mean itself.

VN **GIẢI THÍCH TIẾNG VIỆT**

Ba kiểu chọn lọc khác nhau ở việc **kiểu hình nào được ưu tiên**: chọn lọc **định hướng** (directional) ưu tiên một cực trị, làm **dịch chuyển giá trị trung bình** của quần thể (ví dụ: bướm đêm *Biston betularia* — sau cách mạng công nghiệp, thân cây phủ bồ hóng đen khiến bướm màu tối được nguỵ trang tốt hơn, tần số alen màu tối tăng dần qua các thế hệ). Chọn lọc **ổn định hoá** (stabilizing) ưu tiên kiểu hình trung bình, loại bỏ hai cực trị, làm **giảm phương sai** nhưng KHÔNG đổi giá trị trung bình (ví dụ: cân nặng trẻ sơ sinh). Chọn lọc **phân ly** (disruptive) ưu tiên CẢ HAI cực trị, loại bỏ kiểu trung gian, làm **tăng phương sai** và có thể tạo ra quần thể đa hình (hai đỉnh phân bố) — ví dụ kinh điển là chim mỏ to *Pyrenestes ostrinus* ở châu Phi: cá thể mỏ nhỏ chuyên ăn hạt mềm, cá thể mỏ lớn chuyên ăn hạt cứng, còn cá thể mỏ trung bình kém hiệu quả với cả hai loại hạt nên bị chọn lọc loại bỏ.

7.3 Artificial Selection

Artificial selection is human-directed selective breeding: humans choose which individuals reproduce based on desired traits (crop yield, milk production, coat color, temperament), rather than the environment doing the "choosing." Over generations this produces dramatic phenotypic change — all domestic dog breeds, from Chihuahuas to Great Danes, descend from wolves within roughly the last $15{,}000$–$30{,}000$ years; teosinte was transformed into modern maize through repeated selection for larger, more numerous kernels; wild mustard (*Brassica oleracea*) was selectively bred into broccoli, cauliflower, kale, and cabbage by selecting for different plant organs.

Darwin studied pigeon breeders extensively and used artificial selection as the key analogy that helped him formulate natural selection: if humans could produce such extensive change in a few generations by selecting individuals with desired heritable traits, an analogous process — with the *environment* doing the selecting instead of a breeder, and over a much longer timescale — could plausibly produce the diversity of life.

Artificial vs. natural selection — same mechanism, different source of pressure. Both require heritable variation and differential reproduction. The difference is *who/what determines which individuals reproduce*: a human breeder (artificial) vs. the abiotic and biotic environment — predators, climate, competitors, disease, mates (natural).

VN **GIẢI THÍCH TIẾNG VIỆT**

Chọn lọc nhân tạo và chọn lọc tự nhiên có cùng **cơ chế logic**: biến dị di truyền + sinh sản khác biệt → thay đổi tần số alen qua các thế hệ. Điểm khác biệt duy nhất là **ai/cái gì quyết định** cá thể nào được sinh sản: ở chọn lọc nhân tạo, con người chủ động chọn (ví dụ chọn giống chó, giống lúa, giống bò sữa cho năng suất cao); ở chọn lọc tự nhiên, môi trường "chọn" một cách khách quan thông qua khả năng sống sót và sinh sản. Darwin dùng chọn lọc nhân tạo (đặc biệt là việc lai tạo bồ câu) làm **phép loại suy (analogy)** để thuyết phục người đọc: nếu con người có thể tạo ra thay đổi lớn trong thời gian ngắn, thì tự nhiên — với thời gian địa chất dài hơn rất

nhiều — hoàn toàn có thể tạo ra sự đa dạng sinh học ta thấy ngày nay.

7.4 Population Genetics

Population genetics studies how allele and genotype frequencies change within populations. The **gene pool** is the complete set of alleles at all loci carried by every individual in a population at a given time.

Allele frequency vs. genotype frequency

For a gene with two alleles A (frequency p) and a (frequency q):

$$p + q = 1.$$

Allele frequency is the proportion of all copies of a gene in the gene pool that are a particular allele. **Genotype frequency** is the proportion of individuals in the population with a particular genotype (AA, Aa, or aa). Allele frequency is calculated by counting alleles (each homozygote contributes 2 copies of one allele; each heterozygote contributes 1 copy of each allele) and dividing by the total number of allele copies ($2N$ for a diploid population of size N).

Five factors can change allele frequencies in a population from one generation to the next:

Factor	Effect on allele frequency
Mutation	Creates new alleles; on its own, changes frequencies very slowly (low per-locus mutation rate), but it is the ultimate source of all new genetic variation.
Gene flow (migration)	Movement of individuals (and their alleles) between populations tends to make neighboring populations' allele frequencies more similar to each other.
Genetic drift	Random, chance fluctuation in allele frequency from generation to generation due to sampling error; effect is strongest in **small** populations and is not directed by fitness.
Non-random mating	Individuals choose mates non-randomly (e.g., inbreeding, assortative mating). This changes **genotype** frequencies (typically increasing homozygosity) but, by itself, does *not* directly change allele frequencies.
Natural selection	Differential survival/reproduction based on phenotype systematically changes which alleles are passed to the next generation.

Ví dụ mẫu · Gene flow and allele frequency

A large resident population of 800 snails has allele frequency $q_1 = 0.10$ for a shell-color allele. A group of 200 migrant snails from a neighboring population, with $q_2 = 0.50$ for the same allele, joins and interbreeds freely with the resident population. Find the new allele frequency after the populations merge.

Pool all alleles, weighting by population size:

$$q' = \frac{N_1 q_1 + N_2 q_2}{N_1 + N_2} = \frac{(800)(0.10) + (200)(0.50)}{800 + 200} = \frac{80 + 100}{1000} = \frac{180}{1000} = 0.18.$$

Gene flow pulled the resident population's allele frequency from 0.10 toward the migrants' value, landing at 0.18 — illustrating how migration homogenizes allele frequencies between populations.

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Tần số alen (allele frequency) là tỉ lệ của MỘT loại alen trong tổng số alen của cả locus đó trong quần thể (đếm alen, không đếm cá thể). **Tần số kiểu gen** (genotype frequency) là tỉ lệ cá thể mang một kiểu gen cụ thể. Có 5 yếu tố có thể làm thay đổi tần số alen: đột biến (mutation), di nhập gen (gene flow), biến động di truyền ngẫu nhiên (genetic drift), giao phối không ngẫu nhiên (non-random mating), và chọn lọc tự nhiên (natural selection). Lưu ý: giao phối không ngẫu nhiên (như giao phối cận huyết) chủ yếu làm thay đổi **tần số kiểu gen** (tăng tỉ lệ đồng hợp) chứ KHÔNG trực tiếp làm thay đổi tần số alen.

7.5 Hardy--Weinberg Equilibrium

The **Hardy–Weinberg (HW) model** describes a theoretical population whose allele and genotype frequencies do *not* change from generation to generation — i.e., a population that is **not evolving** at the locus in question. It serves as a null model: real populations are compared against Hardy–Weinberg expectations to detect whether evolution is occurring.

The five Hardy–Weinberg assumptions

A population is in Hardy–Weinberg equilibrium only if **all five** of the following hold:

1. **No mutation** — allele sequences do not change.
2. **No gene flow** — no individuals (and their alleles) enter or leave the population.
3. **Infinitely large population** — no genetic drift (no random sampling error in which alleles are passed on).
4. **Random mating** — individuals do not select mates based on genotype.
5. **No natural selection** — all genotypes have equal survival and reproductive success.

If a real population violates one or more of these assumptions, it is expected to evolve (its allele frequencies will change over time).

Hardy–Weinberg equations. For a two-allele locus with $p =$ frequency of the dominant allele A and $q =$ frequency of the recessive allele a:

$$p + q = 1, \qquad p^2 + 2pq + q^2 = 1,$$

where $p^2 =$ frequency of genotype AA, $2pq =$ frequency of genotype Aa (heterozygotes), and $q^2 =$ frequency of genotype aa.

Ví dụ mẫu · Hardy–Weinberg 1: from phenotype to genotype frequencies

In a population of wildflowers, petal color is controlled by one gene: red (A) is dominant to white (a), so only aa plants show the recessive white phenotype. A survey of the population finds that 16% of the plants have white petals. Assuming Hardy–Weinberg equilibrium, find p, q, and the frequency of each genotype, and state the percentage of plants that are heterozygous carriers.

Step 1 — get q^2. Only aa individuals show the recessive phenotype, so

$$q^2 = 0.16.$$

Step 2 — solve for q.

$$q = \sqrt{0.16} = 0.40.$$

Step 3 — solve for p.

$$p = 1 - q = 1 - 0.40 = 0.60.$$

Step 4 — genotype frequencies.

$$p^2 = (0.60)^2 = 0.36 \ (36\% \ AA), \qquad 2pq = 2(0.60)(0.40) = 0.48 \ (48\% \ Aa),$$

$$q^2 = 0.16 \ (16\% \ aa).$$

Check: $0.36 + 0.48 + 0.16 = 1.00$. 48% **of the population are heterozygous carriers** of the white allele, even though only 16% show the white phenotype.

(!) Lỗi thường gặp: Sai lầm phổ biến nhất khi giải bài Hardy–Weinberg: HỌC SINH LẤY CĂN BẬC HAI CỦA SAI GIÁ TRỊ. Tần số kiểu hình lặn quan sát được LUÔN LUÔN bằng q^2 (tần số kiểu gen aa), KHÔNG bằng q. Phải lấy căn bậc hai của q^2 để ra q: $q = \sqrt{q^2}$. Ví dụ nếu đề cho "16% mang kiểu hình lặn", đó là $q^2 = 0.16$, KHÔNG phải $q = 0.16$ — quên bước lấy căn là lỗi sai điểm số nhiều nhất trong dạng bài này.

Ví dụ mẫu · Hardy–Weinberg 2: from allele frequencies to expected counts

In a population of $2{,}000$ deer, a coat-color gene has allele frequencies $p = 0.7$ (allele B) and $q = 0.3$ (allele b), and the population is assumed to be in Hardy–Weinberg equilibrium. Find the expected genotype frequencies and the expected number of deer of each genotype.

$$p^2 = (0.7)^2 = 0.49, \qquad 2pq = 2(0.7)(0.3) = 0.42, \qquad q^2 = (0.3)^2 = 0.09.$$

Check: $0.49 + 0.42 + 0.09 = 1.00$. Multiply each frequency by $N = 2{,}000$:

$$BB: \ 0.49 \times 2000 = 980, \qquad Bb: \ 0.42 \times 2000 = 840, \qquad bb: \ 0.09 \times 2000 = 180.$$

Check: $980 + 840 + 180 = 2{,}000$. ✓

Ví dụ mẫu · Hardy–Weinberg 3: testing whether a population is in equilibrium

The MN blood-group gene is **codominant**, so all three genotypes (MM, MN, NN) are directly distinguishable. A sample of 500 people gives the observed genotype counts: $MM = 260$, $MN = 180$, $NN = 60$. Determine whether this population appears to be in Hardy–Weinberg equilibrium.

Step 1 — observed allele frequencies. Total alleles $= 2(500) = 1000$.

$$p(M) = \frac{2(260) + 180}{1000} = \frac{700}{1000} = 0.70, \qquad q(N) = \frac{2(60) + 180}{1000} = \frac{300}{1000} = 0.30.$$

Step 2 — Hardy–Weinberg expected counts (using these observed allele frequencies):

$$MM_{\text{exp}} = p^2 N = (0.49)(500) = 245, \quad MN_{\text{exp}} = 2pqN = (0.42)(500) = 210,$$

$$NN_{\text{exp}} = q^2 N = (0.09)(500) = 45.$$

Step 3 — compare.

Genotype	Observed	HW-expected	Difference
MM	260	245	$+15$ (excess)
MN	180	210	-30 (deficit)
NN	60	45	$+15$ (excess)

Observed counts show a clear **excess of homozygotes** and a **deficit of heterozygotes** relative to Hardy–Weinberg expectations. This pattern is the signature of **non-random mating** (e.g., inbreeding or assortative mating) or population subdivision — the population is **not** in Hardy–Weinberg equilibrium, i.e., it appears to be evolving (or at least violating one of the five assumptions) at this locus.

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Định luật Hardy–Weinberg mô tả một quần thể **lý tưởng, KHÔNG tiến hoá**, thoả cả 5 điều kiện: không đột biến, không di nhập gen, quần thể vô hạn lớn (không có biến động di truyền), giao phối ngẫu nhiên, và không có chọn lọc tự nhiên. Hai phương trình cốt lõi: $p + q = 1$ và $p^2 + 2pq + q^2 = 1$. Quy trình giải bài chuẩn: (1) xác định q^2 từ tần số kiểu hình lặn quan sát được; (2) lấy căn bậc hai ra q; (3) tính $p = 1 - q$; (4) thay vào để tính p^2, $2pq$, q^2. Khi tần số kiểu gen QUAN SÁT ĐƯỢC lệch đáng kể so với tần số KỲ VỌNG theo Hardy–Weinberg, đó chính là **bằng chứng cho thấy quần thể đang tiến hoá** — tức có ít nhất một trong 5 điều kiện đang bị vi phạm.

7.6 Evidence of Evolution

Multiple, independent lines of evidence converge to support the theory that all living organisms share common ancestry and have changed over time.

7.6.1 The fossil record

Fossils form when organisms are buried and preserved (e.g., in sediment, ice, amber) and later found in rock layers (**strata**). **Relative dating** places fossils in order using the position of the rock layers they are found in (deeper layers = generally older, by the principle of superposition); **absolute (radiometric) dating** uses the known, constant decay rate of radioactive isotopes (e.g., carbon-14 for material younger than $\sim 50{,}000$ years; potassium-argon or uranium-lead for much older rock) to assign an actual age. The fossil record documents **transitional forms** — organisms with a mix of ancestral and derived traits linking two major groups — such as *Tiktaalik* (a fish with limb-like fins and a mobile neck, linking fish and early tetrapods) and *Archaeopteryx* (feathered, winged, but with teeth and a bony tail, linking non-avian dinosaurs and birds).

7.6.2 Biogeography

Biogeography is the study of the geographic distribution of species. Closely related species tend to be found in geographically close (or once-connected) regions, consistent with descent from a shared ancestor that dispersed and diversified. **Island endemism** — many species found nowhere else in the world evolving on isolated islands (e.g., the Galápagos finches, Hawaiian silverswords) — is best explained by a small founding population diversifying in isolation, not by independent creation. Unrelated species in similar environments on different continents (e.g., Australian marsupials vs. placental mammals elsewhere occupying similar ecological niches) show **convergent evolution** of similar traits under similar selective pressures, rather than shared recent ancestry.

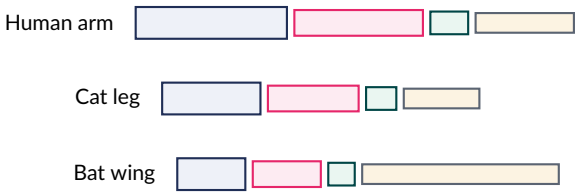
7.6.3 Comparative anatomy

Homologous, analogous, and vestigial structures

Homologous structures are anatomically similar structures that arose from a common ancestor, even if they now serve different functions. The classic example is the vertebrate forelimb: the same set of bones (humerus, radius/ulna, carpals, digits) is found in the human arm, cat leg, whale flipper, and bat wing, modified for grasping, walking, swimming, and flying respectively.

Analogous structures are similar in function (and often outward appearance) but arose **independently** in unrelated lineages — **convergent evolution** — and are *not* inherited from a shared ancestor with that structure. Insect wings (thin cuticle extensions) and bird/bat wings (modified bony forelimbs) are analogous as flight structures: both evolved the ability to fly independently, from completely different starting structures.

Vestigial structures are reduced, seemingly functionless remnants of structures that served an important function in an ancestor — e.g., the human coccyx (tailbone, remnant of an ancestral tail), the human appendix (reduced remnant of a larger ancestral cecum used for digesting cellulose), and small pelvic and leg bones found embedded in the body of some whales (remnants of walking, four-limbed ancestors).



Simplified homology map of the vertebrate forelimb. Navy = humerus; pink = radius/ulna; teal = carpals; amber = digits. All three forelimbs contain the same four skeletal elements in the same sequence — evidence of descent from a common tetrapod ancestor — even though relative proportions and final function (grasping, walking, flying) differ.

Ví dụ mẫu · Classifying homologous, analogous, and vestigial structures

Classify each pair/structure below.

(1) The bone arrangement in a human arm and a bat wing. → **Homologous.** Both are built from the same pentadactyl-limb bones (humerus, radius/ulna, carpals, digits), inherited from a common tetrapod ancestor.

(2) A butterfly wing and a bird wing. → **Analogous.** Both allow flight, but a butterfly wing is a cuticle extension with no bones at all, while a bird wing is a modified bony forelimb — completely different structural origins, so the flight function evolved independently (convergent evolution).

(3) The human coccyx. → **Vestigial.** A reduced remnant of the tail vertebrae present in our ancestors, with no locomotor function today.

(4) A shark's fin and a dolphin's flipper. → **Analogous** in overall external shape — both are streamlined for aquatic locomotion, a case of convergent evolution between a fish and a marine mammal. (Internally, the dolphin's flipper skeleton is actually *homologous* to other tetrapod forelimbs like a bat wing, since dolphins descend from land mammals — it is only the external similarity to the shark's fin that is convergent/analogous.)

(!) Lỗi thường gặp: Nhầm lẫn phổ biến: cấu trúc TƯƠNG ĐỒNG (homologous) và cấu trúc TƯƠNG TỰ (analogous). Chìa khoá phân biệt KHÔNG phải là "trông có giống nhau không" mà là **nguồn gốc tiến hoá**: tương đồng = cùng cấu trúc nền tảng, thừa hưởng từ tổ tiên chung

(dù chức năng hiện tại khác nhau — như xương chi trước ở tay người, chân mèo, cánh dơi); tương tự = chức năng/hình dạng giống nhau nhưng phát sinh ĐỘC LẬP ở hai dòng không có quan hệ họ hàng gần (tiến hoá hội tụ — như cánh côn trùng và cánh chim). Cấu trúc tương đồng là bằng chứng CÓ tổ tiên chung; cấu trúc tương tự KHÔNG phải bằng chứng có tổ tiên chung (chỉ là bằng chứng của áp lực chọn lọc tương tự).

7.6.4 Comparative embryology

Related organisms often share developmental features during embryonic stages that are lost or highly modified by adulthood. All vertebrate embryos — including humans — develop a **notochord**, a **post-anal tail**, and a series of **pharyngeal (branchial) pouches** early in development. In fish, the pharyngeal pouches become gill structures; in humans, the same embryonic pouches develop into structures such as parts of the inner ear, thymus gland, and parathyroid glands. The shared presence of these structures early in development, even in lineages where the adult structure is completely different, points to descent from a common ancestor with a shared developmental program.

7.6.5 Molecular biology

The most direct evidence of common ancestry comes from comparing **DNA and protein sequences** across species. Species that are more closely related (shared a more recent common ancestor) tend to have *more similar* gene and protein sequences than species that are more distantly related, because less time has passed for mutations to accumulate independently in each lineage.

The universal genetic code. Virtually all organisms — bacteria, archaea, plants, fungi, animals — use essentially the *same* genetic code (the same 64 codons specify the same 20 amino acids). This universality is strong evidence that all life shares a single common ancestor: an arbitrary code, once established, would be expected to differ randomly between independent origins of life, but instead it is conserved across the entire tree of life.

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Có 5 nhóm bằng chứng tiến hoá chính: (1) **hoá thạch** — cho thấy dạng trung gian và trình tự thời gian qua các lớp đá; (2) **địa sinh học** — sự phân bố loài (đặc hữu trên đảo) phù hợp với tổ tiên chung phát tán và phân hoá; (3) **giải phẫu so sánh** — cấu trúc tương đồng (cùng nguồn gốc) và cấu trúc thoái hoá/vết tích (vestigial); (4) **phôi học so sánh** — các đặc điểm phát triển phôi giống nhau (dây sống, đuôi sau hậu môn, túi hầu) dù con trưởng thành khác biệt; (5) **sinh học phân tử** — trình tự DNA/protein càng giống nhau thì quan hệ họ hàng càng gần, và **mã di truyền phổ quát** (universal genetic code) — hầu như mọi sinh vật dùng chung một bộ mã — là bằng chứng mạnh mẽ cho tổ tiên chung của toàn bộ sự sống.

7.7 Common Ancestry and Phylogeny

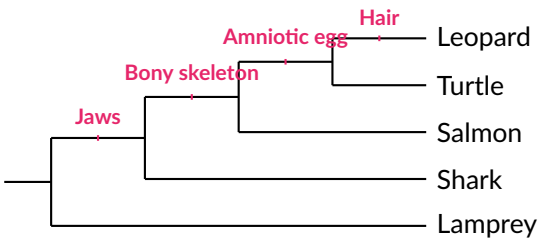
A **phylogenetic tree** (or **cladogram**) is a branching diagram that represents hypothesized evolutionary relationships among taxa. Each branch point (**node**) represents a most recent common ancestor of the taxa descending from it; the taxa at the tips are the groups being compared.

Reading and building a cladogram

Cladograms are built primarily from **shared derived characters**, called **synapomorphies** — traits that arose in the common ancestor of a clade and are shared by all its descendants, distinguishing that clade from other groups. This is different from a **shared ancestral character** (**symplesiomorphy**) — a trait present in the common ancestor of a *larger* group, which is therefore uninformative for defining a smaller subgroup within it (e.g., "has a backbone" is a synapomorphy defining Vertebrata, but it is a symplesiomorphy — not useful for further sorting —

within any subgroup of vertebrates, like mammals).

An **outgroup** is a taxon known (from other evidence) to have diverged *before* the group of interest (the **ingroup**). Comparing ingroup taxa to the outgroup identifies which character states are **ancestral** (also found in the outgroup) versus **derived** (present in some ingroup members but absent in the outgroup), and it is used to root the tree.



A cladogram of five vertebrate taxa (Lamprey as outgroup). Each pink tick mark is a synapomorphy shared by all taxa to its right: jaws unite all but the jawless lamprey; a bony skeleton unites bony fish and tetrapods (sharks retain a cartilaginous skeleton); the amniotic egg unites turtles and leopards (Amniota); hair is unique to (an autapomorphy of) the leopard branch.

Ví dụ mẫu · Constructing a cladogram from a character matrix

Use the character matrix below (outgroup = Sponge; 1 = derived state present, 0 = absent) to construct a cladogram for the remaining three taxa.

Taxon	True tissues	Bilateral symmetry	Segmentation
Sponge (outgroup)	0	0	0
Jellyfish	1	0	0
Flatworm	1	1	0
Earthworm	1	1	1

Reasoning. Sponge lacks all three derived traits, confirming it as the outgroup and rooting the tree. "True tissues" is shared by Jellyfish, Flatworm, and Earthworm $\Rightarrow$ a synapomorphy grouping them together, apart from Sponge. Within that group, "bilateral symmetry" is shared by Flatworm and Earthworm but not Jellyfish $\Rightarrow$ a synapomorphy nesting Flatworm $+$ Earthworm together, apart from Jellyfish. Finally, "segmentation" is unique to Earthworm.

Resulting tree (Newick-style): $(\text{Sponge}, (\text{Jellyfish}, (\text{Flatworm}, \text{Earthworm})))$ — i.e., Flatworm and Earthworm are each other's closest relatives in this matrix, Jellyfish is the next closest relative to that pair, and Sponge is the outgroup.

Ví dụ mẫu · Molecular clock reasoning

A researcher compares the amino acid sequence of the same protein across four species. Using species W as the reference, the number of amino acid differences is: W vs. X $= 6$; W vs. Y $= 18$; W vs. Z $= 40$. Assume, for this exercise, a molecular clock calibrated to 1 amino acid substitution per 3 million years for this protein. Rank X, Y, and Z by how recently each shared a common ancestor with W.

Fewer sequence differences $\Rightarrow$ less time for mutations to accumulate independently $\Rightarrow$ more recent common ancestor. Estimated divergence times:

$$\text{X: } 6 \times 3 = 18 \text{ Mya}, \qquad \text{Y: } 18 \times 3 = 54 \text{ Mya}, \qquad \text{Z: } 40 \times 3 = 120 \text{ Mya}.$$

X shares the most recent common ancestor with W (closest living relative among the three), followed by **Y**, then **Z** (most distantly related, oldest divergence).

VN **GIẢI THÍCH TIẾNG VIỆT**

Cây phát sinh chủng loại (phylogenetic tree/cladogram) được xây dựng chủ yếu dựa trên **đặc điểm phái sinh dùng chung** (synapomorphy) — đặc điểm mới xuất hiện ở tổ tiên chung của một nhánh và được mọi hậu duệ thừa hưởng, dùng để xác định các nhóm (clade). Ngược lại, **đặc điểm tổ tiên dùng chung** (symplesiomorphy) là đặc điểm cũ, có từ tổ tiên xa hơn, KHÔNG giúp phân biệt các nhóm nhỏ bên trong. **Nhóm ngoài** (outgroup) — một loài được biết đã tách ra trước cả nhóm đang nghiên cứu — dùng để xác định đặc điểm nào là nguyên thuỷ (tổ tiên), đặc điểm nào là phái sinh (mới), và để "gắn rễ" cho cây. **Đồng hồ phân tử** (molecular clock) dựa trên giả định số lượng khác biệt trình tự DNA/protein tích luỹ theo tốc độ tương đối ổn định theo thời gian — càng nhiều khác biệt trình tự, thời gian phân tách với tổ tiên chung càng xa.

7.8 Continuing Evolution: Natural Selection in Real Time

Natural selection is not a process confined to the deep past — it is an ongoing, directly observable process, especially in organisms with short generation times and large population sizes.

Real-time natural selection

Antibiotic resistance in bacteria: resistance alleles/mutations pre-exist at low frequency; antibiotic exposure kills susceptible bacteria and selects for resistant survivors, whose frequency rises each generation the antibiotic is used (see the directional-selection example above).

Pesticide resistance in insects: repeated pesticide application selects for pre-existing resistance alleles in insect pest populations (e.g., resistance to DDT in mosquitoes), following the identical logic.

HIV drug resistance: HIV's reverse transcriptase enzyme lacks proofreading, producing a very high mutation rate and enormous standing genetic variation within a single infected patient. A single antiretroviral drug creates strong selection pressure that quickly favors pre-existing resistant viral variants; combination therapy (multiple drugs simultaneously) is far more effective because a virus would need several independent resistance mutations at once, which is far less likely to arise by chance.

(!) Lỗi thường gặp: Sai lầm kiểu Lamarck thường gặp: nói rằng vi khuẩn "phát triển" tính kháng thuốc **ĐỂ PHẢN ỨNG LẠI** với kháng sinh — SAI. Đột biến kháng thuốc xuất hiện **NGẪU NHIÊN**, hoàn toàn độc lập với sự hiện diện của kháng sinh, và đã tồn tại ở tần số thấp trong quần thể TRƯỚC khi tiếp xúc kháng sinh. Kháng sinh không "tạo ra" đột biến có lợi — nó chỉ đóng vai trò là **tác nhân chọn lọc**, giết chết các cá thể không mang alen kháng thuốc và để lại các cá thể mang alen kháng thuốc sinh sản, làm tần số alen đó tăng dần qua các thế hệ.

VN **GIẢI THÍCH TIẾNG VIỆT**

Tiến hoá không chỉ là chuyện của quá khứ xa xôi — nó có thể quan sát được **ngay trong thời gian thực**, đặc biệt ở sinh vật có vòng đời ngắn và quần thể lớn (vi khuẩn, côn trùng, virus). Kháng kháng sinh ở vi khuẩn, kháng thuốc trừ sâu ở côn trùng, và kháng thuốc điều trị ở HIV đều là ví dụ của **chọn lọc định hướng** đang diễn ra: biến dị (đột biến kháng thuốc) đã có sẵn một cách ngẫu nhiên trong quần thể, và tác nhân chọn lọc (thuốc) chỉ làm tăng tần số của biến dị có lợi đó qua các thế hệ — thuốc KHÔNG tạo ra đột biến.

7.9 Speciation

Biological species concept: a species is a group of populations whose members can actually or potentially interbreed in nature and produce viable, fertile offspring, and which are reproductively isolated from other such groups. (Limitation: it cannot be applied to asexually reproducing organisms or to fossils.)

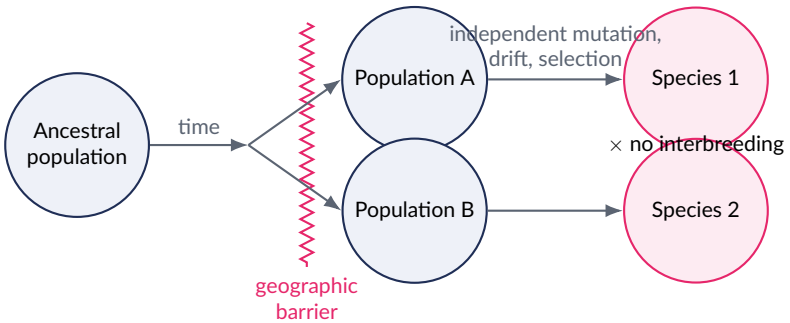
Speciation occurs when **reproductive isolating mechanisms** prevent gene flow between diverging populations long enough for them to become distinct species. These barriers are classified by whether they act before or after fertilization.

Prezygotic barriers (prevent mating or fertilization)	
Habitat isolation	Populations live in different habitats and rarely encounter each other.
Temporal isolation	Populations breed at different times (time of day, season, year).
Behavioral isolation	Differences in courtship rituals/signals prevent mate recognition.
Mechanical isolation	Differences in reproductive anatomy physically prevent mating.
Gametic isolation	Sperm and egg fail to fuse (biochemical incompatibility) even if mating occurs.
Postzygotic barriers (act after a hybrid zygote forms)	
Reduced hybrid viability	Hybrid offspring fail to develop or die before reproductive age.
Reduced hybrid fertility	Hybrids survive but are sterile (e.g., a mule, from horse × donkey).
Hybrid breakdown	First-generation hybrids are viable/fertile, but their offspring (F2) have reduced fitness.

Allopatric vs. sympatric speciation

Allopatric speciation occurs when a population is split by a **geographic barrier** (river, mountain range, land bridge submersion), preventing gene flow; the two isolated populations accumulate independent genetic changes (via mutation, drift, and differing local selection pressures) until reproductive isolation evolves.

Sympatric speciation occurs **without** geographic separation — the diverging populations remain in the same location. Mechanisms include **polyploidy** in plants (an error in meiosis/fertilization produces offspring with extra chromosome sets, which are instantly reproductively isolated from the parent population because hybrid offspring with mismatched chromosome numbers are usually sterile) and **sexual selection** on mate-choice traits that splits a population into groups that no longer interbreed even while sharing the same habitat.



Allopatric speciation: a geographic barrier splits one interbreeding population into two, which accumulate independent genetic changes until reproductive isolation prevents interbreeding even if the barrier later disappears.

VN **GIẢI THÍCH TIẾNG VIỆT**

Khái niệm loài sinh học (biological species concept) định nghĩa loài dựa trên khả năng **giao phối tự nhiên và sinh ra con hữu thụ**. Cơ chế cách li sinh sản chia làm hai nhóm: **cách li trước hợp tử** (prezygotic — ngăn giao phối/thụ tinh xảy ra: cách li nơi ở, thời gian, tập tính, cơ học, giao tử) và **cách li sau hợp tử** (postzygotic — hợp tử đã hình thành nhưng con lai có vấn đề: sức sống giảm, khả năng sinh sản giảm — ví dụ con la vô sinh, hoặc suy thoái con lai ở thế hệ F2). Hình thành loài **khác khu** (allopatric) cần có rào cản địa lý chia cắt quần thể; hình thành loài **cùng khu** (sympatric) xảy ra mà KHÔNG có rào cản địa lý — cơ chế phổ biến nhất ở thực vật là **đa bội hoá** (polyploidy), tạo ra ngay lập tức một quần thể cách li sinh sản với quần thể gốc do không tương thích số lượng nhiễm sắc thể.

7.10 Extinction

Extinction is the permanent disappearance of a species. The **background extinction rate** is the low, relatively steady rate at which species have disappeared throughout most of geologic time, primarily from ordinary causes: environmental change, competition with other species, disease, and localized catastrophes. A **mass extinction** is a much more rapid loss of a large fraction of Earth's species within a short geologic interval, typically triggered by large-scale catastrophic events (e.g., asteroid impact, massive volcanism) or abrupt global environmental change (e.g., rapid climate shifts, ocean anoxia). The best-known mass extinction, the end-Cretaceous (K–Pg) event ~ 66 million years ago, eliminated the non-avian dinosaurs, most likely following a large asteroid impact.

Mass extinction and adaptive radiation. Mass extinctions sharply reduce biodiversity, but by eliminating dominant groups they also open up vacant ecological niches. Surviving lineages often undergo **adaptive radiation** — rapid diversification into many new species that exploit the newly available niches. The extinction of non-avian dinosaurs at the K–Pg boundary is widely credited with opening ecological opportunities that allowed mammals to diversify rapidly in the following epochs.

VN **GIẢI THÍCH TIẾNG VIỆT**

Tỉ lệ tuyệt chủng **nền** (background extinction rate) là mức độ tuyệt chủng thấp, tương đối ổn định diễn ra liên tục trong suốt lịch sử địa chất (do cạnh tranh, thay đổi môi trường cục bộ, bệnh tật...). Ngược lại, **tuyệt chủng hàng loạt** (mass extinction) là sự kiện mất đi một tỉ lệ rất lớn loài trong thời gian địa chất ngắn, thường do thảm hoạ quy mô lớn (va chạm thiên thạch, núi lửa quy mô lớn) hoặc biến đổi môi trường toàn cầu đột ngột. Sau tuyệt chủng hàng loạt, các ổ sinh thái bị bỏ trống tạo điều kiện cho **bức xạ thích nghi** (adaptive radiation) — các dòng sống sót phân hoá nhanh chóng thành nhiều loài mới để lấp đầy những ổ sinh thái đó (ví dụ: động vật có vú đa dạng hoá mạnh sau khi khủng long không phải chim tuyệt chủng).

7.11 Variation in Populations and Genetic Drift

Natural selection can only act on **existing heritable variation**. Two processes generate that variation in the first place:

Sources of genetic variation

Mutation is the ultimate source of *all new* alleles — random changes in DNA sequence (point mutations, insertions, deletions, chromosomal changes). It is rare per gene per generation but

is the only process that creates genuinely new genetic material.

Recombination reshuffles *existing* alleles into new combinations without creating new alleles: **crossing over** during meiosis I exchanges segments between homologous chromosomes, and **independent assortment** of homologous chromosome pairs during meiosis I, together with random fertilization, generates enormous genotypic diversity among offspring each generation.

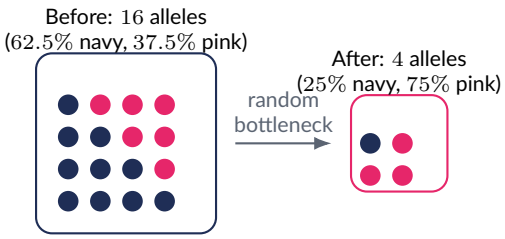
Genetic drift is the random, chance fluctuation of allele frequencies from one generation to the next due to sampling error — which allele copies happen, purely by chance, to be passed on. Because sampling error is proportionally larger in small samples, drift has the strongest effect in **small populations**, and can cause allele frequencies to change regardless of whether the allele is beneficial, neutral, or even mildly harmful. Two special cases are especially important:

Bottleneck effect vs. founder effect

Bottleneck effect: an existing population's size is drastically and suddenly reduced by a random event (natural disaster, disease outbreak, overhunting) unrelated to genotype. The small group of survivors, by chance, carries only a non-representative sample of the original gene pool's alleles — some alleles may be lost entirely, and allele frequencies can shift sharply. Real example: northern elephant seals were hunted to near-extinction (as few as ~ 20 individuals) in the late 1800s; the modern population, though numbering in the tens of thousands again, has unusually low genetic diversity as a legacy of that bottleneck.

Founder effect: a *new* population is established by a small number of individuals who, by chance, carry only a non-representative sample of alleles from the original (source) population's gene pool. Real example: the Amish community of Lancaster County descends from a small number of founders and has an unusually high frequency of certain rare recessive alleles (such as the allele causing Ellis–van Creveld syndrome) that happened to be carried by the founders, compared to the broader population they came from.

Both processes are forms of **genetic drift** and both tend to **reduce genetic diversity** in the resulting population — the difference is simply whether an *existing* population's size crashes (bottleneck) or a *new* population is founded by a small sample (founder effect).



Schematic bottleneck effect: a random, size-independent-of-genotype crash in population size leaves a small, non-representative sample of the original gene pool, sharply — and randomly — shifting allele frequencies and reducing genetic diversity.

Ví dụ mẫu · Bottleneck effect: numeric example

A population of $1{,}000$ beetles has allele frequencies $p(A) = 0.6$, $q(a) = 0.4$ at a color locus. A wildfire kills all but 5 survivors. By chance, the 5 survivors have genotypes: 3 are AA, 2 are Aa, 0 are aa. Find the new allele frequencies after the bottleneck.

Total alleles among survivors: $2 \times 5 = 10$.

$$A \text{ alleles} = 3(2) + 2(1) = 6 + 2 = 8, \qquad a \text{ alleles} = 2(0) + 2(1) = 0 + 2 = 2.$$

$$p' = \frac{8}{10} = 0.80, \qquad q' = \frac{2}{10} = 0.20.$$

Purely by chance, the frequency of a dropped from 0.40 to 0.20 — not because a was less fit, but because the handful of survivors happened not to be representative of the pre-fire gene pool. This is genetic drift acting through a population bottleneck, and it has reduced the population's genetic diversity going forward.

(!) Lỗi thường gặp: Phân biệt **hiệu ứng thắt cổ chai** (bottleneck effect) và **hiệu ứng người sáng lập** (founder effect) — cả hai đều là biến động di truyền ngẫu nhiên (genetic drift) và đều làm GIẢM đa dạng di truyền, nhưng khác nhau ở nguồn gốc: thắt cổ chai xảy ra khi một quần thể ĐANG TỒN TẠI bị giảm kích thước đột ngột (thiên tai, dịch bệnh, săn bắt quá mức); hiệu ứng người sáng lập xảy ra khi một quần thể MỚI được thành lập bởi một nhóm nhỏ cá thể tách ra từ quần thể gốc (ví dụ: một nhóm chim nhỏ bị bão thổi dạt tới đảo mới). Câu hỏi để phân biệt: "quần thể có bị giảm kích thước tại chỗ không (thắt cổ chai), hay có một nhóm nhỏ tách ra lập quần thể mới ở nơi khác không (người sáng lập)?"

VN **GIẢI THÍCH TIẾNG VIỆT**

Biến dị trong quần thể đến từ **đột biến** (nguồn duy nhất tạo alen HOÀN TOÀN MỚI) và **tái tổ hợp** (trao đổi chéo, phân li độc lập — xáo trộn lại các alen ĐÃ CÓ SẴN thành tổ hợp mới, không tạo alen mới). **Biến động di truyền** (genetic drift) là sự thay đổi tần số alen một cách NGẪU NHIÊN do sai số lấy mẫu, tác động mạnh nhất ở quần thể NHỎ. Hai trường hợp đặc biệt của drift: **hiệu ứng thắt cổ chai** (quần thể hiện tại bị giảm kích thước đột ngột và ngẫu nhiên) và **hiệu ứng người sáng lập** (quần thể mới hình thành từ một số ít cá thể mang mẫu alen không đại diện cho quần thể gốc) — cả hai đều làm giảm đa dạng di truyền.

7.12 Practice Problems

Bài tập luyện tập

Which of the following is *not* one of Darwin's original observations or inferences underlying natural selection?

(A) Populations produce more offspring than the environment can support.

(B) Individuals within a population vary, and much of this variation is heritable.

(C) Organisms actively strive to improve themselves in response to need.

(D) Individuals with favorable heritable traits tend to leave more offspring.

Lời giải chi tiết

Darwin's logic is built from overproduction, heritable variation, the resulting struggle for existence, and differential survival/reproduction. The idea that organisms "strive to improve" in response to need is a Lamarckian concept (inheritance of acquired characteristics), not part of Darwin's natural-selection framework. **(C)**.

Bài tập luyện tập

Before widespread pollution, light-colored peppered moths (*Biston betularia*) were far more common than dark moths because they were camouflaged on light, lichen-covered tree bark.

After industrial pollution darkened the trees with soot, dark moths became far more common within a few decades. This is best described as:

(A) Stabilizing selection
(B) Disruptive selection
(C) Directional selection
(D) Genetic drift

Lời giải chi tiết

The population mean phenotype shifted from mostly light-colored to mostly dark-colored as the environment changed in a consistent direction (increasing soot) — one phenotypic extreme was consistently favored over the other. **(C)**.

Bài tập luyện tập

Human infants born near the average birth weight have the lowest mortality rate; both much smaller and much larger infants have higher mortality. This is an example of:

(A) Directional selection
(B) Stabilizing selection
(C) Disruptive selection
(D) Artificial selection

Lời giải chi tiết

Both phenotypic extremes are selected against and the intermediate phenotype is favored, reducing variance around an unchanged mean. **(B)**.

Bài tập luyện tập

In a population of seed-eating finches, individuals with very small bills (efficient at cracking soft seeds) and individuals with very large bills (efficient at cracking hard seeds) both have higher survival than individuals with intermediate bill size, which are inefficient at both. Explain what type of selection this is and predict its effect on the population's bill-size distribution over time.

Lời giải chi tiết

Both phenotypic extremes are favored over the intermediate phenotype, so this is **disruptive (diversifying) selection**. Over time it increases the variance in bill size and can split the single bell-shaped distribution into a **bimodal** distribution (two peaks: small-billed and large-billed), potentially setting the stage for sympatric speciation if the two phenotype classes eventually stop interbreeding (e.g., due to assortative mating within each bill-size class).

Bài tập luyện tập

What is the key difference between artificial selection and natural selection?

(A) Artificial selection does not involve heritable variation.
(B) Artificial selection is driven by human-chosen breeding criteria, while natural selection is driven by the environment.
(C) Artificial selection cannot change allele frequencies.
(D) Natural selection only occurs in wild, undomesticated species.

Lời giải chi tiết

Both processes rely on the same underlying logic (heritable variation + differential reproduction), and both can occur in any species. The distinguishing feature is simply *who/what* determines which individuals reproduce: a human breeder for artificial selection, versus the environment for natural selection. **(B)**.

Bài tập luyện tập

Explain, in 2–3 sentences, how observing artificial selection in domesticated pigeons and crop plants helped Darwin formulate his theory of natural selection.

Lời giải chi tiết

Darwin saw that pigeon breeders could produce dramatic phenotypic change in relatively few generations simply by choosing which birds with desired heritable traits were allowed to reproduce. This showed him that selective, differential reproduction based on heritable variation is a powerful mechanism for change. He reasoned that an analogous process could operate in nature, with the environment (rather than a human breeder) determining which individuals survive and reproduce, and that over the vastly longer timescale of geologic history, this natural process could plausibly produce the full diversity of life.

Bài tập luyện tập

The "gene pool" of a population is best defined as:

(A) The total number of individuals in the population.

(B) The complete set of alleles at all loci carried by every member of the population.

(C) The genotype of a single representative individual.

(D) The set of alleles found only in homozygous individuals.

Lời giải chi tiết

The gene pool is the sum of all alleles, at every gene locus, present in every individual of the population — the raw material on which evolutionary forces act. **(B)**.

Bài tập luyện tập

The MN blood group is codominant. In a sample of 100 people: $MM = 36$, $MN = 48$, $NN = 16$. Calculate the frequency of the M and N alleles.

Lời giải chi tiết

Total alleles $= 2(100) = 200$.

$$\text{freq}(M) = \frac{2(36) + 48}{200} = \frac{120}{200} = 0.60, \qquad \text{freq}(N) = \frac{2(16) + 48}{200} = \frac{80}{200} = 0.40.$$

Check: $0.60 + 0.40 = 1.00$. ✓ (This is a direct genotype count, not a Hardy–Weinberg calculation — no equilibrium assumption is needed since all three genotypes are directly observable.)

Bài tập luyện tập

In a population of pea plants, wrinkled seeds (aa, recessive) occur at a frequency of 4%. Assuming Hardy–Weinberg equilibrium, find p, q, and all three genotype frequencies, and state the percentage of plants that are heterozygous carriers.

Lời giải chi tiết

$q^2 = 0.04 \Rightarrow q = \sqrt{0.04} = 0.20$. Then $p = 1 - 0.20 = 0.80$.

$$p^2 = (0.80)^2 = 0.64\ (64\%\ AA), \qquad 2pq = 2(0.80)(0.20) = 0.32\ (32\%\ Aa),$$

$$q^2 = 0.04\ (4\%\ aa).$$

Check: $0.64 + 0.32 + 0.04 = 1.00$. 32% of the population are heterozygous carriers.

Bài tập luyện tập

In a population of 500 butterflies, a wing-pattern gene has allele frequencies $p = 0.8$ and $q = 0.2$ at Hardy–Weinberg equilibrium. Find the expected number of individuals with each genotype.

Lời giải chi tiết

$$p^2 = 0.64, \qquad 2pq = 2(0.8)(0.2) = 0.32, \qquad q^2 = 0.04.$$

Expected counts: $AA = 0.64 \times 500 = 320$; $Aa = 0.32 \times 500 = 160$; $aa = 0.04 \times 500 = 20$. Check: $320 + 160 + 20 = 500$. ✓

Bài tập luyện tập

Which of the following would most likely cause a real population to deviate from Hardy–Weinberg equilibrium?

(A) An extremely large population size

(B) Completely random mating with respect to the trait

(C) A severe population crash leaving only a handful of survivors

(D) Absence of migration into or out of the population

Lời giải chi tiết

A drastic reduction in population size introduces genetic drift (violating the "infinitely large population" assumption), the classic cause of deviation from Hardy–Weinberg proportions. The other three options describe conditions that are consistent *with* equilibrium, not violations of it. **(C)**.

Bài tập luyện tập

Snapdragon flower color is codominant: C^RC^R = red, C^RC^W = pink, C^WC^W = white. In a sample of 100 plants: red $= 50$, pink $= 40$, white $= 10$. Determine whether this population appears to be in Hardy–Weinberg equilibrium.

Lời giải chi tiết

Observed allele frequencies (total alleles $= 200$):

$$p(C^R) = \frac{2(50)+40}{200} = \frac{140}{200} = 0.70, \qquad q(C^W) = \frac{2(10)+40}{200} = \frac{60}{200} = 0.30.$$

Hardy–Weinberg expected counts: $p^2N = 0.49 \times 100 = 49$; $2pqN = 0.42 \times 100 = 42$; $q^2N = 0.09 \times 100 = 9$. Comparing observed $(50, 40, 10)$ to expected $(49, 42, 9)$: the differences are only ± 1 individual in each category — small enough to be attributed to ordinary sampling variation. The population **appears to be in Hardy–Weinberg equilibrium**.

Bài tập luyện tập

In a population where individuals with a certain phenotype consistently produce more surviving offspring than individuals with other phenotypes, which Hardy–Weinberg assumption is being violated?

(A) No mutation
(B) No natural selection
(C) Random mating
(D) Infinitely large population

Lời giải chi tiết

Consistently unequal reproductive success based on phenotype is, by definition, natural selection — this directly violates the "no natural selection / all genotypes equally fit" assumption. **(B)**.

Bài tập luyện tập

Use the character matrix below (outgroup = Taxon P) to determine the evolutionary relationships among Taxa Q, R, and S.

Taxon	Character 1	Character 2
P (outgroup)	0	0
Q	1	0
R	1	1
S	1	1

Which two taxa are most closely related, and which character is a synapomorphy uniting them?

Lời giải chi tiết

Character 1 is shared by Q, R, and S (absent in outgroup P), so it is a synapomorphy uniting all three relative to P. Character 2 is shared only by R and S (Q lacks it), so it is a synapomorphy uniting **R and S** as each other's closest relatives, with Q branching off earlier. Tree: $(P, (Q, (R, S)))$.

Bài tập luyện tập

A trait present in the common ancestor of an entire class (e.g., "has mammary glands" for all mammals) is of little use for distinguishing individual orders *within* that class (e.g., primates vs. rodents). This trait is best described, in that narrower context, as a:

(A) Synapomorphy
(B) Symplesiomorphy
(C) Analogous structure
(D) Vestigial structure

Lời giải chi tiết

A trait shared because it was already present in an ancestor common to a *larger* group is a shared ancestral character — a symplesiomorphy — and provides no information for resolving relationships *within* that larger group. **(B)**.

Bài tập luyện tập

Explain why systematists include an outgroup when constructing a phylogenetic tree, and give an example of how it is used.

Lời giải chi tiết

An outgroup is a taxon known, from independent evidence, to have diverged before the group under study (the ingroup). Comparing ingroup character states to the outgroup reveals which states are ancestral (shared with the outgroup) and which are derived (present in the ingroup but absent in the outgroup); the derived states are then used as synapomorphies to group ingroup taxa, and the outgroup is used to root the tree. For example, a lamprey (jawless) can serve as an outgroup for a study of jawed vertebrates, since the presence of jaws is then identified as a derived trait of the ingroup.

Bài tập luyện tập

Comparing the same protein across species, with species W as reference: W vs. X differs by 6 amino acids, W vs. Y by 18, and W vs. Z by 40. Using a hypothetical molecular clock rate of 1 substitution per 3 million years for this protein, estimate each divergence time and rank X, Y, Z from most to least closely related to W.

Lời giải chi tiết

$$\text{X: } 6 \times 3 = 18 \text{ Mya}, \qquad \text{Y: } 18 \times 3 = 54 \text{ Mya}, \qquad \text{Z: } 40 \times 3 = 120 \text{ Mya}.$$

Fewer amino acid differences indicate a more recent common ancestor. From most to least closely related to W: **X** $>$ **Y** $>$ **Z**.

Bài tập luyện tập

The fact that nearly all organisms — from bacteria to humans — use the same 64-codon genetic code to specify the same 20 amino acids is considered strong evidence for:

(A) Convergent evolution among unrelated lineages
(B) A single common ancestor for all life
(C) The inheritance of acquired characteristics
(D) Sympatric speciation

Lời giải chi tiết

An arbitrary code, if it originated independently multiple times, would be expected to differ between lineages. Its universality across the entire tree of life instead points to a single com-

mon ancestor from which all life inherited the same code. **(B)**.

Bài tập luyện tập

All vertebrate embryos, including humans, develop pharyngeal (branchial) pouches early in development, even though the adult structures that these pouches become differ enormously between fish and mammals. Explain what this shared embryonic feature suggests about vertebrate evolutionary history.

Lời giải chi tiết

Shared developmental features that appear in the embryos of very different adult organisms suggest that those organisms inherited a common underlying developmental program from a shared ancestor. In fish, the pharyngeal pouches develop into gill structures; in humans, the same embryonic pouches develop into structures such as parts of the inner ear, the thymus, and the parathyroid glands. The retention of this shared early developmental stage, despite very different adult outcomes, is evidence of descent from a common ancestor with that developmental program, later modified differently in each lineage.

Bài tập luyện tập

The wing of a bee and the wing of a bird are best classified as:

(A) Homologous structures
(B) Analogous structures
(C) Vestigial structures
(D) Symplesiomorphies

Lời giải chi tiết

Both structures allow flight, but they have completely different structural origins (chitin exoskeleton extension vs. modified bony forelimb) and evolved independently in unrelated lineages — a case of convergent evolution, making them analogous, not homologous. **(B)**.

Bài tập luyện tập

Small, non-functional pelvic and leg bones found embedded within the body wall of some whale species are best explained as:

(A) Analogous structures shared with fish
(B) Evidence of ongoing directional selection for larger pelvises
(C) Vestigial structures inherited from four-limbed, land-dwelling ancestors
(D) Structures resulting from recent gene flow with land mammals

Lời giải chi tiết

Whales descend from four-limbed land mammals. The small pelvic/leg bones no longer serve a locomotor function but persist as reduced remnants of the ancestral hind-limb skeleton — a vestigial structure. **(C)**.

Bài tập luyện tập

A student claims that bacteria "develop" antibiotic resistance because they need it to survive drug exposure. Explain why this statement misrepresents how antibiotic resistance actually evolves in a bacterial population.

Lời giải chi tiết

This statement incorrectly implies that the antibiotic causes bacteria to acquire resistance in response to need (a Lamarckian idea). In reality, resistance mutations arise randomly, through ordinary mutation, independent of and prior to any antibiotic exposure, and typically exist at low frequency within the population by chance. The antibiotic does not create the mutation — it acts purely as a **selective agent**: bacteria that happen to already carry a resistance allele survive and reproduce, while susceptible bacteria die, so the frequency of the resistance allele rises across generations. This is directional selection acting on pre-existing variation, not an organism-directed response to need.

Bài tập luyện tập

Under the biological species concept, two populations are considered separate species primarily when:

(A) They live on different continents.

(B) They differ noticeably in coloration.

(C) They cannot interbreed and produce fertile offspring in nature.

(D) They have different chromosome numbers under all circumstances.

Lời giải chi tiết

The biological species concept defines species boundaries by reproductive isolation: the inability of two populations to interbreed and produce fertile offspring under natural conditions, regardless of geographic location or superficial appearance. **(C)**.

Bài tập luyện tập

For each scenario, identify the specific reproductive isolating mechanism involved.
(a) Two toad species live in the same pond, but one breeds only in early spring and the other only in autumn.
(b) Two firefly species use distinct, species-specific flash patterns during courtship, and females only respond to their own species' pattern.
(c) Horses and donkeys can mate and produce mules, but mules are almost always sterile.
(d) Two land snail species have shells that coil in opposite directions, physically preventing successful mating between them.

Lời giải chi tiết

(a) **Temporal isolation** (prezygotic) — different breeding seasons prevent mating.
(b) **Behavioral isolation** (prezygotic) — species-specific courtship signals prevent mate recognition.
(c) **Reduced hybrid fertility** (postzygotic) — a viable hybrid forms but cannot itself reproduce.
(d) **Mechanical isolation** (prezygotic) — incompatible reproductive anatomy prevents mating.

Bài tập luyện tập

An error during meiosis produces a plant offspring with double the normal chromosome number. This new plant can no longer produce fertile offspring with the parent population but can self-fertilize or mate with other polyploid individuals. This is an example of:

(A) Allopatric speciation
(B) Sympatric speciation via polyploidy
(C) The founder effect
(D) Gametic isolation only

Lời giải chi tiết

No geographic barrier is involved — reproductive isolation arises instantly in the same location due to a chromosome-number mismatch with the parent population. This is sympatric speciation via polyploidy. **(B)**.

Bài tập luyện tập

A river changes course over thousands of years, permanently splitting a single population of rodents into two groups that can no longer contact each other. Over many generations, the two groups accumulate different adaptations and, when researchers later test them, can no longer produce fertile offspring together. This is an example of:

(A) Sympatric speciation
(B) Allopatric speciation
(C) Postzygotic-only isolation with no prezygotic barriers
(D) Artificial selection

Lời giải chi tiết

A geographic barrier (the river's new course) physically separated the population, preventing gene flow while each group evolved independently — the defining feature of allopatric speciation. **(B)**.

Bài tập luyện tập

Explain the relationship between the K–Pg mass extinction event and the subsequent diversification of mammals.

Lời giải chi tiết

The K–Pg mass extinction (~ 66 million years ago) eliminated the non-avian dinosaurs and many other groups, which had previously dominated most terrestrial ecological niches. Their disappearance left numerous niches vacant. Surviving mammal lineages, no longer excluded from those niches by dinosaur dominance and competition, underwent adaptive radiation — rapidly diversifying in body size, diet, and habitat to exploit the newly available ecological opportunities, giving rise to the wide range of mammalian orders present today.

Bài tập luyện tập

The steady, low-level rate of species loss that has occurred throughout most of geologic time, distinct from rare episodes of much higher species loss, is called:

(A) Mass extinction rate
(B) Background extinction rate
(C) Adaptive radiation rate
(D) Founder extinction rate

Lời giải chi tiết

The ordinary, low, ongoing rate of extinction (from competition, disease, localized environmental change) is the background extinction rate, contrasted with mass extinction events, which involve a much larger fraction of species lost over a much shorter geologic interval. **(B)**.

Bài tập luyện tập

For each scenario, identify whether it illustrates the bottleneck effect or the founder effect.
(a) A severe hurricane kills 95% of a lizard population on an island, leaving only a small, randomly surviving group.
(b) A small flock of finches is blown off course by a storm and colonizes a previously uninhabited island, establishing a new population.

Lời giải chi tiết

(a) **Bottleneck effect** — an existing population's size is drastically and randomly reduced in place.
(b) **Founder effect** — a new population is established elsewhere by a small, non-representative sample of individuals from the source population.

Bài tập luyện tập

A population of 800 rabbits has allele frequencies $p = q = 0.5$ before a disease epidemic. Only 6 rabbits survive: 4 are AA, 1 is Aa, and 1 is aa. Calculate the new allele frequencies after the epidemic.

Lời giải chi tiết

Total alleles among survivors: $2 \times 6 = 12$.

$$A \text{ alleles} = 4(2) + 1(1) = 8 + 1 = 9, \qquad a \text{ alleles} = 1(1) + 1(2) = 1 + 2 = 3.$$

$$p' = \frac{9}{12} = 0.75, \qquad q' = \frac{3}{12} = 0.25.$$

The allele frequencies shifted sharply, from $0.50/0.50$ to $0.75/0.25$, purely due to the random identity of the few survivors — a clear illustration of genetic drift through a population bottleneck.

Bài tập luyện tập

Which process is capable of introducing a genuinely *new* allele into a population's gene pool for the first time?

(A) Independent assortment
(B) Crossing over
(C) Mutation
(D) Random fertilization

Lời giải chi tiết

Crossing over, independent assortment, and random fertilization all reshuffle *existing* alleles into new combinations, but none of them create new allele sequences. Only mutation generates genuinely new genetic variants. **(C)**.

Ecology

Mục tiêu Unit: Phản ứng của sinh vật với môi trường (tập tính bẩm sinh và tập tính học được, taxis, kinesis, fixed action pattern, đáp ứng sinh lý như điều hoà thân nhiệt và di cư); dòng năng lượng qua hệ sinh thái (bậc dinh dưỡng, GPP/NPP, quy tắc 10%, tháp năng lượng và tháp sinh khối); sinh thái học quần thể (kích thước, mật độ, kiểu phân bố, mô hình tăng trưởng hàm mũ và logistic, sức chứa môi trường K, chiến lược sống r/K); ảnh hưởng của mật độ lên tăng trưởng quần thể (nhân tố phụ thuộc và không phụ thuộc mật độ); sinh thái học quần xã (cạnh tranh khác loài, ăn thịt, ăn cỏ, cộng sinh, ổ sinh thái, loài chủ chốt, diễn thế sinh thái); đa dạng sinh học; và các tác nhân gây xáo trộn hệ sinh thái (phá huỷ/chia cắt môi trường sống, loài xâm lấn, biến đổi khí hậu, ô nhiễm, phú dưỡng, khuếch đại sinh học).

8.1 Responses to the Environment

8.1.1 Behavioral Responses: Innate and Learned Behavior

A **behavior** is a coordinated, observable response of an organism to a stimulus. Like anatomical or biochemical traits, behaviors have costs and benefits for survival and reproduction, so behaviors that raise fitness tend to persist and spread in a population through natural selection.

Innate behavior is largely genetically programmed: it appears in essentially the same form in every individual of a species regardless of prior experience, and does not need to be learned (though it may be fine-tuned somewhat by experience). **Learned behavior** is modified by individual experience and can therefore vary among individuals of the same species. Forms of learning include **habituation** (a decreased response to a repeated, harmless stimulus), **imprinting** (rapid, often irreversible learning during a brief sensitive period early in development — e.g. newly hatched geese following and forming an attachment to the first moving object they see), classical and operant conditioning, and social learning through observation and imitation.

Three classic patterns of innate behavior

Fixed action pattern (FAP): a highly stereotyped, species-typical behavioral sequence that, once triggered by a specific **sign stimulus** (releaser), runs to completion essentially unchanged even if conditions change partway through. Classic example: a greylag goose that sees an egg outside its nest performs a fixed head-and-neck "rolling" motion to bring it back; if the egg is removed mid-sequence, the goose completes the same rolling motion regardless.

Taxis (pl. taxes): *directed* movement toward (positive) or away from (negative) a specific stimulus — the organism orients its body relative to the stimulus and moves along that axis. Examples: phototaxis (light), chemotaxis (a chemical gradient), geotaxis (gravity).

Kinesis: an *undirected* change in the *rate* of movement (e.g. speed, turning frequency) in response to a stimulus. The organism does not orient toward or away from the stimulus itself; instead, random movement increases in unfavorable conditions and decreases in favorable ones, which statistically leaves individuals aggregated in favorable patches even though no single movement was "aimed" there.

Ví dụ mẫu · Taxis vs. kinesis

Two observations: (1) a planarian flatworm placed in a dish with a light source consistently swims to the darkest corner of the dish. (2) A pillbug (terrestrial isopod) placed in a dish with a dry half and a humid half moves in short, frequent, randomly-directed bursts while on the dry side, but moves in long, infrequent bursts once it wanders onto the humid side — with no tendency to turn specifically toward the humid side. After some time, most pillbugs end up clustered on the humid side.

Classify each. (1) The planarian orients its body *directly away from* the light stimulus and moves along that axis ⇒ **negative phototaxis** (directed movement). (2) The pillbug does not orient toward humidity at all — it simply moves less (lower turning/movement rate) once conditions become favorable ⇒ **kinesis**. The pillbugs' eventual aggregation on the humid side is an indirect statistical consequence of reduced movement in a favorable patch, not directed navigation toward it.

VN **GIẢI THÍCH TIẾNG VIỆT**

Ba khái niệm dễ nhầm: **FAP** (mô thức hành vi cố định) là một chuỗi động tác rập khuôn, khi đã được một *tín hiệu kích hoạt* (sign stimulus) khởi động thì chạy hết chuỗi động tác dù hoàn cảnh có đổi. **Taxis** là di chuyển *có định hướng* — sinh vật quay cơ thể hướng về (dương) hoặc lánh xa (âm) nguồn kích thích rồi di chuyển theo hướng đó, ví dụ trùng roi bơi về phía ánh sáng (phototaxis dương). **Kinesis** là thay đổi *tốc độ/tần suất di chuyển* một cách KHÔNG định hướng — con vật không hướng về hay tránh xa nguồn kích thích, mà chỉ di chuyển ngẫu nhiên nhiều hơn khi điều kiện bất lợi và ít hơn khi điều kiện thuận lợi; kết quả là quần thể "vô tình" tụ lại ở nơi thuận lợi dù từng cá thể không hề biết hướng đi. Cả ba đều là tập tính **bẩm sinh** (innate), khác với tập tính **học được** (learned) như in vết (imprinting) hay quen nhờn (habituation), vốn phụ thuộc vào kinh nghiệm cá thể.

8.1.2 Physiological Responses and Fitness

Organisms also respond to environmental change with internal, physiological adjustments, not just behavior.

Thermoregulation: endotherms (birds, mammals) generate their own metabolic heat and use physiological mechanisms — vasodilation/vasoconstriction of blood vessels near the skin, shivering thermogenesis, sweating or panting — to hold body temperature within a narrow range largely independent of the external environment. **Ectotherms** (most reptiles, amphibians, fish, and invertebrates) rely much more heavily on *behavior* (basking in sun, seeking shade, burrowing) because their body temperature tracks ambient temperature; they spend far less energy on internal heat production, which frees up more energy for growth and reproduction, but limits their activity when it is cold.

Migration timing: many species time seasonal migration, breeding, or dormancy (hibernation, diapause) to environmental cues — especially **photoperiod** (day length, a highly reliable predictor of season) and temperature — often relayed through hormonal signaling (e.g. melatonin, thyroid hormones). This timing maximizes overlap between resource availability (food, nesting sites, mates) and the energetically demanding stages of the life cycle.

Fitness, precisely defined, is an individual's (or genotype's) relative reproductive success — the number of viable, fertile offspring it contributes to the next generation compared to other individuals in the population. Behavioral and physiological responses matter evolutionarily only insofar as they raise or lower fitness: a migratory bird arriving at breeding grounds in sync with peak food (insect) abundance raises more surviving chicks than one arriving too early or too late; an animal that thermoregulates efficiently spends less energy compensating for temperature stress and has more energy left over for growth and reproduction. Because these responses have a heritable component, natural selection can shape and fine-tune them across generations.

VN **GIẢI THÍCH TIẾNG VIỆT**

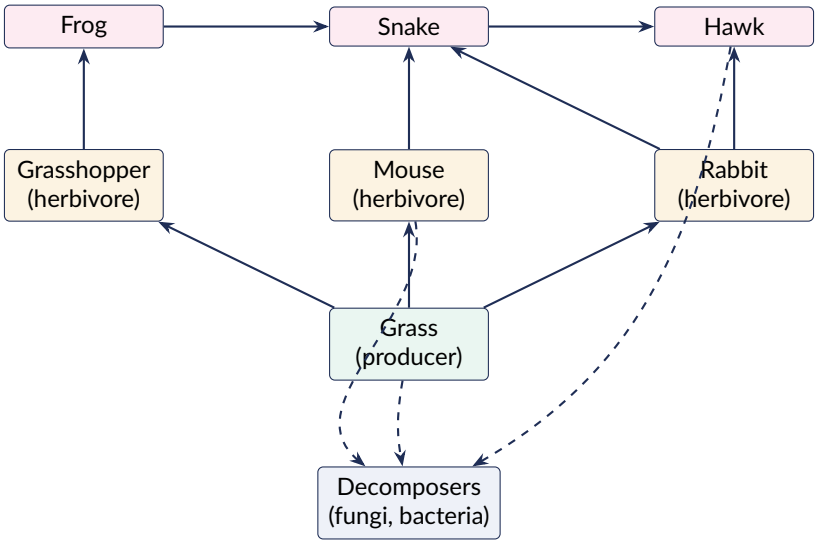
Đáp ứng sinh lý khác đáp ứng tập tính ở chỗ nó diễn ra *bên trong cơ thể* thay vì qua hành động quan sát được. Động vật **đẳng nhiệt** (endotherm — chim, thú) tự sinh nhiệt bằng chuyển hoá và điều chỉnh (co/giãn mạch máu, run cơ, đổ mồ hôi) để giữ thân nhiệt ổn định bất kể nhiệt độ môi trường; động vật **biến nhiệt** (ectotherm — bò sát, lưỡng cư, cá, đa số động vật không xương sống) dựa chủ yếu vào *tập tính* (phơi nắng, tìm bóng râm) vì thân nhiệt biến đổi theo môi trường. Thời điểm di cư/sinh sản của nhiều loài được đồng bộ hoá với **độ dài ngày** (photoperiod) — tín hiệu đáng tin cậy nhất về mùa. Điểm mấu chốt: các đáp ứng này chỉ có ý nghĩa tiến hoá nếu chúng ảnh hưởng đến **độ thích nghi** (fitness) — tức khả năng sinh sản thành công tương đối của cá thể.

8.2 Energy Flow Through Ecosystems

8.2.1 Trophic Levels, Food Chains, and Food Webs

Energy enters most ecosystems as sunlight and is captured by **producers** (autotrophs — plants, algae, cyanobacteria, and, in chemosynthetic ecosystems, certain bacteria/archaea that oxidize inorganic compounds instead of using light). Producers occupy the first **trophic level**. **Primary consumers** (herbivores) eat producers and occupy the second trophic level; **secondary consumers** eat primary consumers (third trophic level); **tertiary consumers** eat secondary consumers (fourth trophic level); some ecosystems support quaternary consumers at a fifth level. **Decomposers and detritivores** (fungi, many bacteria, earthworms, and other scavengers) break down dead organic matter and waste from *every* trophic level, releasing inorganic nutrients (N, P, etc.) back into the soil or water for producers to take up again — this recycling loop is what allows *matter*, unlike energy, to cycle repeatedly through an ecosystem.

A **food chain** is a single linear pathway of energy transfer (e.g. grass → grasshopper → frog → snake → hawk). A **food web** is the full network of interconnected, overlapping food chains within a community, since most consumers eat — and are eaten by — more than one species.



A simplified terrestrial food web. Solid arrows point from food source toward consumer (direction of energy flow) — the snake and hawk each feed at more than one point in the web, which is why a *web* is a more realistic model than a single linear *chain*. Dashed arrows show a sample of the continuous transfer of dead organic matter to decomposers from every trophic level.

VN **GIẢI THÍCH TIẾNG VIỆT**

Bậc dinh dưỡng (trophic level) là vị trí của một sinh vật trong chuỗi truyền năng lượng: sinh vật sản xuất (bậc 1) → sinh vật tiêu thụ bậc 1/ăn cỏ (bậc 2) → tiêu thụ bậc 2 (bậc 3) → tiêu thụ bậc 3 (bậc 4). **Chuỗi thức ăn** là một đường thẳng đơn lẻ; **lưới thức ăn** là tập hợp nhiều chuỗi thức ăn đan xen nhau vì hầu hết sinh vật ăn — và bị ăn bởi — nhiều hơn một loài. Sinh vật phân giải (decomposer/detritivore — nấm, vi khuẩn, giun đất) đóng vai trò đặc biệt: chúng phân giải xác chết và chất thải từ *mọi* bậc dinh dưỡng, trả lại chất dinh dưỡng vô cơ cho môi trường để sinh vật sản xuất tái sử dụng — đây chính là cơ chế giúp **vật chất được tuần hoàn**, khác hẳn với năng lượng (chỉ đi một chiều, xem mục tiếp theo).

8.2.2 Gross and Net Primary Productivity

Gross primary productivity (GPP) is the total rate at which producers convert light (or chemical) energy into chemical energy stored in organic compounds via photosynthesis, typically expressed per unit area per unit time (e.g. kcal/m^2/yr or g/m^2/yr). Producers use part of this captured energy to run their own cellular respiration (R), fueling their own growth and maintenance. **Net primary productivity (NPP)** is what remains after subtracting that respiration:

$$\text{NPP} = \text{GPP} - R.$$

NPP is the rate of new producer biomass accumulation, and it is the only portion of captured energy actually available to enter the rest of the food web — i.e. available to primary consumers (and, indirectly, every level above them) or to be stored as standing plant biomass.

Ví dụ mẫu · GPP, respiration, and NPP

A patch of forest has producers with gross primary productivity GPP $= 12{,}000$ kcal/m^2/yr. The producers themselves use $R = 4{,}500$ kcal/m^2/yr for their own cellular respiration. Find the net primary productivity.

$$\text{NPP} = \text{GPP} - R = 12{,}000 - 4{,}500 = 7{,}500 \text{ kcal/m}^2\text{/yr}.$$

Only this $7{,}500$ kcal/m^2/yr — not the full $12{,}000$ — is available to primary consumers and everything above them in the food web, or to accumulate as new plant biomass.

VN **GIẢI THÍCH TIẾNG VIỆT**

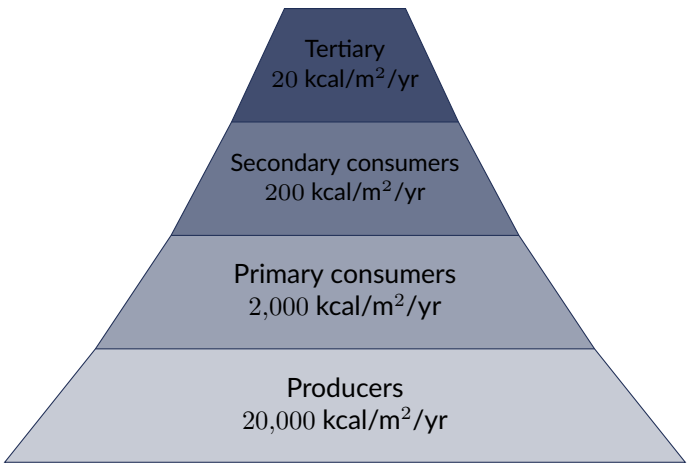
GPP là **tổng** năng lượng sinh vật sản xuất cố định được qua quang hợp; nhưng bản thân sinh vật sản xuất phải "tiêu" bớt một phần cho hô hấp tế bào của chính nó (R) để duy trì sự sống. Phần **còn lại thực sự tích luỹ thành sinh khối mới** — và là phần duy nhất sẵn có cho các sinh vật tiêu thụ phía trên — gọi là NPP $=$ GPP $-R$. Nhầm lẫn phổ biến nhất: tưởng rằng toàn bộ GPP được chuyển lên bậc dinh dưỡng kế tiếp; thực ra chỉ có NPP mới "đi tiếp" vào lưới thức ăn.

8.2.3 The 10% Rule and Energy Pyramids

When energy passes from one trophic level to the next, only a small fraction — on average roughly 10% — is incorporated into the consumer's own biomass and thus becomes available to the *next* trophic level. The other approximately 90% is lost from that transfer, for several reasons:

- most is released as **heat** through cellular respiration and everyday metabolic activity — a direct consequence of the second law of thermodynamics, since no energy transformation is 100% efficient;
- some is used for movement, and for growth of body parts (bones, fur, shells) that the next consumer does not eat or cannot digest;
- some of what is eaten is not digested at all and is **egested** as waste, which is then processed by decomposers rather than becoming consumer biomass.

Because roughly 90% of available energy is lost at every single transfer, total energy available shrinks by a factor of about 10 at each successive trophic level. This has two major consequences: (1) food chains rarely extend beyond about **4 to 5 trophic levels**, because there is simply too little energy left to support a viable population at a sixth or seventh level; (2) a given land area (or amount of grain) can support far more biomass — and far more people — if its energy is consumed *directly* (a plant-based diet) than if that same energy is first funneled through livestock before being eaten (a meat-based diet), since each additional trophic level "spends" roughly 90% of the available energy just getting there.



Energy pyramid: each trophic level retains only about 10% of the energy available in the level below it. Illustrative values (kcal/m^2/yr) shown for four trophic levels.

Ví dụ mẫu · The 10% rule across four trophic levels

Producers in a wetland fix NPP $= 20{,}000$ kcal/m^2/yr. Assuming an average 10% transfer efficiency between trophic levels, find the energy available to primary, secondary, and tertiary consumers.

Primary consumers: $20{,}000 \times 0.10 = 2{,}000$ kcal/m^2/yr.
Secondary consumers: $2{,}000 \times 0.10 = 200$ kcal/m^2/yr.
Tertiary consumers: $200 \times 0.10 = 20$ kcal/m^2/yr.

Equivalently, energy at trophic level n (producers $=$ level 1) is $20{,}000 \times (0.10)^{n-1}$. A hypothetical quaternary consumer (level 5) would have only $20 \times 0.10 = 2$ kcal/m^2/yr available — under one hundred-thousandth of the original producer energy — which is why a fifth trophic level is rarely energetically viable and food chains almost never extend further. This same math is why eating lower on the food chain (grain → human, one transfer) supports roughly ten times more people per unit land than eating higher on it (grain → cattle → human, two transfers), since each extra transfer forfeits about 90% of the energy.

Energy pyramids are always upright — each level strictly narrower than the one beneath it — because energy strictly decreases moving up the food chain (thermodynamics guarantees this; an energy pyramid can never be inverted). **Biomass pyramids** are usually upright too, but can occasionally appear *inverted at a single snapshot in time* in fast-turnover aquatic systems: a small standing crop of phytoplankton with an extremely fast reproduction/turnover rate can support a larger standing biomass of zooplankton at any given instant, even though the phytoplankton's *productivity* (biomass produced per unit time) is still greater than the zooplankton's over any extended period.

(!) Lỗi thường gặp: Students often treat GPP as if it were the energy available to the rest of the food web. It is not — producers first spend part of GPP on their own respiration; only **NPP** $=$ **GPP** $-$ **R** is available to primary consumers and beyond. Likewise, "10% efficiency" is an average rule of thumb, not an exact law — actual transfer efficiencies vary by ecosystem and organism, but AP-level calculations should use 10% unless another value is explicitly given.

(!) Lỗi thường gặp: A very common error is assuming energy is recycled through an ecosystem the way matter is. It is not: matter (carbon, nitrogen, water, phosphorus) genuinely cycles between organisms and the physical environment via biogeochemical cycles, but **energy flows through an ecosystem in one direction only** — captured by producers, passed (with roughly 90% loss at each step) to consumers, and ultimately lost from the ecosystem entirely as heat. An ecosystem must therefore continuously receive new energy input (almost always sunlight) to keep functioning; unlike nutrients, "used" energy can never be recaptured and reused.

VN **GIẢI THÍCH TIẾNG VIỆT**

Quy tắc 10%: trung bình chỉ khoảng 10% năng lượng ở một bậc dinh dưỡng được chuyển thành sinh khối ở bậc kế tiếp; khoảng 90% còn lại mất đi chủ yếu dưới dạng **nhiệt** qua hô hấp tế bào (hệ quả của định luật II nhiệt động lực học), phần còn lại là chất thải không tiêu hoá được hoặc bộ phận cơ thể sinh vật ở bậc sau không ăn. Vì vậy năng lượng giảm theo cấp số nhân (nhân 10 lần mỗi bậc) — đây là lý do chuỗi thức ăn hiếm khi vượt quá 4–5 bậc, và vì sao ăn ở bậc dinh dưỡng thấp hơn (ví dụ ăn ngũ cốc trực tiếp thay vì ăn thịt động vật được nuôi bằng ngũ cốc đó) nuôi được nhiều người hơn trên cùng diện tích đất. **Lưu ý quan trọng:** năng lượng KHÔNG được tuần hoàn lại — nó đi một chiều và mất dần thành nhiệt; chỉ có **vật chất**

(carbon, nitơ, nước...) mới được tuần hoàn qua các chu trình sinh địa hoá.

8.3 Population Ecology

8.3.1 Population Size, Density, and Dispersion

A **population** is a group of interbreeding individuals of the same species living in the same area at the same time. Ecologists commonly describe populations using: **population size** (N, the total number of individuals), **population density** (individuals per unit area or volume), and **dispersion pattern** — how individuals are arranged in space relative to one another.

Three dispersion patterns

Clumped (most common in nature): individuals cluster in patches, typically tracking unevenly distributed resources (water, food, shelter, favorable microclimate) or reflecting social behavior (herds, flocks, schools) and limited offspring dispersal.

Uniform (regular): individuals are evenly spaced, often the result of territoriality or direct competitive interactions between neighbors (e.g. nesting seabirds each defending a fixed territory radius; allelopathic spacing in some desert shrubs).

Random: individuals are positioned independently of one another, with no strong attraction or repulsion between them; this pattern occurs when resources are fairly uniform and individuals do not interact strongly, and is comparatively uncommon in nature.

VN **GIẢI THÍCH TIẾNG VIỆT**

Ba kiểu phân bố cá thể trong không gian: **tụ tập** (clumped — phổ biến nhất, do tài nguyên phân bố không đều hoặc do tập tính xã hội, ví dụ đàn voi quanh hồ nước); **đều** (uniform — thường do tính lãnh thổ hoặc cạnh tranh trực tiếp, ví dụ chim biển làm tổ cách đều nhau); **ngẫu nhiên** (random — hiếm gặp, khi tài nguyên đồng đều và cá thể không tương tác mạnh với nhau). Phân biệt với **mật độ** (density — số cá thể/đơn vị diện tích) và **kích thước quần thể** (size — tổng số cá thể): hai quần thể có cùng kích thước có thể có mật độ và kiểu phân bố hoàn toàn khác nhau.

8.3.2 Exponential Growth

When resources are effectively unlimited (a population colonizing a new habitat, or a culture early in laboratory growth), population growth follows the **exponential growth model**:

$$\frac{dN}{dt} = rN,$$

where N is population size, t is time, and r is the **intrinsic (per capita) rate of increase**, $r = b - d$ (per capita birth rate minus per capita death rate, ignoring migration). Because the growth *rate* is proportional to the current population size, growth accelerates continuously, producing the characteristic **J-shaped curve** described by $N_t = N_0 e^{rt}$: population size increases without bound as long as $r > 0$ remains constant, with no built-in limit. A convenient related quantity is the **doubling time**, approximated by the "rule of 70":

$$t_{\text{double}} \approx \frac{70}{100r} = \frac{70}{r(\%)}.$$

Ví dụ mẫu · Exponential growth and doubling time

A population of $N = 8{,}000{,}000$ has an intrinsic growth rate $r = 0.025$ (2.5% per year), and resources are currently not limiting. (a) Find the instantaneous rate of increase, dN/dt. (b) Estimate the population's doubling time.

(a) $\dfrac{dN}{dt} = rN = (0.025)(8{,}000{,}000) = 200{,}000$ individuals/year are being added at this instant.

(b) Using the rule of 70: $t_{\text{double}} \approx \dfrac{70}{100(0.025)} = \dfrac{70}{2.5} = 28$ years. (This is an approximation of the exact value $\ln(2)/r \approx 0.693/0.025 \approx 27.7$ years.)

VN **GIẢI THÍCH TIẾNG VIỆT**

Mô hình tăng trưởng hàm mũ ($dN/dt = rN$) áp dụng khi tài nguyên gần như KHÔNG giới hạn — tốc độ tăng trưởng tỉ lệ thuận với kích thước quần thể hiện tại, nên quần thể tăng ngày càng nhanh, tạo đường cong hình chữ J. r là tốc độ tăng trưởng nội tại theo đầu người ($r = b - d$, birth rate trừ death rate). **Quy tắc** 70: thời gian để quần thể tăng gấp đôi ≈ 70 chia cho tốc độ tăng trưởng phần trăm ($r \times 100$). Mô hình này chỉ đúng trong thời gian ngắn hoặc khi quần thể mới xâm chiếm môi trường còn dư thừa tài nguyên (ví dụ loài xâm lấn giai đoạn đầu, vi khuẩn trong môi trường nuôi cấy mới) — không thể duy trì mãi mãi trong tự nhiên.

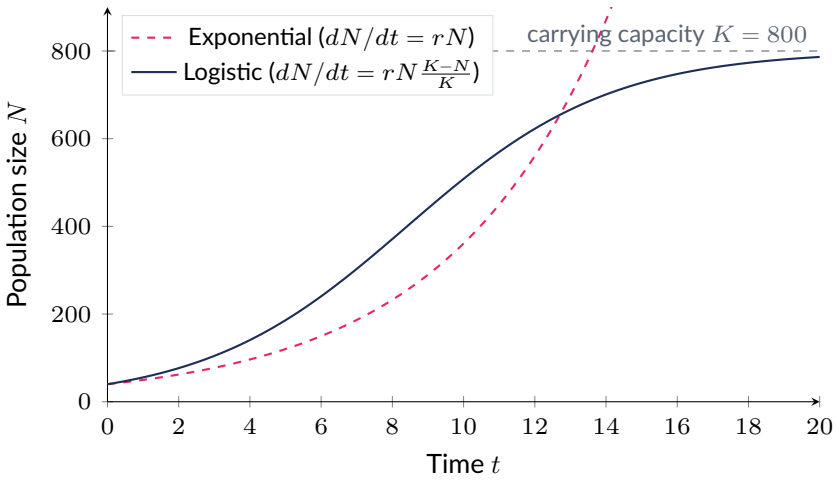
(!) Lỗi thường gặp: Exponential growth ($dN/dt = rN$) assumes resources are unlimited — an idealization that can only hold briefly (e.g. a population just beginning to colonize an unoccupied habitat, or the early phase of a lab culture). Almost every natural population eventually experiences resource limitation and shifts toward **logistic**, not exponential, dynamics as it approaches carrying capacity. Do not assume unbounded exponential growth continues indefinitely for a real, established population.

8.3.3 Logistic Growth and Carrying Capacity

Real environments have finite resources (food, space, nutrients, mates), so as a population grows, resources per individual decline and growth slows. The **logistic growth model** builds in this negative feedback:

$$\frac{dN}{dt} = rN\left(\frac{K - N}{K}\right),$$

where K is the **carrying capacity** — the maximum population size the environment can sustainably support given available resources. The factor $\dfrac{K - N}{K}$ scales growth rate down as N approaches K: when $N \ll K$, this factor is close to 1 and growth is nearly exponential; as $N \to K$, the factor approaches 0 and so does the growth rate; if N ever exceeded K, the factor turns negative and the model predicts population decline back toward K. This produces the characteristic **S-shaped (sigmoid) curve**: nearly exponential at first, with maximum growth *rate* at the inflection point $N = K/2$, leveling off asymptotically at K.



Exponential growth (dashed pink, J-shaped, unbounded) versus logistic growth (solid navy, S-shaped) starting from the same initial population $N_0 = 40$; the logistic curve levels off at carrying capacity $K = 800$.

Ví dụ mẫu · Logistic growth rate at different population sizes

A population has $K = 1{,}000$ and intrinsic growth rate $r = 0.4$/year. Find dN/dt when (i) $N = 100$ (small), (ii) $N = 500$ (near $K/2$), and (iii) $N = 900$ (near K). Comment on the trend.

(i) $\dfrac{dN}{dt} = (0.4)(100)\left(\dfrac{1{,}000 - 100}{1{,}000}\right) = (0.4)(100)(0.90) = 36$ individuals/year.

(ii) $\dfrac{dN}{dt} = (0.4)(500)\left(\dfrac{1{,}000 - 500}{1{,}000}\right) = (0.4)(500)(0.50) = 100$ individuals/year.

(iii) $\dfrac{dN}{dt} = (0.4)(900)\left(\dfrac{1{,}000 - 900}{1{,}000}\right) = (0.4)(900)(0.10) = 36$ individuals/year.

Growth rate rises from $N = 100$ to a **maximum at** $N = K/2 = 500$ (where $dN/dt = 100$/year), then falls again as N approaches K. If we continued to $N = 990$: $dN/dt = (0.4)(990)(0.01) = 3.96$/year — confirming $dN/dt \to 0$ as $N \to K$, exactly as the logistic model predicts.

Ví dụ mẫu · Reading carrying capacity from population data

A yeast culture is sampled every 10 hours:

Time (h)	0	10	20	30	40	50	60
Population ($\times 10^3$ cells)	20	65	180	340	410	430	432

Estimate the carrying capacity K from this data.

Population growth is rapid between $t = 0$ and $t \approx 30$ h (still climbing steeply — the exponential-like early phase), then slows sharply and **plateaus** around $t = 50$–60 h at approximately 430–432×10^3 cells, with almost no further increase between the last two readings. This plateau value *is* the carrying capacity: $K \approx 430 \times 10^3 = 4.3 \times 10^5$ cells — the population size the culture's resources (nutrients, space, and its own waste accumulation) can sustainably support.

VN **GIẢI THÍCH TIẾNG VIỆT**

Mô hình logistic ($dN/dt = rN\frac{K-N}{K}$) mô tả tăng trưởng khi tài nguyên **có giới hạn**: tốc độ tăng trưởng đạt cực đại khi $N = K/2$ (điểm uốn của đường cong hình chữ S) rồi giảm dần về 0 khi N tiến gần K — sức chứa môi trường (carrying capacity), tức số cá thể tối đa mà môi trường có thể nuôi bền vững. Trên đồ thị hoặc bảng số liệu, K chính là giá trị mà quần thể **dừng lại/đi**

ngang (plateau) sau giai đoạn tăng nhanh ban đầu.

8.3.4 Life History Strategies: r-Selected and K-Selected Species

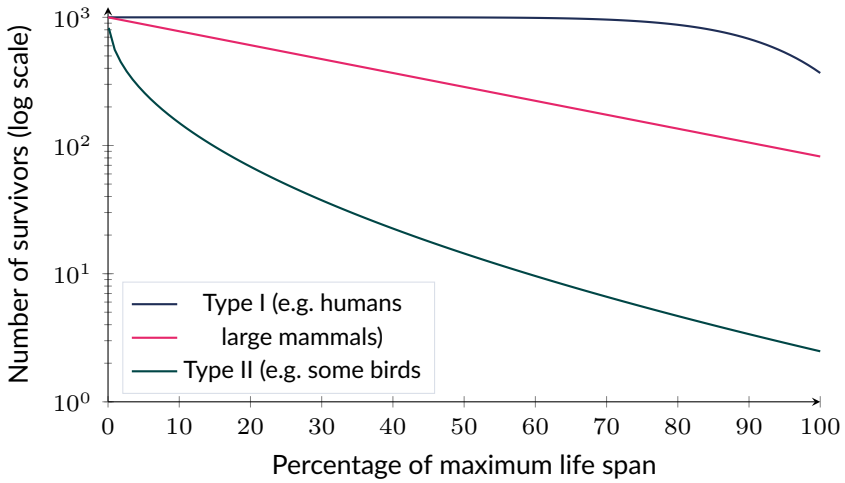
Species differ systematically in the reproductive "strategy" favored by their typical ecological conditions.

r-selected vs. K-selected life histories

r-selected species are favored in unstable, unpredictable, or frequently-disturbed environments where population size rarely approaches carrying capacity. Selection favors traits that maximize the intrinsic growth rate r: small body size, early sexual maturity, short lifespan, many offspring per reproductive event, and little or no parental care. Populations often show "boom-and-bust" fluctuations. Examples: bacteria, most insects, weeds, mice.

K-selected species are favored in stable, predictable environments where populations remain near carrying capacity K and competition for limited resources is the dominant pressure. Selection favors traits that maximize competitive ability at high density: larger body size, delayed sexual maturity, longer lifespan, few offspring per reproductive event, and substantial parental investment per offspring. Examples: elephants, whales, most large-bodied birds and mammals, humans.

These are two ends of a continuum rather than a strict either/or — most species combine traits from both strategies.



Survivorship curves (semi-log scale, starting cohort of $1{,}000$). Type I: low mortality until late in life (typically K-selected). Type II: roughly constant mortality rate at every age. Type III: very high early mortality, with the rare survivors then having good long-term survival (typically r-selected).

Survivorship curves plot the proportion of a starting cohort still alive at each age, usually on a logarithmic y-axis. **Type I** (concave, most mortality late in life): typical of K-selected species with few offspring and extensive parental care — high survival through most of the lifespan, with a steep drop-off only in old age. **Type II** (roughly linear on a semi-log plot): a roughly constant mortality rate at every age. **Type III** (convex, most mortality early in life): typical of r-selected species producing huge numbers of offspring with no parental care, most of which die very young, while the rare survivors then have a good chance of living long.

VN **GIẢI THÍCH TIẾNG VIỆT**

Chiến lược **r-selected** ("chọn lọc theo r"): sinh vật nhỏ, trưởng thành sớm, đẻ rất nhiều con nhưng gần như không chăm sóc con, phù hợp môi trường bất ổn/khó đoán (ví dụ côn trùng,

cỏ dại, vi khuẩn) — thường có đường cong sống sót **Type III** (chết nhiều lúc còn nhỏ). Chiến lược **K-selected**: sinh vật lớn, trưởng thành muộn, đẻ ít con nhưng đầu tư chăm sóc kỹ, phù hợp môi trường ổn định gần sức chứa K (ví dụ voi, cá voi, con người) — thường có đường cong sống sót **Type I** (tỉ lệ sống cao đến tận cuối đời). Đây là một **phổ liên tục**, không phải hai nhóm tách biệt tuyệt đối.

8.3.5 Population Growth Rate: Births, Deaths, and Migration

A full accounting of how a population's size changes over an interval requires tracking not only births and deaths but also movement of individuals into (**immigration**) and out of (**emigration**) the population:

$$\Delta N = (B + I) - (D + E),$$

where B = births, I = immigrants, D = deaths, and E = emigrants over the interval. Dividing by N gives the per capita growth rate for that interval.

Ví dụ mẫu · Population growth rate from birth, death, and migration data

A town has a population of $N = 25{,}000$. Over one year: 520 babies are born, 310 residents die, 180 people move in (immigration), and 95 people move away (emigration). Find the population's per capita growth rate and its new size after one year.

$$\Delta N = (B + I) - (D + E) = (520 + 180) - (310 + 95) = 700 - 405 = 295.$$

Per capita growth rate: $\dfrac{\Delta N}{N} = \dfrac{295}{25{,}000} = 0.0118 = 1.18\%$ per year. New population: $25{,}000 + 295 = 25{,}295$.

8.4 Effects of Density on Population Growth

Limiting factors are the resources or conditions that restrict population growth. They are classified by whether their effect depends on population density.

Density-dependent vs. density-independent factors

Density-dependent limiting factors: their effect on birth rate, death rate, or growth rate *intensifies as population density increases*. Examples: **intraspecific competition** for food, water, space, or mates (more individuals sharing the same resource pool means less available per individual); **predation** (dense prey populations can be easier for predators to find, or may draw in more predators); **disease and parasitism** (transmission rates rise with the contact rate between individuals, which rises with density); accumulation of **metabolic waste products**. Density-dependent factors act as negative feedback that pushes growth rate toward zero as N approaches K — this is exactly the mechanism captured by the $(K - N)/K$ term of the logistic model.

Density-independent limiting factors: their effect removes roughly the *same proportion* of individuals *regardless* of population density. Examples: natural disasters (wildfire, flood, hurricane, volcanic eruption), sudden extreme weather (an early hard frost, prolonged drought), and some forms of abrupt human habitat destruction. A severe storm kills roughly the same *fraction* of a population whether that population is sparse or dense.

(!) Lỗi thường gặp: The dividing line is whether the factor's *effect intensifies with density*, not whether the factor is "natural" or "biological." A disease outbreak is density-dependent (it

spreads faster when individuals are crowded together and contact each other more often), while a hurricane or wildfire is density-independent (it destroys roughly the same proportion of habitat/individuals whether the population is at low or high density). Do not classify factors simply as "biotic = density-dependent" and "abiotic = density-independent" — although this is a useful rough guide, the true test is always whether the *severity of impact scales with density*.

VN **GIẢI THÍCH TIẾNG VIỆT**

Nhân tố **phụ thuộc mật độ** (density-dependent): tác động MẠNH hơn khi mật độ quần thể CAO hơn — ví dụ cạnh tranh cùng loài, dịch bệnh (lây lan nhanh hơn khi cá thể ở gần nhau), động vật ăn thịt tìm con mồi dễ hơn khi con mồi đông đúc. Đây chính là cơ chế đứng sau số hạng $(K - N)/K$ trong mô hình logistic. Nhân tố **không phụ thuộc mật độ** (density-independent): tác động giết chết cùng một **tỉ lệ** cá thể bất kể mật độ cao hay thấp — ví dụ thiên tai (cháy rừng, lũ lụt, bão), thời tiết khắc nghiệt đột ngột. Mẹo phân biệt: hỏi "tác động của nhân tố này có TĂNG khi quần thể đông hơn không?" — nếu có thì phụ thuộc mật độ, nếu không (tác động như nhau dù đông hay thưa) thì không phụ thuộc mật độ.

8.5 Community Ecology

8.5.1 Interspecific Competition and Ecological Niche

A **community** is all the interacting populations of different species living in the same area. **Interspecific competition** occurs when individuals of different species compete for the same limited resource, reducing the fitness of both. The **competitive exclusion principle** (Gause's principle, demonstrated experimentally with two *Paramecium* species competing for the same food source) states that two species with identical ecological niches — competing for exactly the same limiting resource in exactly the same way — cannot coexist indefinitely in the same location; the species that is even marginally more efficient will eventually outcompete and locally eliminate the other.

In nature, competing species more commonly persist together by evolving differences that reduce competitive overlap: **resource partitioning**, in which competing species divide a shared resource by using different portions of it (different feeding times, locations, food sizes, etc. — e.g. several *Dendroica* warbler species that coexist in the same spruce trees by foraging in different zones of the canopy). This can produce visible **character displacement**, where competing species evolve measurable morphological differences (e.g. beak size in *Anolis* lizards or Darwin's finches) specifically where their geographic ranges overlap, reducing niche overlap and allowing coexistence.

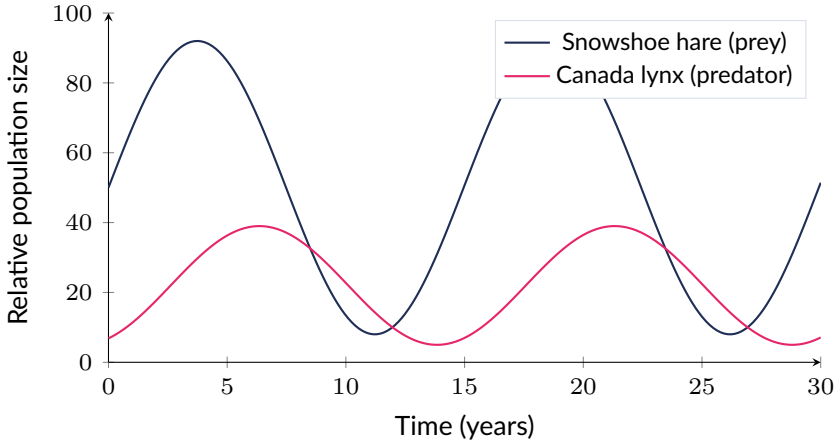
An organism's **ecological niche** is the full set of biotic and abiotic conditions and resources it uses — its functional "role" in the community. The **fundamental niche** is the full range of conditions/resources a species could theoretically use in the complete absence of competitors or predators. The **realized niche** is the (typically smaller) portion of the fundamental niche a species actually occupies once competition, predation, and other biotic interactions are accounted for.

VN **GIẢI THÍCH TIẾNG VIỆT**

Nguyên lý loại trừ cạnh tranh (competitive exclusion): hai loài chiếm cùng một ổ sinh thái, cạnh tranh cùng một nguồn tài nguyên giới hạn theo cùng một cách, KHÔNG thể cùng tồn tại lâu dài — loài hiệu quả hơn dù chỉ một chút cũng sẽ dần loại bỏ loài kia. Trong tự nhiên, các loài thường tránh bị loại trừ bằng **phân chia nguồn tài nguyên** (resource partitioning) — mỗi loài chuyên hoá sử dụng một phần khác của nguồn tài nguyên chung (khác thời điểm kiếm ăn, khác vị trí, khác kích cỡ mồi...). **Ổ sinh thái cơ bản** (fundamental niche) là toàn bộ điều kiện/tài nguyên một loài CÓ THỂ sử dụng nếu không có đối thủ cạnh tranh; **ổ sinh thái hiện thực** (realized niche) là phần THỰC SỰ loài đó sử dụng sau khi bị giới hạn bởi cạnh tranh và kẻ thù tự nhiên — luôn nhỏ hơn hoặc bằng ổ sinh thái cơ bản.

8.5.2 Predation and Predator–Prey Cycles

Predation is an interaction in which one organism (the predator) kills and consumes another (the prey); it benefits the predator (+) and harms the prey (−). Predator and prey populations can show recurring, coupled oscillations over time: as prey become abundant, predators have abundant food and their population grows (with a time lag, since it takes time to convert food into new predators); the growing predator population then depresses the prey population; as prey become scarce, predator numbers subsequently decline (again with a lag) from starvation and reduced reproduction, which allows the prey population to recover and the cycle to repeat. One of the best-documented examples is the roughly decade-long cycle between the snowshoe hare and its main predator, the Canada lynx, reconstructed from about a century of Hudson's Bay Company fur-trapping records: lynx population peaks consistently lag one to two years behind hare population peaks.



Schematic predator–prey population cycle (pattern based on the classic snowshoe hare–Canada lynx cycle): the predator population rises and falls with a time lag behind the prey population.

Ví dụ mẫu · Interpreting a predator–prey cycle graph

In the figure above, the hare population peaks at roughly $t \approx 4$, $t \approx 19$, and again near $t \approx 34$ years (period ≈ 15 years), while the lynx population peaks slightly *after* each hare peak. Explain this lag using population growth reasoning.

When hares are abundant, lynx have plentiful food, so lynx survival and reproduction increase — but it takes time (gestation, growth to reproductive age) for that abundance of food to translate into *more lynx*, so the lynx peak trails the hare peak. As the growing lynx population then intensifies predation pressure, the hare population is driven down; with less food, lynx reproduction and survival then decline in turn (again with a lag), releasing predation pressure and allowing hares to rebound — restarting the cycle. This lagged, reciprocal feedback between predator and prey abundance is the hallmark of coupled predator–prey population dynamics.

VN **GIẢI THÍCH TIẾNG VIỆT**

Chu kỳ con mồi–vật ăn thịt (predator–prey cycle) kinh điển nhất là thỏ tuyết (snowshoe hare) và mèo rừng Canada (Canada lynx), với chu kỳ khoảng 10 năm được ghi nhận qua số liệu buôn bán lông thú của công ty Hudson's Bay suốt hơn một thế kỷ. Đỉnh số lượng vật ăn thịt luôn **trễ pha** so với đỉnh số lượng con mồi — vì cần thời gian để lượng thức ăn dồi dào chuyển hoá thành số lượng vật ăn thịt tăng thêm (qua sinh sản, nuôi con lớn). Đây là ví dụ về **phản hồi ngược có độ trễ** giữa hai quần thể tương tác.

8.5.3 Herbivory and Symbiosis

Herbivory is the consumption of plant (or algal) tissue by an animal; it resembles predation, but the "prey" (the plant) is usually not killed outright, though its fitness is reduced. **Symbiosis** refers to a close, long-term physical association between individuals of two different species. Three main categories are distinguished by the net effect on each partner:

- **Mutualism** ($+/+$): both species benefit. Examples: mycorrhizal fungi and plant roots (the fungus receives sugars; the plant gains improved water/nutrient uptake); nitrogen-fixing *Rhizobium* bacteria housed in legume root nodules; flowering plants and their pollinators (bees, hummingbirds); the gut microbiome and its animal host.
- **Commensalism** ($+/0$): one species benefits, the other is essentially unaffected. Examples: cattle egrets following grazing cattle to catch insects the cattle stir up (egret benefits, cattle largely unaffected); epiphytic plants such as many orchids growing on tree branches purely for physical support, without drawing nutrients from the tree; barnacles attached to a whale's skin (barnacle gains a mobile substrate and access to nutrient-rich water; the whale is largely unaffected).
- **Parasitism** ($+/-$): the parasite benefits at the host's expense, typically without killing the host outright (unlike predation). Examples: tapeworms and ticks on vertebrate hosts; mistletoe (a photosynthetic parasite) tapping into a host tree's vascular tissue; the malaria parasite *Plasmodium* in the human bloodstream.

Interaction	Effect on A	Effect on B	Example
Mutualism	$+$	$+$	Mycorrhizal fungi and plant roots; flowering plants and pollinators
Commensalism	$+$	0	Cattle egrets following grazing cattle; epiphytic orchids on tree branches
Parasitism	$+$	$-$	Tapeworm in a vertebrate gut; mistletoe tapping a host tree
Predation	$+$	$-$	Canada lynx killing and eating a snowshoe hare
Interspecific competition	$-$	$-$	Two bird species competing for the same nest cavities

Net effect of each interspecific interaction on species A and species B ($+$ = benefit, $-$ = harm, 0 = no significant effect).

(!) Lỗi thường gặp: Students frequently mix up the signs of the three symbiosis types. Remember: **mutualism** is $+/+$ (both win); **commensalism** is $+/0$ (one wins, the other is unaffected — NOT $0/0$, since one species genuinely does benefit); **parasitism** is $+/-$ (one wins, the other is actively harmed, but — unlike predation — usually not killed outright, at least not immediately). A quick check: if removing the interaction would clearly hurt one species and leave the other essentially unchanged, that is commensalism, not mutualism.

VN GIẢI THÍCH TIẾNG VIỆT

Ba kiểu cộng sinh phân biệt theo **dấu tác động** lên mỗi bên: **hội sinh/tương hỗ** (mutualism, $+/+$) — cả hai cùng có lợi (ví dụ nấm rễ cộng sinh với rễ cây); **hợp sinh** (commensalism, $+/0$) — một bên có lợi, bên kia không ảnh hưởng đáng kể (ví dụ chim diệc bạc đi theo đàn gia súc để bắt côn trùng); **ký sinh** (parasitism, $+/-$) — một bên có lợi, bên kia bị hại nhưng thường không chết ngay (ví dụ sán dây trong ruột vật chủ). Lỗi sai phổ biến: nhầm hợp sinh ($+/0$) thành "không bên nào ảnh hưởng" ($0/0$) — thực ra luôn có MỘT bên hưởng lợi rõ ràng.

8.5.4 Keystone Species and Ecological Succession

A **keystone species** has a disproportionately large effect on community structure relative to its own abundance or biomass — removing it triggers dramatic, cascading changes throughout the rest of the community. Classic example: sea otters prey on sea urchins; where otters are present, urchin populations stay low and kelp forests (which urchins graze heavily) flourish, supporting a rich community of fish and invertebrates; where otters are removed (historically, by fur hunting), urchin populations explode and can destroy entire kelp forests ("urchin barrens"), collapsing the community that depended on the kelp. Another widely cited example: wolves reintroduced to Yellowstone reduced elk overgrazing along streams, indirectly allowing willow and aspen regeneration — a **trophic cascade** rippling down through multiple trophic levels from a single keystone predator.

Ecological succession is the predictable, gradual change in a community's species composition over time following a disturbance.

- **Primary succession** begins in an area with *no pre-existing soil and essentially no life* — bare rock exposed by a retreating glacier, newly cooled volcanic lava, or a new sandbar. **Pioneer species** (typically lichens and mosses, which can grow directly on rock and begin breaking it down) colonize first; as organic matter slowly accumulates, soil gradually forms, allowing progressively larger plants (grasses, then shrubs, then trees) to establish. Primary succession takes a very long time — often centuries.
- **Secondary succession** begins in an area where soil already exists but the existing community has been disturbed or removed (wildfire, farmland abandonment, hurricane, logging). Because soil — and often a seed bank — is already present, secondary succession proceeds much faster than primary succession.

VN **GIẢI THÍCH TIẾNG VIỆT**

Loài chủ chốt (keystone species) có ảnh hưởng lên cấu trúc quần xã LỚN HƠN nhiều so với độ phong phú (số lượng/sinh khối) của nó — mất loài này kéo theo xáo trộn dây chuyền (trophic cascade) cho cả quần xã. Ví dụ kinh điển: rái cá biển ăn nhím biển, giữ số lượng nhím thấp để rừng tảo bẹ (kelp) phát triển; mất rái cá → nhím biển bùng nổ → rừng tảo bẹ bị phá huỷ. **Diễn thế nguyên sinh** (primary succession) bắt đầu từ nơi CHƯA CÓ đất và sự sống (đá trần, dung nham nguội) — loài tiên phong thường là địa y/rêu, quá trình rất chậm (hàng thế kỷ). **Diễn thế thứ sinh** (secondary succession) bắt đầu từ nơi ĐÃ CÓ đất nhưng quần xã bị phá huỷ (cháy rừng, đất nông nghiệp bỏ hoang) — nhanh hơn nhiều vì đất và hạt giống có sẵn.

8.6 Biodiversity

8.6.1 Species Richness, Evenness, and Diversity Indices

Biodiversity at the community level is commonly described by two components: **species richness** (the number of different species present) and **species evenness** (how equally individuals are distributed among those species). Two communities can have identical richness yet very different diversity if one is dominated numerically by a single species while the other has individuals spread evenly across all species. Diversity indices combine richness and evenness into a single number; a widely used one is **Simpson's Diversity Index**:

$$D = 1 - \sum_{i} p_i^2,$$

where p_i is the proportion of all individuals belonging to species i. D ranges from near 0 (very low diversity — one species dominates) toward 1 (high diversity — many species, evenly represented).

Ví dụ mẫu · Simpson's Diversity Index

Two 100-individual plant communities each contain the same 4 species (equal richness). Community A: 25 individuals of each species (perfectly even). Community B: 91, 3, 3, 3 individuals (one species dominates). Compute D for each and compare.

Community A: $p_i = 0.25$ for each of 4 species. $\sum p_i^2 = 4(0.25)^2 = 4(0.0625) = 0.25$. $D_A = 1 - 0.25 = 0.75$.

Community B: $p_i = 0.91, 0.03, 0.03, 0.03$. $\sum p_i^2 = (0.91)^2 + 3(0.03)^2 = 0.8281 + 0.0027 = 0.8308$. $D_B = 1 - 0.8308 \approx 0.17$.

Although both communities have identical species *richness* (4 species), Community A is far more diverse ($D_A = 0.75$) than Community B ($D_B \approx 0.17$) because A has much higher species *evenness*. This illustrates why richness alone is an incomplete measure of biodiversity.

VN **GIẢI THÍCH TIẾNG VIỆT**

Độ phong phú loài (species richness) chỉ đếm SỐ LƯỢNG loài; **độ đồng đều** (species evenness) đo mức độ số cá thể được phân bố đều giữa các loài đó. Hai quần xã có thể có cùng số loài nhưng độ đa dạng thực tế rất khác nhau nếu một loài áp đảo về số lượng. **Chỉ số đa dạng Simpson** $D = 1 - \sum p_i^2$ kết hợp cả hai yếu tố: D càng gần 1, quần xã càng đa dạng (nhiều loài, phân bố đều); D càng gần 0, càng kém đa dạng (một loài chiếm ưu thế áp đảo).

8.6.2 Biodiversity, Ecosystem Stability, and Ecosystem Services

Higher biodiversity generally increases a community's **stability** — its **resistance** (ability to withstand a disturbance without changing much) and **resilience** (ability to recover afterward, returning to something like its original state). Diverse communities tend to have more functional redundancy (multiple species performing similar ecological roles, so losing any one species has a smaller overall effect) and a wider range of responses to any given disturbance, making the whole community less likely to collapse from a single shock.

Biodiversity also underlies **ecosystem services** — benefits humans derive from natural ecosystems, including pollination of crops, water purification and flood control by wetlands, carbon storage and climate regulation by forests and oceans, nutrient cycling and soil formation, and a genetic reservoir of wild species (many pharmaceuticals are derived from natural compounds). Human activities — habitat destruction, overharvesting, pollution, introduction of invasive species, and climate change — are collectively driving biodiversity loss at a rate far above historical background extinction rates, threatening both ecosystem stability and the services ecosystems provide.

> More species (richness) *and* more even abundance among them (evenness) both raise measured biodiversity and diversity-index values such as Simpson's D. Greater biodiversity tends to raise both the **resistance** and **resilience** of a community to disturbance, largely through functional redundancy among species.

8.7 Disruptions to Ecosystems

8.7.1 Habitat Destruction, Fragmentation, and Invasive Species

Habitat destruction (converting natural habitat to agriculture, urban development, logging, mining, etc.) is the leading direct cause of biodiversity loss, since it removes the resources and living space a species needs outright. **Habitat fragmentation** breaks large, continuous habitat into smaller, isolated patches; this increases "edge effects" (altered microclimate near patch boundaries, easier access for predators/invasive species/human disturbance), reduces the total area of undisturbed interior habitat, and can isolate populations from one another — reducing gene flow and raising local extinction

risk, since smaller, more isolated populations are more vulnerable to demographic and environmental fluctuations and to inbreeding depression.

An **invasive species** is a non-native species introduced (often through human trade, travel, or intentional release) into a new region where it establishes and spreads aggressively, causing ecological or economic harm. Invasive species often thrive precisely because they arrive *without* the natural predators, parasites, diseases, or competitors that kept their population in check in their native range, while native species and predators in the new region typically have not evolved recognition of, or defenses against, the newcomer. Invasive species can outcompete natives for resources, prey heavily on native species that have no evolved defenses, alter physical habitat structure, or introduce novel diseases to which native species have no resistance.

VN **GIẢI THÍCH TIẾNG VIỆT**

Phá huỷ môi trường sống là nguyên nhân trực tiếp hàng đầu gây mất đa dạng sinh học. **Chia cắt môi trường sống** (fragmentation) biến một vùng sống liên tục lớn thành nhiều mảnh nhỏ cách biệt, làm tăng "hiệu ứng rìa" (edge effect), giảm diện tích lõi (interior habitat), và cô lập các quần thể — giảm dòng gen, tăng nguy cơ tuyệt chủng cục bộ. **Loài xâm lấn** (invasive species) thường bùng phát mạnh vì đến một môi trường mới KHÔNG CÓ kẻ thù tự nhiên (thiên địch, ký sinh trùng, đối thủ cạnh tranh) từng kiểm soát chúng ở quê hương — trong khi loài bản địa chưa từng tiến hoá cơ chế phòng vệ chống lại loài mới này.

8.7.2 Climate Change: Range Shifts and Phenology

Rising global temperatures — driven substantially by human release of greenhouse gases, especially CO_2 from fossil fuel combustion — are shifting the geographic **ranges** of many species poleward and to higher elevations as organisms track the climate conditions to which they are adapted; species that cannot disperse fast enough, or that are already at a mountaintop or a pole, have nowhere left to go and face increased extinction risk. Climate change also disrupts **phenology** — the timing of seasonal biological events such as flowering, breeding, migration, and emergence from dormancy — which is often cued by temperature or day length. When interacting species respond to different environmental cues (e.g. a plant's flowering time shifts earlier with warming spring temperatures, while a pollinator's migration timing is cued mainly by day length, which does not shift with climate warming), the result can be a **phenological mismatch**: resources and the consumers that depend on them fall out of sync in time, reducing the fitness of one or both species — for example, migratory birds arriving at breeding grounds after the seasonal peak abundance of the insects their chicks need to grow.

8.7.3 Pollution, Eutrophication, and Biomagnification

Eutrophication results from excess nutrient input — chiefly nitrogen and phosphorus from agricultural fertilizer runoff, sewage, or detergents — into a body of water. The sequence runs: excess nutrients enter the water → explosive growth of algae/cyanobacteria (an **algal bloom**) → the bloom eventually dies off and is decomposed by aerobic bacteria, whose respiration rapidly depletes dissolved oxygen → resulting **hypoxia** (very low dissolved oxygen) can create a "dead zone" that suffocates fish and other aerobic organisms, sometimes causing mass die-offs.

Biomagnification is the increase in tissue concentration of a persistent, poorly-metabolized toxin (e.g. the pesticide DDT, methylmercury, PCBs — typically fat-soluble compounds) at successively higher trophic levels. It occurs because each consumer must eat many times its own body mass of prey over its lifetime to grow, yet excretes or breaks down the toxin only very slowly — so the toxin **bioaccumulates** within an individual's tissues over its lifetime, then transfers up nearly undiminished when that individual is eaten. Top predators, at the end of long food chains, end up with by far the highest tissue concentrations, even when the toxin was present only at very low, seemingly "safe" concentrations in the water or soil at the base of the food chain.

Ví dụ mẫu · Biomagnification calculation

A persistent pollutant is present in lake water at a background concentration and concentrates by a factor of $8\times$ at each successive trophic transfer (a simplified illustrative model — real biomagnification factors vary by chemical and species). Phytoplankton (producers) have a tissue concentration of 0.002 ppm. Find the concentration in zooplankton (primary consumers), small fish (secondary consumers), and large fish (tertiary consumers).

Zooplankton: $0.002 \times 8 = 0.016$ ppm.
Small fish: $0.016 \times 8 = 0.128$ ppm.
Large fish: $0.128 \times 8 = 1.024$ ppm.

Across the three trophic transfers from phytoplankton to large fish (a tertiary consumer), the concentration rose by a factor of $8^3 = 512$ — from 0.002 ppm to about 1.024 ppm — even though the toxin's concentration at the base of the food chain was extremely low. This is exactly why top predators (including humans who eat large predatory fish) accumulate the highest body burdens of persistent pollutants such as DDT and methylmercury.

VN **GIẢI THÍCH TIẾNG VIỆT**

Phú dưỡng hoá (eutrophication): dư thừa dinh dưỡng (N, P từ phân bón nông nghiệp, nước thải) chảy vào nguồn nước → tảo/vi khuẩn lam bùng phát (algal bloom) → tảo chết, vi khuẩn hiếu khí phân giải tiêu tốn oxy hoà tan → **thiếu oxy** (hypoxia), tạo "vùng chết" làm cá và sinh vật hiếu khí chết hàng loạt. **Khuếch đại sinh học** (biomagnification): chất độc khó phân huỷ, tan trong mỡ (như DDT, thuỷ ngân hữu cơ) tích luỹ ngày càng đậm đặc hơn ở mỗi bậc dinh dưỡng cao hơn, vì mỗi sinh vật tiêu thụ ăn rất nhiều con mồi trong đời nhưng đào thải chất độc rất chậm — kết quả là sinh vật ở đỉnh chuỗi thức ăn (kể cả con người) tích luỹ nồng độ độc tố cao nhất, dù nồng độ ở gốc chuỗi thức ăn rất thấp.

8.8 Problem Bank

Bài tập luyện tập

A pillbug placed on dry soil turns and moves erratically at a high rate; once it wanders onto damp soil, its movement rate drops sharply, with no tendency to turn toward the damp area specifically. This behavior is best classified as:

(A) Positive taxis
(B) Negative taxis
(C) Kinesis
(D) A fixed action pattern

Lời giải chi tiết

The pillbug does not orient its body toward or away from moisture — it only changes its *rate* of random movement depending on conditions, with no directed component. This undirected change in movement rate is the definition of **kinesis**. **(C)**.

Bài tập luyện tập

A newly hatched duckling follows the first moving object it sees during a brief critical period shortly after hatching, and continues to follow that object (even a human researcher) afterward. This is an example of:

(A) A fixed action pattern
(B) Imprinting
(C) Negative taxis
(D) Habituation

Lời giải chi tiết

This is **imprinting** — a form of learning restricted to a brief sensitive period early in development, in which the young animal forms a lasting attachment to (or recognition of) a stimulus encountered during that window. **(B)**.

Bài tập luyện tập

Producers in a meadow ecosystem fix NPP $= 50{,}000$ kcal/m^2/yr. Assuming a 10% transfer efficiency at each step, find the energy available to (a) primary consumers, (b) secondary consumers, (c) tertiary consumers, and (d) quaternary consumers.

Lời giải chi tiết

Multiply by 0.10 at each successive level: (a) primary consumers $= 50{,}000 \times 0.10 = 5{,}000$ kcal/m^2/yr. (b) secondary consumers $= 5{,}000 \times 0.10 = 500$ kcal/m^2/yr. (c) tertiary consumers $= 500 \times 0.10 = 50$ kcal/m^2/yr. (d) quaternary consumers $= 50 \times 0.10 = 5$ kcal/m^2/yr. By the fifth trophic level, only 5 kcal/m^2/yr remains — under one ten-thousandth of the original producer energy — illustrating why a viable population rarely persists at a fifth or sixth trophic level.

Bài tập luyện tập

Producers in a lake ecosystem capture GPP $= 9{,}000$ kcal/m^2/yr and use $R = 3{,}200$ kcal/m^2/yr for their own cellular respiration. What is the net primary productivity available to the rest of the food web?

(A) $9{,}000$ kcal/m^2/yr
(B) $5{,}800$ kcal/m^2/yr
(C) $3{,}200$ kcal/m^2/yr
(D) $12{,}200$ kcal/m^2/yr

Lời giải chi tiết

NPP $=$ GPP $- R = 9{,}000 - 3{,}200 = 5{,}800$ kcal/m^2/yr. **(B)**.

Bài tập luyện tập

Which pyramid can, at a single instant in time, occasionally appear inverted in a fast-turnover aquatic ecosystem, and why?

(A) The energy pyramid, because energy can occasionally flow backward down a food chain
(B) The biomass pyramid, because a small, fast-reproducing phytoplankton population can support a larger standing biomass of zooplankton at a given moment
(C) The biomass pyramid, because decomposers always outweigh producers
(D) Neither pyramid can ever be inverted

Lời giải chi tiết

Energy pyramids can never be inverted (energy strictly decreases moving up any food chain, by the second law of thermodynamics). **Biomass** pyramids are usually upright too, but in some aquatic systems a small standing crop of fast-turnover phytoplankton can, at a single snapshot, support a larger standing biomass of zooplankton, even though phytoplankton *productivity* (biomass produced per unit time) remains higher than the zooplankton's over any extended period. **(B)**.

Bài tập luyện tập

A population of $N = 15{,}000$ has an intrinsic growth rate $r = 0.045$ (unlimited resources). (a) Find dN/dt. (b) Estimate the doubling time using the rule of 70.

Lời giải chi tiết

(a) $\dfrac{dN}{dt} = rN = (0.045)(15{,}000) = 675$ individuals added per unit time. (b) $t_{\text{double}} \approx \dfrac{70}{100(0.045)} = \dfrac{70}{4.5} \approx 15.6$ time units.

Bài tập luyện tập

An invasive plant population is estimated at $N_0 = 200$ upon first detection, growing exponentially with $r = 0.30$/year in an environment with abundant unused resources. Approximately how long until the population doubles?

(A) About 2.3 years
(B) About 7 years
(C) About 23 years
(D) About 70 years

Lời giải chi tiết

Using the rule of 70: $t_{\text{double}} \approx \dfrac{70}{100(0.30)} = \dfrac{70}{30} \approx 2.3$ years. **(A)**.

Bài tập luyện tập

A population has carrying capacity $K = 2{,}000$ and intrinsic growth rate $r = 0.25$/year. Find dN/dt when $N = 1{,}500$.

(A) 375 individuals/year
(B) 93.75 individuals/year
(C) 500 individuals/year
(D) $1{,}500$ individuals/year

Lời giải chi tiết

$\dfrac{dN}{dt} = rN\left(\dfrac{K-N}{K}\right) = (0.25)(1{,}500)\left(\dfrac{2{,}000-1{,}500}{2{,}000}\right) = (0.25)(1{,}500)(0.25) = 93.75$ individuals/year. **(B)**.

Bài tập luyện tập

In the logistic growth model, at what population size N is the instantaneous growth rate dN/dt at its maximum?

(A) $N = K$
(B) $N = 0$
(C) $N = K/2$
(D) $N = 2K$

Lời giải chi tiết

$dN/dt = rN(K - N)/K$ is a downward-opening parabola in N (product of a term rising with N and a term falling with N); its maximum occurs at the midpoint, $N = K/2$, where the population is growing fastest in absolute numbers even though its per-capita growth rate has already fallen below the maximum it had when N was small. **(C)**.

Bài tập luyện tập

A population of deer is monitored over several decades: rapid growth from $N = 50$ to $N \approx 1{,}800$ over the first 15 years, followed by size fluctuating narrowly between $1{,}950$ and $2{,}050$ for the next 10 years with no further net increase. Estimate the carrying capacity K for this deer population.

Lời giải chi tiết

The population's sustained plateau — fluctuating narrowly around $2{,}000$ with no further net growth over 10 years — indicates the population has reached the environment's carrying capacity. $K \approx 2{,}000$ deer.

Bài tập luyện tập

A city of $N = 40{,}000$ records the following over one year: 890 births, 610 deaths, 240 immigrants, and 310 emigrants. Find (a) the net change in population ΔN, and (b) the per capita growth rate.

Lời giải chi tiết

(a) $\Delta N = (B + I) - (D + E) = (890 + 240) - (610 + 310) = 1{,}130 - 920 = 210$. (b) Per capita growth rate $= \Delta N/N = 210/40{,}000 = 0.00525 = 0.525\%$ per year.

Bài tập luyện tập

Which set of traits describes a typical K-selected species?

(A) Small body size, early maturity, many offspring, no parental care
(B) Large body size, delayed maturity, few offspring, extensive parental care
(C) Rapid population fluctuation with unstable "boom-and-bust" dynamics
(D) A Type III survivorship curve

Lời giải chi tiết

K-selected species are adapted to stable environments near carrying capacity: large body size, delayed sexual maturity, long lifespan, few offspring with heavy parental investment, and typ-

ically a Type I survivorship curve (not Type III, which is characteristic of r-selected species). **(B)**.

Bài tập luyện tập

A rodent species produces large litters several times per year, reaches sexual maturity within weeks, and provides minimal parental care; its populations frequently crash and rebound. Which survivorship curve type would you expect, and why?

(A) Type I, because most individuals die of old age

(B) Type II, because mortality is constant at every age

(C) Type III, because most offspring die very young, with only a few surviving to reproduce

(D) Survivorship curves do not apply to r-selected species

Lời giải chi tiết

This rodent shows classic **r-selected** traits (early maturity, many offspring, little parental care). r-selected species typically show **Type III** survivorship: very high mortality among the huge number of young offspring, with the rare survivors then having a decent chance of reaching reproductive age. **(C)**.

Bài tập luyện tập

Classify each scenario as density-dependent (DD) or density-independent (DI), and briefly justify each: (1) A wildfire burns 70% of a forest regardless of the deer population size within it. (2) A respiratory infection spreads through a seabird colony, with faster transmission when the colony is more crowded. (3) An unusually early frost kills a fixed fraction of an insect population no matter how large that population is. (4) Intense competition for nesting sites reduces reproductive success more severely as a bird population grows denser.

Lời giải chi tiết

(1) **DI** — the wildfire destroys roughly the same proportion of habitat/population regardless of population size. (2) **DD** — transmission rate scales with contact rate, which rises with density; more crowding means faster spread and greater impact. (3) **DI** — the frost affects the same fraction of the population regardless of density. (4) **DD** — competition for a fixed number of nesting sites intensifies, and therefore its negative effect on reproduction intensifies, as population density increases.

Bài tập luyện tập

Two bird species in the same forest both nest primarily in tree cavities of a particular size range and both feed on similar insect prey. Over many generations, one species begins foraging mainly in the forest canopy while the other shifts almost entirely to foraging near the ground, and both persist stably. This outcome best illustrates:

(A) Competitive exclusion, since one species clearly displaced the other

(B) Resource partitioning, reducing niche overlap enough for coexistence

(C) Mutualism between the two bird species

(D) Density-independent population regulation

Lời giải chi tiết

Rather than one species driving the other to local extinction (competitive exclusion), the two species diverged in *how* they use a shared resource (foraging zone), reducing niche overlap enough that both can persist — this is **resource partitioning**. **(B)**.

Bài tập luyện tập

A species of barnacle could theoretically survive across a wide range of intertidal heights if grown alone in the laboratory, but in the wild it is consistently outcompeted and excluded from the lower intertidal zone by a competitively superior barnacle species, surviving only in the upper zone. Its laboratory range represents its _____, and its actual wild range represents its _____.

(A) realized niche; fundamental niche
(B) fundamental niche; realized niche
(C) niche breadth; niche width
(D) trophic level; ecological role

Lời giải chi tiết

The full range it could occupy *without* competitors (shown in the lab) is its **fundamental niche**; the smaller range it actually occupies once competition is factored in (shown in the wild) is its **realized niche**. **(B)**.

Bài tập luyện tập

In the classic snowshoe hare–Canada lynx predator–prey system, lynx population peaks consistently occur:

(A) At exactly the same time as hare population peaks
(B) One to two years after hare population peaks
(C) One to two years before hare population peaks
(D) With no consistent relationship to hare population size

Lời giải chi tiết

Long-term fur-trapping records show lynx (predator) population peaks lag **one to two years after** hare (prey) population peaks, reflecting the time needed for abundant prey to translate into increased predator survival and reproduction. **(B)**.

Bài tập luyện tập

A clownfish lives among the stinging tentacles of a sea anemone, gaining protection from predators (the clownfish is immune to the anemone's sting), while in return it drives off some anemone-eating fish and provides the anemone with nutrients from its waste. This relationship is best classified as:

(A) Commensalism
(B) Parasitism
(C) Mutualism
(D) Predation

Lời giải chi tiết

Both partners benefit — the clownfish gains protection, and the anemone gains defense against predators and extra nutrients — so this is **mutualism** $(+/+)$. **(C)**.

Bài tập luyện tập

Classify each relationship as mutualism, commensalism, or parasitism: (1) A tick feeds on a deer's blood, weakening the deer over time. (2) Remora fish attach to a shark and feed on scraps from the shark's meals, with no measurable effect on the shark. (3) Bees collect nectar from flowers while transferring pollen that fertilizes the plant.

Lời giải chi tiết

(1) **Parasitism** $(+/-)$ — the tick benefits, the deer is harmed. (2) **Commensalism** $(+/0)$ — the remora benefits, the shark is essentially unaffected. (3) **Mutualism** $(+/+)$ — the bee gains food (nectar), and the plant gains pollination/reproduction.

Bài tập luyện tập

Sea otters are considered a keystone species in kelp forest ecosystems primarily because:

(A) They are the most numerous species in the ecosystem

(B) They have the largest biomass of any species present

(C) Their predation on sea urchins prevents urchins from destroying the kelp forest, despite the otters' relatively low abundance

(D) They are the only species capable of photosynthesis in the ecosystem

Lời giải chi tiết

A keystone species is defined by its disproportionately *large effect relative to its abundance*, not by being the most numerous or highest-biomass species. Sea otters control sea urchin populations through predation; without otters, urchins overgraze and destroy the kelp forest that supports the entire community. **(C)**.

Bài tập luyện tập

A volcanic island forms from cooled lava with no soil present. Order the following stages of the succession that will occur there, from earliest to latest: (i) shrubs and small trees, (ii) lichens and mosses, (iii) grasses in thin developing soil, (iv) a mature forest community.

(A) (iv) → (iii) → (ii) → (i)

(B) (ii) → (iii) → (i) → (iv)

(C) (iii) → (ii) → (iv) → (i)

(D) (i) → (ii) → (iii) → (iv)

Lời giải chi tiết

This is **primary succession** (bare rock, no pre-existing soil). Pioneer species (lichens and mosses) colonize first and begin soil formation → as thin soil develops, grasses can establish → enough soil and organic matter accumulates for shrubs and small trees → eventually a mature forest community. Order: (ii) → (iii) → (i) → (iv). **(B)**.

Bài tập luyện tập

Two wetlands each contain 100 individuals across 5 species. Wetland C: counts of 40, 30, 15, 10, 5. Wetland D: counts of 20 each (perfectly even). Calculate Simpson's Diversity Index $D = 1 - \sum p_i^2$ for each wetland and state which is more diverse.

Lời giải chi tiết

Wetland C: $p_i = 0.40, 0.30, 0.15, 0.10, 0.05$. $\sum p_i^2 = 0.16 + 0.09 + 0.0225 + 0.01 + 0.0025 = 0.285$. $D_C = 1 - 0.285 = 0.715$.
Wetland D: $p_i = 0.20$ each. $\sum p_i^2 = 5(0.04) = 0.20$. $D_D = 1 - 0.20 = 0.80$.
Both wetlands have identical species richness (5 species), but Wetland D has perfectly even abundance and therefore the higher diversity index ($D_D = 0.80 > D_C = 0.715$) — evenness raises measured diversity even when richness is unchanged.

Bài tập luyện tập

Which statement correctly distinguishes species richness from species evenness?

(A) Richness measures how equally individuals are distributed among species; evenness counts the number of species

(B) Richness counts the number of species present; evenness measures how equally individuals are distributed among those species

(C) They are two names for exactly the same quantity

(D) Richness can only be measured in aquatic ecosystems

Lời giải chi tiết

Richness = the number of different species present; **evenness** = how equally individuals are distributed among those species. Both feed into overall diversity, but they measure different things. **(B)**.

Bài tập luyện tập

Higher biodiversity generally makes an ecosystem more stable primarily because:

(A) More species means the ecosystem needs less energy input from the sun

(B) Functional redundancy among species reduces the impact of losing any single species, improving resistance and resilience to disturbance

(C) Diverse ecosystems are immune to invasive species

(D) Diverse ecosystems no longer require decomposers

Lời giải chi tiết

With more species performing similar ecological roles (functional redundancy), the loss or decline of any one species has a smaller overall effect on ecosystem function, and the community has a broader range of ways to respond to disturbance — raising both resistance (withstanding change) and resilience (recovering afterward). **(B)**.

Bài tập luyện tập

A lake receives heavy fertilizer runoff from surrounding farmland. Explain, step by step, the mechanism by which this runoff can lead to a fish kill, and identify the process by name.

Lời giải chi tiết

This is **eutrophication**. Step 1: excess nitrogen and phosphorus from fertilizer runoff enter the lake. Step 2: these nutrients fuel an explosive **algal bloom** at the water's surface. Step 3: as the bloom's algae die (from age, self-shading, or nutrient exhaustion), their remains sink and are broken down by aerobic decomposer bacteria. Step 4: this decomposition consumes large amounts of dissolved oxygen from the water. Step 5: the resulting **hypoxia** (oxygen depletion) leaves too little dissolved oxygen for fish and other aerobic organisms, causing a fish kill.

Bài tập luyện tập

A persistent pesticide concentrates by a factor of $6\times$ at each trophic transfer. Background water concentration is 0.0015 ppm, and phytoplankton have already concentrated it to 0.009 ppm. Find the concentration in a tertiary consumer fish, which sits two trophic transfers above the phytoplankton (phytoplankton $\rightarrow$ zooplankton $\rightarrow$ small fish $\rightarrow$ tertiary consumer fish is three transfers total from phytoplankton — use the transfer count carefully).

Lời giải chi tiết

From phytoplankton to the tertiary consumer fish, there are three trophic transfers (phytoplankton $\rightarrow$ zooplankton $\rightarrow$ small fish $\rightarrow$ tertiary consumer). Multiply by 6 three times, i.e. by $6^3 = 216$: $0.009 \times 216 = 1.944$ ppm. The tertiary consumer's tissue concentration (≈ 1.94 ppm) is more than 200 times the phytoplankton's concentration and over $1{,}000$ times the original water concentration (0.0015 ppm), illustrating how sharply persistent toxins concentrate up a food chain.

Bài tập luyện tập

An invasive insect species is accidentally introduced to a new continent and its population explodes within a few years, far outpacing any native insect in the region. What is the most likely primary explanation?

(A) The invasive species photosynthesizes more efficiently than native insects

(B) The new environment lacks the natural predators, parasites, and diseases that controlled the species in its native range

(C) Invasive species always have a higher intrinsic growth rate r than every native species

(D) The invasive species has switched from r-selected to K-selected life history

Lời giải chi tiết

Invasive species frequently proliferate because they have escaped the natural enemies (predators, parasites, pathogens, competitors) that regulated their population size in their native range, while native species/predators in the new region have not evolved recognition of or defenses against the newcomer. **(B)**.

Bài tập luyện tập

A migratory songbird times its arrival at northern breeding grounds using day length (photoperiod) as its primary cue, while the caterpillars its chicks depend on for food emerge in response to local spring temperature, which has been arriving progressively earlier due to climate warming. Explain the likely consequence for the bird population using the concept of phenological mismatch.

Lời giải chi tiết

Because the caterpillar food source is now emerging (and peaking) earlier due to warming spring temperatures, while the bird's migration timing — cued by day length, a signal unaffected by climate change — has not shifted correspondingly earlier, the bird's chicks are increasingly likely to hatch *after* the peak caterpillar abundance has already passed. This **phenological mismatch** between predator need and prey availability reduces the amount of food available to growing chicks, which can lower chick survival and, over time, reduce the fitness and population size of the bird species.

Bài tập luyện tập

Habitat fragmentation is most directly associated with which of the following consequences for a wildlife population?

(A) Increased gene flow between formerly separated populations

(B) Reduced edge effects and larger interior habitat area

(C) Isolation of smaller populations, reduced gene flow, and increased vulnerability to local extinction

(D) Guaranteed population growth due to increased habitat diversity

Lời giải chi tiết

Fragmentation breaks continuous habitat into smaller, more isolated patches. This typically *reduces* gene flow between now-separated subpopulations, increases edge effects and reduces interior habitat area, and leaves smaller populations more vulnerable to demographic/environmental fluctuations, inbreeding depression, and local extinction. **(C)**.

Bài tập luyện tập

A pond has producers with GPP $= 6{,}400$ kcal/m^2/yr; producer respiration is $R = 1{,}600$ kcal/m^2/yr. Using the resulting NPP and a 10% transfer efficiency, find the energy available to secondary consumers (two trophic transfers above the producers).

Lời giải chi tiết

NPP $=$ GPP $- R = 6{,}400 - 1{,}600 = 4{,}800$ kcal/m^2/yr. Primary consumers: $4{,}800 \times 0.10 = 480$ kcal/m^2/yr. Secondary consumers: $480 \times 0.10 = 48$ kcal/m^2/yr.

Bài tập luyện tập

A prairie population is observed to be spread evenly across the landscape, with individuals maintaining almost identical minimum distances from their nearest neighbors at all times. This dispersion pattern is most likely maintained by:

(A) Highly clumped, unevenly distributed resources

(B) Strong territoriality or direct antagonistic interactions between neighboring individuals

(C) Completely random settlement with no biological interactions

(D) An algal bloom in a nearby pond

Lời giải chi tiết

Evenly spaced (**uniform**) dispersion typically arises from territorial behavior or direct competitive/antagonistic interactions that keep individuals apart at a roughly constant minimum distance. **(B)**.

Bài tập luyện tập

A grassland is destroyed by an unusually intense, fast-moving wildfire that kills the same proportion of grasshoppers whether the local grasshopper population was sparse or dense beforehand. Classify this limiting factor and explain your reasoning in one sentence.

Lời giải chi tiết

This is a **density-independent** limiting factor, because its impact (the proportion of the population killed) does not scale with population density — the fire kills roughly the same fraction of grasshoppers regardless of whether the population was sparse or dense beforehand.

Ôn tập nhanh: (1) Đại phân tử: khử nước để nối đơn phân, thủy phân để cắt; bốn nhóm đại phân tử là carbohydrate, lipid, protein, nucleic acid. (2) Màng tế bào: nước di chuyển từ nơi có thế nước (Ψ) cao đến nơi có thế nước thấp; tỉ lệ diện tích bề mặt trên thể tích giảm khi tế bào lớn lên, đây là lý do tế bào phải giữ kích thước nhỏ hoặc phân chia. (3) Enzyme làm giảm năng lượng hoạt hóa E_a chứ không làm thay đổi ΔG của phản ứng; trong hô hấp tế bào, phần lớn ATP được tạo ra ở chuỗi truyền electron nhờ hóa thẩm thấu. (4) Phản hồi âm giúp duy trì ổn định nội môi, còn phản hồi dương đẩy nhanh một quá trình đến khi hoàn tất; chu kỳ tế bào được kiểm soát chặt chẽ tại các điểm kiểm soát G1/S, G2/M và M nhờ cyclin và CDK. (5) Trong di truyền học, dùng quy tắc nhân xác suất cho các gene phân li độc lập và quy tắc cộng cho các biến cố loại trừ nhau; kiểm định chi bình phương dùng để so sánh tỉ lệ quan sát được với tỉ lệ lý thuyết mong đợi. (6) Chiều trung tâm của sinh học phân tử: DNA $\rightarrow$ RNA $\rightarrow$ protein; đột biến dịch khung (mất hoặc thêm số nucleotide không phải bội số của 3) thường gây hậu quả nghiêm trọng hơn đột biến thay thế một cặp base đơn lẻ. (7) Định luật Hardy-Weinberg: $p + q = 1$ và $p^2 + 2pq + q^2 = 1$; tần số allele lặn được suy ra bằng $q = \sqrt{q^2}$ từ tần số kiểu hình lặn, không phải lấy trực tiếp q^2. (8) Quần thể tăng trưởng theo mô hình logistic sẽ chậm dần khi kích thước quần thể N tiến gần đến sức chứa môi trường K; năng lượng chỉ được truyền khoảng 10% giữa hai bậc dinh dưỡng liên tiếp, phần còn lại mất dưới dạng nhiệt.

Đồng hành cùng 8020 English

Cảm ơn bạn đã học cùng bộ giáo trình quốc tế 8020. **Điểm thật · Thầy thật · Kết quả thật** — nhiều học viên chỉ cần 1–2 khoá để đạt kết quả mong muốn.

Chương trình đào tạo tại 8020 English

IELTS Academic/General · **SAT** · PTE · Duolingo · TOEFL | **AP** (College Board) · **IB** Diploma · **Cambridge** IGCSE / A-Level | săn học bổng du học.

Vì sao chọn 8020 English?

- **100% giáo viên** đạt tối thiểu 8.0 IELTS hoặc 1500 SAT — đội ngũ Giáo sư · Tiến sĩ · Thạc sĩ tốt nghiệp trường top đầu thế giới (Carnegie Mellon — #1 Hoa Kỳ về Khoa học Máy tính).
- **Kèm 1–1** mọi độ tuổi; lớp sĩ số nhỏ 2–5 bạn (đa số dưới 10 bạn/lớp).
- Lộ trình cá nhân hoá, theo sát tiến độ từng học viên; lớp OFFLINE tại TP.HCM & ONLINE toàn quốc.

Bảng vàng học viên

AP 5/5 — Calculus AB/BC	**AP** 4–5 — Biology, Chemistry	**IB** 90/100 — Economics
SAT 1590 / 1570 / 1550	**IELTS** 8.0–9.0	**Duolingo** 110 · **PTE** 90

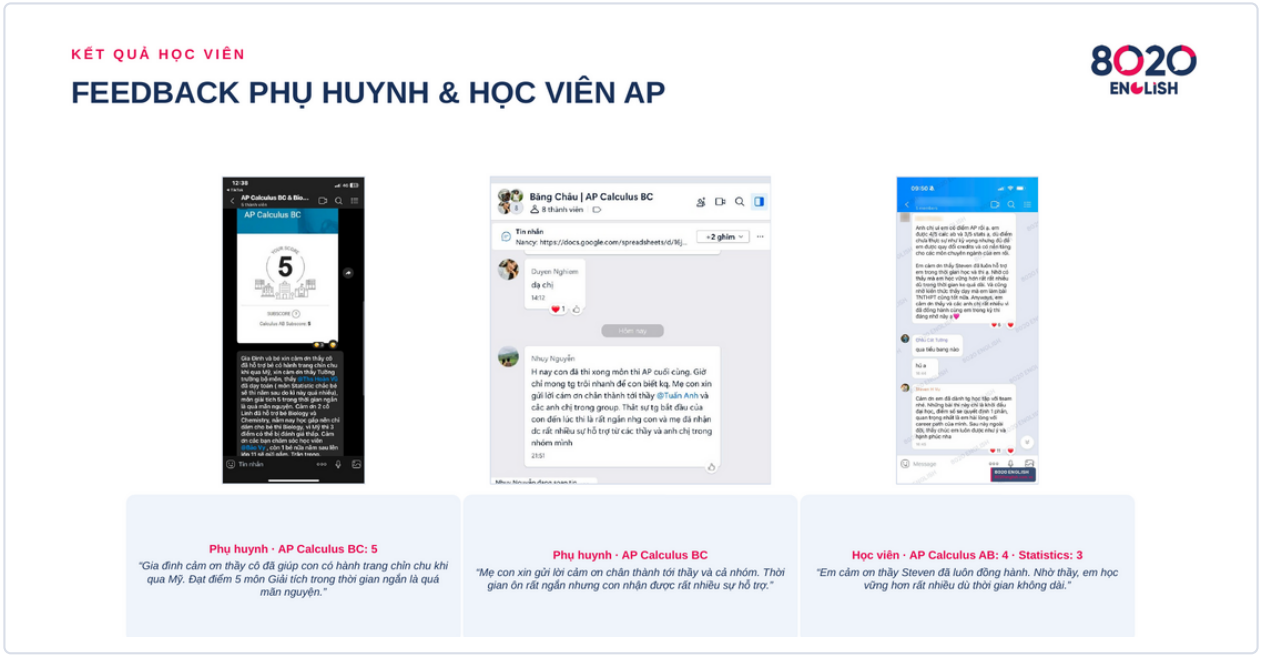
Cảm nhận học viên & phụ huynh

> *"Bạn đã cải thiện được tư duy Writing — kỹ năng từng là nỗi sợ lớn nhất — và cuối cùng đã đậu vào trường top như mong muốn. Thái độ học tập cực kỳ nghiêm túc; ngay cả khi nằm viện vẫn cố gắng học đều đặn."*
>
> — Phan Thị Thanh Hằng · IELTS Overall 8.5

> *"Cần tất cả kỹ năng trên 7.5 để xét vào trường top 1 Anh Quốc về Y học (chương trình UKFPO của NHS) — và đã đạt mục tiêu sau khi học Writing 1–1."*
>
> — Trần Hoàng Bảo Ngọc · IELTS Overall 8.0 (Writing 6.0 → 7.5)

> *"Gia đình và bé xin cảm ơn thầy cô đã giúp con có hành trang chỉn chu khi qua Mỹ. Đạt điểm 5 môn Giải tích trong thời gian ngắn là quá mãn nguyện."*
>
> — Phụ huynh · AP Calculus BC 5/5

> *"Em cảm ơn thầy đã luôn đồng hành. Nhờ thầy, em học vững hơn rất nhiều dù thời gian ôn không dài."*
>
> — Học viên · AP Calculus AB 4

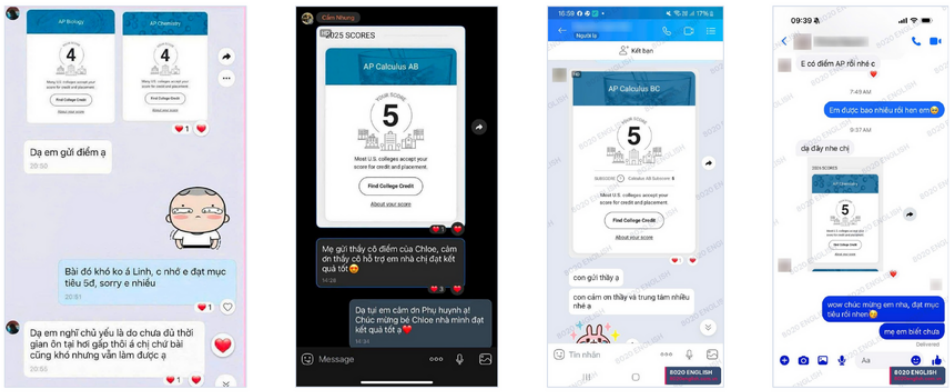


Feedback phụ huynh & học viên AP — nhiều môn đạt điểm 4 & 5

Điểm thi thật của học viên

KẾT QUẢ HỌC VIÊN

ĐIỂM SỐ AP

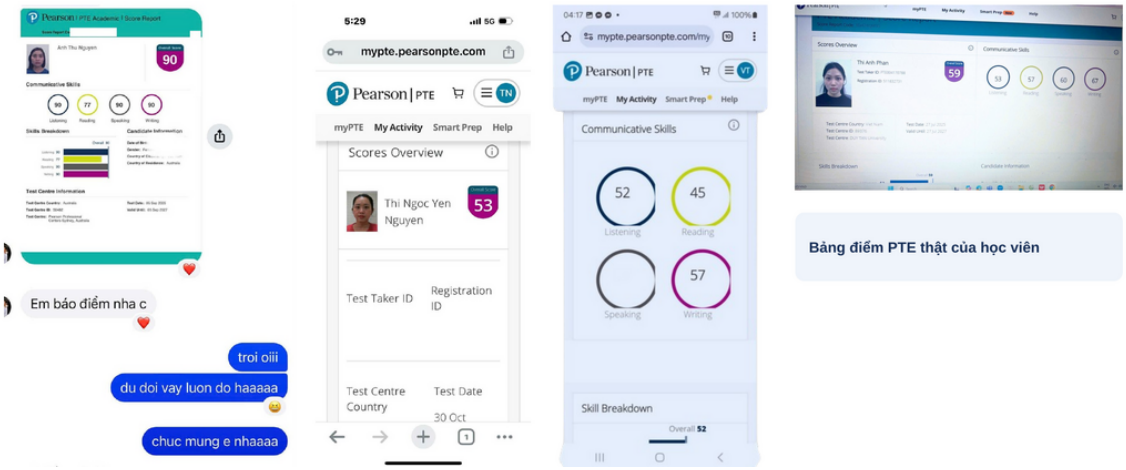


Bảng điểm AP thật của học viên – nhiều môn đạt điểm 4 & 5

Bảng điểm AP thật — Calculus AB/BC 5/5 · Biology & Chemistry 4–5 (College Board)

KẾT QUẢ HỌC VIÊN

ĐIỂM SỐ PTE

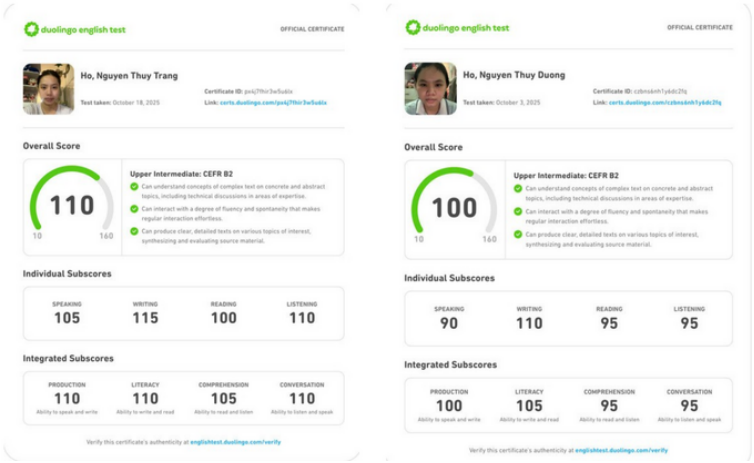


Bảng điểm PTE thật của học viên

Học viên 8020 — PTE Academic 90

KẾT QUẢ HỌC VIÊN

ĐIỂM SỐ DUOLINGO



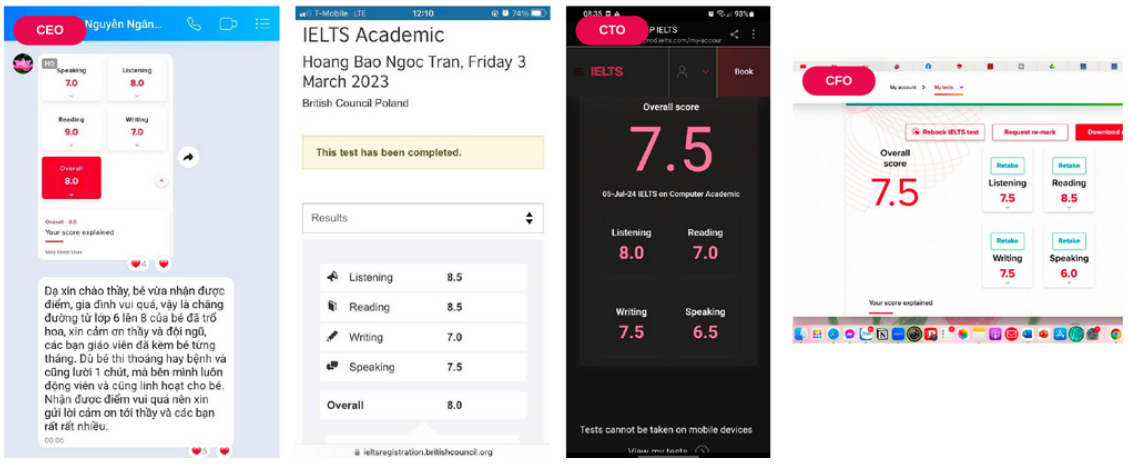
Duolingo English Test – 110 & 100

Học viên 8020 — Duolingo English Test 110 & 100

KẾT QUẢ HỌC VIÊN

THÀNH TÍCH HỌC VIÊN

Bảng điểm thi thật – chất lượng được giám sát nghiêm ngặt. Một số học viên chỉ cần 1–2 khóa để đạt kết quả mong muốn.



Học viên 8020 — IELTS 8.0 / 7.5 / 8.5 (báo điểm thật)