2026–2027 OFFICIAL COURSEBOOK EDITION

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# AP Biology Complete Master Textbook

Units 1–8 Comprehensive Cellular & Molecular Mechanisms, Comparison Tables & Quantitative Problems

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|---|---|
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| CHAPTER 2 — Cell Structure and Function | 10–13% |
| CHAPTER 3 — Cellular Energetics | 12–16% |
| CHAPTER 4 — Cell Communication and Cell Cycle | 10–15% |
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📘 Structured Theory · Comparison Tables · Step-by-Step Worked Examples · FRQ Traps

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**AP Exam Weighting: 8–11%**

# Unit 1: Chemistry of Life

Biological systems depend on the physical and chemical properties of water, versatile carbon skeletons modified by functional groups, and the hierarchical assembly of biological macromolecules. Understanding how electronegativity, hydrogen bonding, and stereochemistry dictate molecular conformation is foundational to all cellular processes.

### CHAPTER 1 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| $\text{Dehydration Synthesis: Monomer}_1 + \text{Monomer}_2 \rightarrow \text{Covalent Bond} + H_2O$ | Anabolic enzymatic polymerization removing −OH and −H to link monomers |
| $\text{Hydrolysis: Polymer} + H_2O \rightarrow \text{Monomer}_1 + \text{Monomer}_2$ | Catabolic enzymatic cleavage inserting $H_2O$ across a covalent linkage |
| $pH = -\log_{10}[H^+]$ and $[H^+][OH^-] = 10^{-14}\ M^2$ (at 25 °C) | Each 1-unit decrease in pH represents a 10-fold increase in proton ($H^+$) concentration |
| $\text{Chargaff's Rules: \%A} = \text{\%T (2 H-bonds) and \%G} = \text{\%C (3 H-bonds)}$ | Complementary purine–pyrimidine base pairing in double-stranded DNA |

## § 1.1 Structure of Water, Polarity, Hydrogen Bonding & pH

Within a single water molecule ($H_2O$), one oxygen atom shares electrons with two hydrogen atoms through strong intramolecular **polar covalent bonds**. Because oxygen is significantly more **electronegative** than hydrogen, it pulls shared valence electrons closer to its nucleus, conferring a partial negative charge (**$\delta^-$**) on the oxygen apex and leaving each hydrogen with a partial positive charge (**$\delta^+$**). This asymmetrical V-shaped charge distribution makes water a highly **polar molecule**.

When multiple water molecules approach one another, the partially negative oxygen ($\delta^-$) of one molecule electrostatically attracts the partially positive hydrogen ($\delta^+$) of an adjacent molecule, forming an intermolecular **hydrogen bond**. Although an individual hydrogen bond is roughly 20 times weaker than a covalent bond, the collective network of billions of transient hydrogen bonds endows water with emergent thermal and cohesive properties essential for life, and stabilizes the three-dimensional conformations of DNA and proteins.

Living cells are exquisitely sensitive to fluctuations in **pH**, which quantifies the concentration of hydrogen ions (protons, $H^+$) in aqueous solution. In pure neutral water at pH 7, $[H^+] = [OH^-] = 10^{-7}$ M. Acids (such as HCl) dissociate to donate $H^+$ and lower pH below 7, whereas bases (such as NaOH) accept $H^+$ or release $OH^-$ to raise pH above 7.

- **Cohesion & Thermal Stability:** Hydrogen bonding between water molecules resists thermal agitation, giving water a **high specific heat capacity** (buffering coastal and cellular temperatures) and a **high heat of vaporization** (enabling evaporative cooling via sweating and transpiration).
- **Adhesion & Transpiration Pull:** Hydrogen bonding between polar water molecules and polar cellulose fibers in plant **xylem walls** (adhesion) works with water-to-water cohesion to pull a continuous water column upward from roots to leaves against gravity as water evaporates through stomata.
- **Surface Tension:** At the air–water interface, surface water molecules hydrogen-bond tightly to neighbors below and beside them, creating an elastic film across which small insects can walk.
- **Macromolecular Stabilization:** Hydrogen bonds pair complementary DNA strands (**A=T** with two H-bonds; **G≡C** with three H-bonds) so enzymes can unzip the helix without breaking the covalent backbone, and stabilize protein **α-helices** and **β-pleated sheets**.

**EXAMPLE 1.1** **Logarithmic pH Scale & Proton Concentration Calculations**

**Problem:** Compare the hydrogen ion concentration $[H^+]$ of gastric juice at pH 2, acid rain at pH 4, and healthy human blood near pH 7. How many times more acidic is pH 4 compared to pH 5 and pH 6?

**STEP-BY-STEP SOLUTION:**

1. Step 1: Recall that $pH = -\log_{10}[H^+]$, meaning each 1-unit decrease on the pH scale corresponds to a $10^1 = 10$-fold increase in $[H^+]$.
2. Step 2: Compare pH 4 to pH 5: $\Delta pH = 5 - 4 = 1$ unit $\rightarrow 10^1 = 10$ times higher $[H^+]$ (10× more acidic).
3. Step 3: Compare pH 4 to pH 6: $\Delta pH = 6 - 4 = 2$ units $\rightarrow 10^2 = 100$ times higher $[H^+]$ (100× more acidic).
4. Step 4: Compare pH 2 to pH 7: $\Delta pH = 7 - 2 = 5$ units $\rightarrow 10^5 = 100{,}000$ times higher $[H^+]$ in gastric juice than in neutral water.

**Final Answer: A solution at pH 4 is 10 times more acidic than pH 5 and 100 times more acidic than pH 6; gastric juice at pH 2 has 100,000-fold higher $[H^+]$ than pH 7.**

**⚠ AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Evaporative boiling or heating water breaks INTERMOLECULAR hydrogen bonds between separate $H_2O$ molecules—it NEVER breaks the INTRAMOLECULAR polar covalent O–H bonds within a water molecule!

## § 1.2 Elements of Life (CHNOPS) & Carbon Functional Groups

Living matter is constructed primarily from six essential elements summarized by the acronym **CHNOPS**: Carbon, Hydrogen, Nitrogen, Oxygen, Phosphorus, and Sulfur. **Carbon (C)** is life's central structural element because its four valence electrons allow it to form up to four stable covalent bonds—including single bonds, double bonds, branched hydrocarbon chains, and aromatic or aliphatic rings.

While carbon, hydrogen, and oxygen form the core framework of all four classes of macromolecules, specific chemical clusters called **functional groups** attached to carbon skeletons govern molecular polarity, solubility, charge, and chemical reactivity.

- **Carbon, Hydrogen & Oxygen (C, H, O):** Present in all four biological macromolecules (carbohydrates, lipids, proteins, nucleic acids); hydrogen and electrons also drive cellular energy transfer via **$NAD^+$/NADH** and mitochondrial proton gradients.
- **Nitrogen (N):** Signature element of all **proteins** (within amino groups and peptide bonds) and all **nucleic acids** (within purine and pyrimidine nitrogenous bases).
- **Phosphorus (P):** Forms the negatively charged phosphate groups of **ATP**, amphipathic **phospholipids**, and the **sugar–phosphate backbone** of DNA and RNA.
- **Sulfur (S):** Found in the amino acids cysteine and methionine; **cysteine** sulfhydryl (−SH) groups oxidize to form covalent **disulfide bridges (−S–S−)** that lock tertiary protein structure.

**Table 1.1 · Eight Essential Functional Groups in AP Biology**

| Functional Group | Formula / Structure | Chemical Property | Biological Role & Examples |
|---|---|---|---|
| Hydroxyl | −OH | Polar, hydrophilic | Forms H-bonds with water; helps sugars (glucose) and alcohols dissolve |
| Carbonyl | >C=O | Polar, hydrophilic | Aldehyde or ketone group in monosaccharides and metabolic intermediates |
| Carboxyl | $-COOH \rightleftharpoons -COO^- + H^+$ | Acidic, negatively charged | Donates $H^+$ at physiological pH; found in all amino acids and fatty acids |
| Amino | $-NH_2 + H^+ \rightleftharpoons -NH_3^+$ | Basic, positively charged | Accepts $H^+$ at physiological pH; found at the N-terminus of all amino acids |
| Sulfhydryl | −SH | Polar, reactive | Two cysteine −SH groups oxidize into a covalent disulfide bridge (−S–S−) |
| Phosphate | $-OPO_3^{2-}$ | Strongly acidic (2− charge) | Transfers high-energy bonds in ATP; links nucleotides in DNA/RNA backbones |
| Methyl | $-CH_3$ | Nonpolar, hydrophobic | Added to cytosine bases in DNA to condense chromatin and silence transcription |
| Acetyl | $-COCH_3$ | Neutral modifier | Added to histone tails (acetylation) to loosen chromatin and activate transcription |

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Carbohydrates and triglycerides contain ONLY Carbon, Hydrogen, and Oxygen (CHO). If an unknown macromolecule contains Sulfur (S) but no Phosphorus (P), it is a protein (as demonstrated in the Hershey–Chase experiment)!

## § 1.3 Polymerization, Carbohydrates & Lipids

Three of the four major macromolecule classes—carbohydrates, proteins, and nucleic acids—are **polymers** assembled by linking repeating **monomers** into long chains. Enzymes build polymers via **dehydration synthesis (condensation)**, removing a hydroxyl group (−OH) from one monomer and a hydrogen atom (−H) from the next to release one molecule of $H_2O$ per covalent bond formed. Conversely, digestive enzymes break polymers down into free monomers via **hydrolysis** ('to break with water') by inserting one $H_2O$ molecule across the covalent linkage.

**Carbohydrates** contain C, H, and O in an approximate **1:2:1 ratio** $(CH_2O)_n$. Simple sugars or **monosaccharides** (glucose, fructose, galactose) provide immediate fuel for cellular respiration. Joining two monosaccharides via a covalent **glycosidic linkage** yields a disaccharide (sucrose, maltose, or lactose). Linking hundreds of glucose monomers forms polysaccharides whose biological function depends strictly on stereochemistry: **α-1,4 glycosidic linkages** produce digestible helical energy-storage polymers (plant **starch** and highly branched animal **glycogen**), whereas **β-1,4 glycosidic linkages** flip every other β-glucose monomer upside down, forming straight, hydrogen-bonded microfibrils of structural **cellulose** in plant cell walls.

Unlike the other three classes, **lipids are not polymers** built from repeating monomers; they are grouped together because they are wholly or partially nonpolar and **hydrophobic** due to abundant nonpolar C–H bonds. **Triglycerides** (fats and oils) consist of one 3-carbon glycerol ester-linked to three fatty acid tails. **Saturated fatty acids** lack double bonds and pack tightly as solids at room temperature (butter), whereas **unsaturated fatty acids** contain one or more *cis* C=C double bonds that introduce rigid kinks, keeping plant oils liquid. **Phospholipids** are **amphipathic**—possessing one hydrophilic polar phosphate head and two hydrophobic fatty acid tails—and spontaneously self-assemble in water into a selective **phospholipid bilayer**.

- **Starch vs. Cellulose Stereochemistry:** Humans possess amylase enzymes that hydrolyze **α-1,4** linkages in potato or bread starch, but lack enzymes to bind alternating **β-1,4** linkages in cellulose; ruminants (cows) and termites rely on symbiotic gut microbes producing cellulase.
- **Lactase Persistence:** Most adult mammals downregulate the intestinal enzyme **lactase** after weaning, but independent regulatory mutations arose 5,000–10,000 years ago in pastoral human populations, maintaining lactase expression into adulthood as a classic adaptation by natural selection.
- **Steroids & Waxes: Steroids** (cholesterol, estrogen, testosterone, cortisol) share a characteristic hydrophobic backbone of four fused carbon rings.

**Table 1.2 · Four Major Classes of Biological Macromolecules**

| Macromolecule Class | Monomer / Subcomponents | Covalent Linkage | Elemental Composition | Primary Biological Functions |
|---|---|---|---|---|
| Carbohydrates | Monosaccharides (glucose, fructose) | Glycosidic linkage (α-1,4 or β-1,4) | C, H, O (1:2:1 ratio) | Immediate/short-term energy (starch, glycogen); structural cell walls (cellulose, chitin) |
| Lipids (Non-polymer) | Glycerol + Fatty Acids; 4 fused rings | Ester linkage (in triglycerides/phospholipids) | C, H, O (high C–H ratio; P in phospholipids) | Long-term energy storage, thermal insulation, cell membrane bilayers, steroid hormones |
| Proteins | 20 Amino Acids | Peptide bond (C–N linkage) | C, H, O, N, S (in Cys, Met) | Enzymatic catalysis, transport channels, antibodies, cytoskeleton, receptors |
| Nucleic Acids | Nucleotides (pentose + base + $PO_4^{3-}$) | Phosphodiester bond (3'–OH to 5'–$PO_4$) | C, H, O, N, P | Hereditary storage (DNA), gene expression & catalysis (mRNA, tRNA, rRNA), energy (ATP) |

**EXAMPLE 1.2** **Stoichiometry of Dehydration Synthesis & Hydrolysis**

> **Problem:** An enzyme polymerizes 150 α-glucose monomers into a single unbranched amylose (starch) chain. How many glycosidic bonds are formed, how many water molecules are released, and what is the molecular formula of a maltose disaccharide synthesized from two $C_6H_{12}O_6$ glucose monomers?

**STEP-BY-STEP SOLUTION:**

1. Step 1: Linking n monomers into a single linear polymer requires (n − 1) covalent bonds and releases (n − 1) water molecules.
2. Step 2: For n = 150 glucose monomers: 150 − 1 = 149 glycosidic linkages formed and 149 $H_2O$ molecules released.
3. Step 3: For maltose (2 glucose monomers): add 2 × $C_6H_{12}O_6$ = $C_{12}H_{24}O_{12}$, then subtract 1 $H_2O$ (2 H and 1 O) removed during dehydration synthesis → $C_{12}H_{22}O_{11}$.

**Final Answer: 149 glycosidic bonds and 149 $H_2O$ molecules are produced; the chemical formula of maltose is $C_{12}H_{22}O_{11}$.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Lipids are NOT true polymers because they are not built from long chains of identical repeating monomers, and dehydration synthesis of a triglyceride removes 3 $H_2O$ molecules (one for each of the three fatty acid tails attached to glycerol)!

## § 1.4 Proteins: Amino Acid Structure, Four Folding Levels & Sickle-Cell Disease

**Proteins** are the most functionally diverse macromolecules in living cells, acting as enzymes, membrane channels, antibodies, motor fibers, and signaling receptors. Every protein is a polymer constructed from combinations of 20 standard **amino acid** monomers. All 20 amino acids share an identical central **asymmetric α-carbon** covalently bonded to a hydrogen atom (−H), a basic **amino group (−$NH_2$ / −$NH_3^+$)**, and an acidic **carboxyl group (−COOH / −$COO^-$)**, differing only in their fourth attachment: the variable side chain or **R-group**.

At the ribosome, amino acids are joined head-to-tail by dehydration synthesis, forming a planar covalent **peptide bond (C–N)** between the carboxyl carbon of one amino acid and the amino nitrogen of the next. This creates a directional polypeptide backbone with a free **N-terminus (amino end)** and a free **C-terminus (carboxyl end)** that folds across four hierarchical levels (1° through 4°) into its native functional conformation.

- **Primary (1°) Structure:** The unique, genetically determined linear sequence of amino acids linked by covalent **peptide bonds** from N-terminus to C-terminus.
- **Secondary (2°) Structure:** Local folding of the polypeptide backbone into **α-helices** and **β-pleated sheets** stabilized strictly by hydrogen bonds between backbone carbonyl oxygens (C=O) and backbone amino hydrogens (N–H). *R-groups do not participate in 2° bonding.*
- **Tertiary (3°) Structure:** Overall 3D conformation of a single polypeptide chain stabilized by four chemical interactions among variable **R-groups**: (1) **hydrophobic clustering** of nonpolar R-groups in the interior away from water, (2) **hydrogen bonds** between polar R-groups, (3) **ionic bonds (salt bridges)** between acidic (−) and basic (+) R-groups, and (4) covalent **disulfide bridges (−S–S−)** between oxidized cysteine sulfhydryl groups.
- **Quaternary (4°) Structure:** Assembly of two or more folded polypeptide subunits into a functional multi-subunit complex, such as adult **hemoglobin** (4 subunits: 2α + 2β) or viral spike trimers.

### EXAMPLE 1.3 Case Study: Sickle-Cell Hemoglobin & Amino Acid R-Group Substitution

> **Problem:** In sickle-cell disease, a single point mutation in the β-globin gene replaces the 6th amino acid, glutamic acid (hydrophilic, negatively charged), with valine (hydrophobic, nonpolar). Explain how this 1° change cascades through 3° and 4° structure to impair red blood cell function, and predict what would happen if glutamic acid were instead replaced by aspartic acid (also hydrophilic, negatively charged).

**STEP-BY-STEP SOLUTION:**

1. Step 1: Replacing hydrophilic glutamic acid with nonpolar valine in the 1° sequence places a hydrophobic R-group on the exterior surface of the folded β-globin subunit (3° structure).
2. Step 2: Under low-oxygen conditions in tissues, exposed hydrophobic valine patches stick together to exclude water, causing hemoglobin tetramers (4° structure) to polymerize into rigid rod-like fibers.
3. Step 3: These rigid fibers deform flexible biconcave red blood cells into sickle shapes that clog capillaries, causing pain crises and organ damage (while heterozygotes gain malaria resistance).
4. Step 4: If glutamic acid were replaced by aspartic acid (conservative substitution with the same negative charge and hydrophilicity), the exterior surface would remain hydrophilic and normal protein folding/function would likely be preserved.

**Final Answer: Nonpolar valine creates an external sticky hydrophobic patch that causes deoxygenated hemoglobin tetramers to aggregate into rigid fibers; substituting another negatively charged hydrophilic amino acid like aspartate typically preserves native 3°/4° folding.**

**⚠ AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: High heat or extreme pH denatures a protein by disrupting weak hydrogen bonds, ionic bonds, and hydrophobic interactions in 2°, 3°, and 4° structure, but denaturation NEVER breaks covalent peptide bonds in the 1° sequence! Only hydrolytic enzymes (proteases) or strong acid hydrolysis cleave peptide bonds.

## § 1.5 Nucleic Acids: DNA vs. RNA Structure & 5' → 3' Directionality

**Nucleic acids**—deoxyribonucleic acid (**DNA**) and ribonucleic acid (**RNA**)—store, transmit, and express hereditary information. Both are polymers built from **nucleotide** monomers. Every nucleotide consists of three covalently linked components: a central 5-carbon **pentose sugar** (numbered 1' to 5'), a nitrogenous base attached to the **1' carbon**, and one to three negatively charged **phosphate groups** attached to the **5' carbon**. Notably, **ATP (adenosine triphosphate)** is itself an RNA nucleotide monomer (adenine + ribose + 3 serial phosphates) whose terminal phosphoanhydride bond hydrolysis powers cellular work.

During polymerization, enzymes join nucleotides via covalent **phosphodiester bonds** linking the **3' hydroxyl (−OH) group** of one pentose sugar to the **5' phosphate group** of the next incoming nucleotide. This creates a directional sugar–phosphate backbone with a free 5' phosphate at one end and a free 3' hydroxyl at the other. In a DNA double helix, the two complementary strands run in opposite directions (**5' → 3'** and **3' → 5'**)—an arrangement termed **antiparallel**.

- **Pentose Sugar (2' Carbon):** RNA contains **ribose** with a reactive hydroxyl group (**−OH**) on the 2' carbon, making RNA chemically less stable; DNA contains **deoxyribose** with only a hydrogen atom (**−H**) on the 2' carbon (one fewer oxygen atom), making DNA highly stable for long-term genetic storage.
- **Nitrogenous Bases:** Both DNA and RNA use double-ring **purines** (Adenine, Guanine) and the single-ring **pyrimidine** Cytosine, but DNA uses **Thymine (T)** whereas RNA uses **Uracil (U)**.
- **Strand Architecture:** DNA typically forms a double-stranded antiparallel helix, whereas RNA is synthesized as a single strand that can fold back on itself via intramolecular A–U and G–C base pairing into complex 3D structures (tRNA cloverleafs, rRNA ribozymes).
- **Universal 5' → 3' Synthesis Rule:** Both DNA polymerases and RNA polymerases can ONLY add new nucleotides to the free **3' −OH end** of a growing strand; therefore, all nucleic acid synthesis proceeds strictly in the **5' → 3' direction**.

**Table 1.3 · Molecular Comparison of DNA and RNA**

| Structural Feature | DNA (Deoxyribonucleic Acid) | RNA (Ribonucleic Acid) |
|---|---|---|
| Pentose Sugar | Deoxyribose (2' carbon has −H) | Ribose (2' carbon has reactive −OH) |
| Purine Bases (2 rings) | Adenine (A), Guanine (G) | Adenine (A), Guanine (G) |
| Pyrimidine Bases (1 ring) | Cytosine (C), Thymine (T) | Cytosine (C), Uracil (U) |
| Base-Pairing Rules | A = T (2 H-bonds), G ≡ C (3 H-bonds) | A = U (2 H-bonds), G ≡ C (3 H-bonds) |
| Strand Structure | Double-stranded antiparallel helix | Single-stranded (folds into 3D secondary structures) |
| Primary Cellular Roles | Long-term hereditary blueprint in nucleus/nucleoid | mRNA coding, tRNA amino acid delivery, rRNA catalysis, gene regulation |

⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Never confuse the bonds inside DNA! Covalent PHOSPHODIESTER bonds link adjacent nucleotides along a single strand (5' to 3' backbone), whereas weak HYDROGEN bonds connect complementary nitrogenous bases (A–T, G–C) across the two opposite strands.

### ✅ CHAPTER 1 MASTERY CHECKLIST (AP EXAM READINESS)

☑ Explain how oxygen's high electronegativity creates polar covalent bonds ($\delta^-/\delta^+$) and intermolecular hydrogen bonding, driving cohesion, adhesion, surface tension, and thermal buffering.

☑ Identify the CHNOPS elements and 8 functional groups in carbohydrates, lipids, proteins, and nucleic acids, and compare dehydration synthesis with hydrolysis.

☑ Contrast α-1,4 vs. β-1,4 glycosidic linkages in starch/glycogen vs. cellulose, and explain why amphipathic phospholipids self-assemble into bilayers.

☑ Trace the four hierarchical levels of protein structure (1°–4°) and predict how R-group substitutions (hydrophobic vs. hydrophilic/charged) alter protein folding.

☑ Compare DNA and RNA across 2' sugar carbon chemistry, nitrogenous bases, and antiparallel 5' → 3' phosphodiester directionality.

CHAPTER 2 · CORE CURRICULUM

**AP Exam Weighting: 10–13%**

# Unit 2: Cell Structure and Function

Cells are the fundamental structural and functional units of life across all three domains. This unit examines how surface-area-to-volume ratios constrain cell size, how eukaryotic compartmentalization and endosymbiosis enhance metabolic efficiency, and how the selectively permeable fluid mosaic membrane regulates passive transport, active transport, and water potential.

### CHAPTER 2 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Cube Surface-Area-to-Volume Ratio: $SA / V = 6s^2 / s^3 = 6 / s$ | As linear dimension s increases, volume grows faster than surface area, lowering SA:V |
| Total Water Potential: $\Psi = \Psi_p + \Psi_s$ | Water always flows passively from higher (less negative) Ψ to lower (more negative) Ψ |
| Solute Potential: $\Psi_s = -iCRT$ | i = ionization constant, C = molarity (mol/L), R = 0.0831 L·bar/(mol·K), T = Kelvin (K = °C + 273) |

## § 2.1 Universal Cell Features, Prokaryotes vs. Eukaryotes & SA:V Ratio

Despite immense evolutionary diversity, all living cells across the three domains—**Bacteria, Archaea, and Eukarya**—share four universal structural features that provide compelling evidence for descent from a single common ancestor (LUCA): (1) an enclosing, selectively permeable **plasma membrane** built from a phospholipid bilayer, (2) a semifluid aqueous **cytosol** containing dissolved ions and metabolic enzymes, (3) hereditary genetic material stored in **DNA chromosomes**, and (4) **ribosomes** (composed of rRNA and protein) that translate mRNA into polypeptides.

Cells are classified into two structural groups. **Prokaryotic cells** (Bacteria and Archaea) are small (1–5 μm), lack a membrane-bound nucleus—housing their single circular DNA chromosome in an unenclosed cytoplasmic region called the **nucleoid** alongside small circular **plasmids**—lack membrane-bound organelles, and possess smaller **70S ribosomes**. **Eukaryotic cells** (protists, fungi, plants, animals) are much larger (10–100 μm), enclose multiple linear DNA chromosomes wrapped around **histone proteins** inside a double-membrane **nucleus**, contain **80S cytoplasmic ribosomes**, and partition their cytoplasm into specialized membrane-bound organelles.

Why are nearly all cells microscopic? A cell's metabolic demand scales with its cytoplasmic **volume (V)**, which dictates how much $O_2$ and nutrients are consumed and how much waste and heat are generated per second. However, the maximum rate of material exchange scales with plasma membrane **surface area (SA)**. As a cell enlarges, volume increases by the cube ($s^3$) while surface area increases only by the square ($s^2$), causing the **SA:V ratio to plummet** and starving the cell's interior.

- **Morphological Adaptations for High SA:V:** Cells and tissues specialized for rapid exchange maximize surface area via thin, elongated, or highly folded geometries—such as **intestinal microvilli**, plant **root hairs**, alveolar sacs, fish gill lamellae, and flattened mammal ears.
- **Body Size & Metabolic Scaling in Endotherms:** Small mammals (such as a 2 g Etruscan shrew or a sea otter in cold water) have a very high SA:V ratio and lose body heat rapidly across their skin, requiring an ultra-high **mass-specific metabolic rate** (80 cal/g/day and 1,200 bpm heart rate in shrews) compared to massive whales or elephants (0.01 cal/g/day) whose low SA:V ratio conserves internal heat.

**EXAMPLE 2.1** **Quantitative Surface-Area-to-Volume (SA:V) Ratio Scaling**

**Problem:** Compare a small cuboidal bacterial cell with side length s = 1 μm to a larger cuboidal eukaryotic cell with side length s = 10 μm. Calculate the surface area, volume, and SA:V ratio for each cell.

**STEP-BY-STEP SOLUTION:**

1. Step 1: For the s = 1 μm cube: SA = $6s^2 = 6(1)^2 = 6\ \mu m^2$; Volume V = $s^3 = (1)^3 = 1\ \mu m^3$; Ratio SA:V = 6 / 1 = 6 : 1.
2. Step 2: For the s = 10 μm cube: SA = $6s^2 = 6(10)^2 = 600\ \mu m^2$ (a 100-fold increase); Volume V = $s^3 = (10)^3 = 1{,}000\ \mu m^3$ (a 1,000-fold increase).
3. Step 3: Calculate the new SA:V ratio: 600 $\mu m^2$ / 1,000 $\mu m^3$ = 0.6 : 1 (a 10-fold decrease in surface area per unit volume).

**Final Answer: Scaling side length up 10-fold (from 1 μm to 10 μm) drops the SA:V ratio 10-fold from 6:1 down to 0.6:1, explaining why large eukaryotic cells require internal membrane compartmentalization.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: As an endotherm's total body mass increases (mouse → elephant), its TOTAL daily calorie consumption increases, but its RELATIVE (mass-specific) metabolic rate per gram of tissue ($O_2$/g/hr) decreases dramatically because its SA:V ratio is much smaller!

## § 2.2 Subcellular Organelles, Endomembrane Trafficking & Endosymbiosis

Large eukaryotic cells overcome their low outer SA:V ratio through **cellular compartmentalization**. Extensive internal membranes partition the cytoplasm into specialized organelles that (1) maintain distinct local chemical microenvironments (e.g., an acidic **lysosome** at pH ~4.8 vs. neutral cytosol at pH 7.2) so incompatible reactions occur simultaneously without interference, and (2) vastly expand internal membrane surface area for membrane-embedded enzymes.

In the **secretory pathway** of the **endomembrane system**, polypeptides destined for membranes, lysosomes, or extracellular secretion are translated by **bound ribosomes** attached to the **rough endoplasmic reticulum (Rough ER)**. Inside the Rough ER lumen, the nascent chain folds and receives a carbohydrate tag to become a **glycoprotein**. Transport vesicles bud off the Rough ER and fuse with the receiving *cis* face of the **Golgi complex**, where enzymes modify carbohydrate tags into molecular zip codes as the cargo moves toward the shipping *trans* face. Finally, vesicles bud from the *trans* Golgi to either fuse with the plasma membrane for **exocytosis** or form hydrolytic **lysosomes**.

Whereas the nuclear envelope and ER evolved from inward infoldings of the ancestral plasma membrane, **mitochondria and chloroplasts** originated via **endosymbiosis**. Roughly 1.8 billion years ago, an ancestral archaeal host cell engulfed an aerobic α-proteobacterium that evolved into the mitochondrion present in all eukaryotes; later, a eukaryotic lineage engulfed a photosynthetic cyanobacterium that became the chloroplast of plants and algae.

- **Free vs. Bound Ribosomes: Free ribosomes** suspended in the cytosol synthesize proteins that function inside the cytosol itself (e.g., glycolysis enzymes), whereas **bound ribosomes** on the Rough ER synthesize secreted, transmembrane, and lysosomal proteins.
- **Smooth ER & Lysosomes:** The ribosome-free **Smooth ER** synthesizes lipids and steroid hormones, detoxifies drugs/alcohol in hepatocytes, and stores $Ca^{2+}$ ions in muscle sarcoplasmic reticulum. **Lysosomes** (pH ~4.8) mediate phagocytosis digestion, **autophagy** (recycling damaged organelles), and **apoptosis** (programmed cell death, such as removing interdigital webbing in human embryos).
- **Four Lines of Evidence for Endosymbiosis:** Both mitochondria and chloroplasts (1) are enclosed by **double membranes**, (2) contain their own **circular, histone-free DNA** genome, (3) possess prokaryote-sized **70S ribosomes**, and (4) reproduce independently inside the cell via **binary fission**.

**Table 2.1 · Structure–Function Coupling in Eukaryotic Organelles**

| Organelle | Structural Architecture | Primary Cellular Function | Cell Distribution |
|---|---|---|---|
| Nucleus & Nucleolus | Double nuclear envelope with nuclear pores; dense nucleolus | Houses linear DNA + histones (chromatin); nucleolus transcribes rRNA & assembles ribosomal subunits | All eukaryotes |
| Rough ER | Membrane network studded with bound 80S ribosomes | Folds & glycosylates secretory, membrane, and lysosomal proteins; packages transport vesicles | All eukaryotes |
| Smooth ER | Tubular lipid membrane network lacking ribosomes | Synthesizes lipids/steroids, detoxifies poisons in liver, sequesters $Ca^{2+}$ in muscle | All eukaryotes |
| Golgi Complex | Polarity of flattened membrane sacs (cisternae: cis → trans) | Modifies carbohydrate tags on glycoproteins; sorts and ships vesicles to membrane or lysosomes | All eukaryotes |
| Lysosome | Single membrane sac maintained at acidic pH ~4.8 by $H^+$ pumps | Intracellular digestion (phagocytosis), organelle recycling (autophagy), programmed cell death (apoptosis) | Animal cells (vacuoles in plants) |
| Mitochondrion | Smooth outer membrane + highly folded inner membrane (cristae) + matrix | Aerobic respiration: Krebs cycle in matrix; ETC & ATP synthase on cristae maximize ATP output | All eukaryotes (plants & animals!) |
| Chloroplast | Double outer membrane + stacked thylakoids (grana) + fluid stroma | Photosynthesis: light reactions in thylakoid membranes; Calvin cycle (RuBisCO) in stroma | Plants and photosynthetic algae |
| Central Vacuole & Cell Wall | Large tonoplast sac (80% volume); rigid β-1,4 cellulose cell wall | Stores water/ions; osmotic water influx pushes membrane against wall to generate turgor pressure | Plants (chitin wall in fungi) |

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Plant cells have BOTH chloroplasts AND mitochondria! Chloroplasts synthesize sugar from sunlight, while mitochondria oxidize that sugar to generate ATP for the plant cell day and night. Also remember that why the inner mitochondrial membrane is folded into cristae is ALWAYS to increase surface area for ETC complexes and ATP synthase.

## § 2.3 The Fluid Mosaic Membrane & Selective Permeability

The plasma membrane is described by the **fluid mosaic model**: it behaves as a two-dimensional fluid because amphipathic phospholipids and many proteins drift laterally within each leaflet, and as a mosaic because diverse proteins, sterols, and carbohydrates are embedded in the bilayer. **Integral (transmembrane) proteins** span the entire bilayer—anchoring their nonpolar hydrophobic amino acid R-groups within the fatty acid core while exposing their polar hydrophilic domains to aqueous fluid on both sides—whereas **peripheral proteins** bind loosely to the membrane surface.

On the extracellular face, short branched oligosaccharides covalently attached to lipids (**glycolipids**) and proteins (**glycoproteins**) serve as cell-to-cell recognition badges (such as MHC antigens and ABO blood group markers). In animal membranes, steroid **cholesterol** molecules wedge between phospholipid tails to act as a **bidirectional fluidity buffer**: at high temperatures, cholesterol restrains phospholipid movement to prevent excess fluidity; at low temperatures, it disrupts tight tail packing to prevent solidification.

Because the interior core of the phospholipid bilayer is nonpolar and hydrophobic, the plasma membrane exhibits strict **selective permeability**.

- **Simple Diffusion (No Protein Required):** Small, **nonpolar hydrophobic molecules**—specifically dissolved gases (**$O_2$, $CO_2$, $N_2$**) as well as nonpolar lipids and steroid hormones—dissolve directly through the hydrophobic fatty acid interior down their concentration gradient.
- **Facilitated Diffusion (Channel or Carrier Protein Required):** Charged **ions** ($Na^+$, $K^+$, $Ca^{2+}$, $Cl^-$) and large **polar hydrophilic molecules** (glucose, amino acids) are repelled by the hydrophobic core and must cross passively down their gradient via specific transmembrane **channel proteins** or conformation-shifting **carrier proteins** with zero ATP expenditure.
- **Aquaporins:** Although water ($H_2O$) is small enough to leak slowly across the bilayer, rapid osmosis across cell membranes occurs through specialized hydrophilic channel proteins called **aquaporins**.

> ⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
> AP Exam Trap: Facilitated diffusion uses transmembrane channel or carrier proteins and is saturable at V_max when all transporters are occupied, but it is still 100% PASSIVE transport (moves solutes high → low down their gradient and requires ZERO ATP)!

## § 2.4 Active Transport, Electrochemical Gradients & Bulk Transport

Whereas passive transport (simple diffusion, osmosis, facilitated diffusion) moves substances spontaneously down their concentration gradient (high → low) using only thermal kinetic energy, **active transport** pumps solutes **uphill against their concentration gradient (low → high)**. This thermodynamically unfavorable work requires the cell to expend metabolic energy, typically by hydrolyzing **ATP into ADP + $P_i$** and transferring the terminal phosphate group directly onto a transmembrane carrier pump to drive a conformational change.

When electrogenic pumps move charged ions unequally across a membrane, they establish both a chemical concentration gradient and an electrical voltage across the membrane (**membrane potential**), creating a combined **electrochemical gradient** that stores potential energy for nerve impulses, cotransport, and chemiosmotic ATP synthesis.

Macromolecules (polysaccharides, polypeptides) and whole bacterial cells that are too large to pass through any transport protein cross the membrane via ATP-requiring **bulk transport** using lipid vesicles propelled along cytoskeleton tracks.

- **Sodium–Potassium Pump ($Na^+/K^+$ ATPase):** In animal neurons, each cycle hydrolyzes **1 ATP** to pump **3 $Na^+$ ions out** of the cell and **2 $K^+$ ions into** the cell against both gradients, leaving the cytoplasm net negatively charged (resting potential ≈ −70 mV).
- **Proton Pumps ($H^+$ ATPase):** In plants, fungi, and bacteria, proton pumps actively extrude $H^+$ out of the cell, generating a proton motive force used to cotransport sucrose or ions into the cell.
- **Exocytosis:** Intracellular secretory vesicles from the trans-Golgi travel along microtubule tracks and fuse with the plasma membrane, spilling hormones (insulin), neurotransmitters, or extracellular matrix proteins outside the cell (and expanding plasma membrane area).
- **Three Modes of Endocytosis:** (1) **Phagocytosis ('cellular eating')**: pseudopods engulf solid particles or bacteria into a food vacuole for lysosomal digestion; (2) **Pinocytosis ('cellular drinking')**: tiny vesicles non-specifically gulp extracellular fluid; (3) **Receptor-mediated endocytosis**: specific ligands (such as cholesterol-carrying LDL particles) bind surface receptors clustered in clathrin-coated pits.

> ⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
> AP Exam Trap: Never reverse the stoichiometry of the $Na^+/K^+$ pump! It always pumps 3 $Na^+$ OUT and 2 $K^+$ IN per ATP hydrolyzed, creating a net export of one positive charge per cycle.

## § 2.5 Osmosis, Tonicity, Osmoregulation & Quantitative Water Potential (Ψ)

**Osmosis** is the passive diffusion of free water across a selectively permeable membrane. The golden rule of osmosis states that water always moves from a **hypotonic solution** (lower solute concentration, higher free water concentration)

toward a **hypertonic solution** (higher solute concentration, lower free water concentration) until osmotic equilibrium (**isotonic** conditions) or opposing physical pressure stops net flow.

Because animal cells (such as red blood cells) lack cell walls, they thrive in an **isotonic** extracellular fluid; in a hypertonic solution they lose water and shrivel (**crenate**), whereas in a hypotonic solution water rushes in until the cell swells and bursts (**lyses**). By contrast, plant cells are surrounded by a rigid cellulose cell wall: in a hypertonic environment the plasma membrane pulls away from the cell wall (**plasmolysis**, causing wilting), in an isotonic solution the cell becomes limp (**flaccid**), and in a **hypotonic** solution water enters the central vacuole and pushes the membrane against the rigid wall to generate healthy **turgor pressure**.

Quantitatively, biophysicists predict water movement using **water potential (Ψ)**, measured in megapascals (MPa) or bars (1 MPa = 10 bar). Water always flows passively from regions of **higher (less negative) Ψ to lower (more negative) Ψ** according to **$\Psi = \Psi_p + \Psi_s$**. Pure water in an open beaker has $\Psi_p = 0$ and $\Psi_s = 0$, so $\Psi = 0$. Dissolving solutes binds water molecules and always reduces free water, meaning solute potential **$\Psi_s = -iCRT$ is always ≤ 0**.

- **Paramecium Contractile Vacuole:** Freshwater protists like *Paramecium* are strongly hypertonic to pond water; as water constantly floods in by osmosis, a specialized **contractile vacuole** uses ATP to pump water back out. Increasing external pond salinity shrinks the osmotic gradient and slows the vacuole's contraction rate.
- **Plant Stomatal Guard Cells:** To open a leaf stoma for gas exchange, $H^+$ pumps drive **$K^+$ and $Cl^-$ ions into guard cells**, making them hypertonic; water follows by osmosis via aquaporins, swelling the guard cells with turgor pressure so the pore bows open. During drought, abscisic acid triggers $K^+$ efflux, water exits by osmosis, guard cells go flaccid, and the stoma closes.

**Table 2.2 · Osmotic Behavior of Animal vs. Plant Cells Across Tonicities**

| External Solution Tonicity | Net Direction of Water Flow | Effect on Animal Cell (No Cell Wall) | Effect on Plant Cell (Rigid Cell Wall) |
|---|---|---|---|
| Hypertonic (Higher external solute) | Net $H_2O$ flows OUT of the cell | Shrivels / Crenates | Plasmolysis (membrane detaches from wall; wilts) |
| Isotonic (Equal solute concentration) | No net $H_2O$ flow (dynamic equilibrium) | Normal / Optimal physiological shape | Flaccid (limp; $\Psi_p = 0$) |
| Hypotonic (Lower external solute) | Net $H_2O$ flows INTO the cell | Swells and bursts (Cytolysis) | Turgid / Optimal (rigid wall exerts $+\Psi_p$ turgor pressure) |

### EXAMPLE 2.2 Calculating Solute Potential (Ψ_s) & Equilibrium Turgor Pressure (Ψ_p)

**Problem:** A plant root cell with an internal solute potential of Ψ_s = −6.5 bar is placed in an open beaker containing a 0.15 M NaCl solution at 27 °C. Given R = 0.0831 L·bar/(mol·K), calculate the water potential of the NaCl solution, determine the initial direction of water flow, and find the equilibrium pressure potential (Ψ_p) if the cell instead reaches osmotic equilibrium in pure distilled water (Ψ_beaker = 0 bar).

**STEP-BY-STEP SOLUTION:**

1. Step 1: Determine parameters for the 0.15 M NaCl beaker: NaCl dissociates into 2 ions ($Na^+$ + $Cl^-$), so i = 2; C = 0.15 mol/L; R = 0.0831 L·bar/(mol·K); T = 27 + 273 = 300 K.
2. Step 2: Calculate beaker solute potential: Ψ_s = −iCRT = −(2)(0.15)(0.0831)(300) = −7.48 bar. Since the beaker is open to the atmosphere, Ψ_p = 0, so Ψ_beaker = −7.48 bar.
3. Step 3: If the plant cell initially has Ψ_s = −6.5 bar and Ψ_p = 0 (Ψ_cell = −6.5 bar), water flows from higher (less negative) Ψ (−6.5 bar in the cell) to lower (more negative) Ψ (−7.48 bar in the beaker), so water exits the cell.
4. Step 4: If the cell with Ψ_s = −6.5 bar reaches osmotic equilibrium in pure water (Ψ_beaker = 0 bar), then Ψ_cell = Ψ_beaker = 0 → Ψ_p + (−6.5 bar) = 0 → Ψ_p = +6.5 bar of turgor pressure.

**Final Answer: The 0.15 M NaCl beaker has Ψ = −7.48 bar (water flows out of a −6.5 bar flaccid cell); in pure water (Ψ = 0), the cell reaches equilibrium at a turgor pressure of Ψ_p = +6.5 bar.**

### ⚠ AP EXAM TRAP & FRQ SCORING GUIDELINE

AP Exam Trap: When using Ψ_s = −iCRT, ALWAYS check whether the solute is covalent/non-ionizing (sucrose or glucose → i = 1) or ionic (NaCl → i = 2; $CaCl_2$ → i = 3), and never forget to convert Celsius to Kelvin (T = °C + 273)!

### ✅ CHAPTER 2 MASTERY CHECKLIST (AP EXAM READINESS)

☑ List the four universal structures shared by all cells and contrast prokaryotic vs. eukaryotic cellular organization.

☑ Calculate surface-area-to-volume (SA:V) ratios for cells of varying geometries and relate SA:V scaling to metabolic rates in endotherms.

☑ Trace the secretory pathway (Rough ER → transport vesicle → cis/trans Golgi → secretory vesicle/lysosome) and state the four lines of evidence for the endosymbiotic origin of mitochondria and chloroplasts.

☑ Predict how molecule polarity, size, and charge govern simple diffusion, facilitated diffusion (channels/carriers/aquaporins), active transport ($Na^+/K^+$ pump, $H^+$ pump), and bulk transport.

☑ Solve quantitative water potential problems using Ψ = Ψ_p + Ψ_s and Ψ_s = −iCRT, and predict cell behavior in hypotonic, isotonic, and hypertonic solutions.

CHAPTER 3 · CORE CURRICULUM

**AP Exam Weighting: 12–16%**

# Unit 3: Cellular Energetics

Living systems require a constant input of free energy to maintain order, grow, and reproduce. This unit explores how protein enzymes catalyze metabolic reactions by lowering activation energy, how exergonic ATP hydrolysis couples to endergonic cellular work, and how chloroplasts and mitochondria harvest and transform energy via photosynthesis, aerobic cellular respiration, and anaerobic fermentation.

### CHAPTER 3 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Gibbs Free Energy: $\Delta G < 0$ (Exergonic, spontaneous) vs. $\Delta G > 0$ (Endergonic, requires energy input) | Enzymes lower activation energy (E_A) but NEVER alter ΔG of a reaction |
| Photosynthesis: $6\ CO_2 + 6\ H_2O + \text{Light Energy} \rightarrow C_6H_{12}O_6 + 6\ O_2$ ($\Delta G = +686$ kcal/mol) | Anabolic endergonic pathway; $O_2$ gas comes exclusively from splitting $H_2O$ at Photosystem II |
| Cellular Respiration: $C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O + \sim 30–32$ ATP ($\Delta G = -686$ kcal/mol) | Catabolic exergonic pathway oxidizing glucose via Glycolysis, Krebs Cycle, and Oxidative Phosphorylation |

## § 3.1 Enzyme Structure, Induced-Fit Catalysis, Kinetics & Inhibition

**Enzymes** are biological catalysts—almost always tertiary or quaternary proteins (alongside catalytic RNA ribozymes)—that accelerate cellular reaction rates by millions of times without being consumed or permanently altered. Every chemical reaction must overcome an initial energy barrier called **activation energy (E_A)** to contort reactant bonds into the unstable **transition state**. Enzymes speed up reactions strictly by **lowering E_A**; crucially, an enzyme never changes the free energy of reactants or products, so the net **Gibbs free energy change (ΔG)** remains completely unchanged.

Each enzyme possesses a uniquely shaped 3D pocket called the **active site** lined with specific amino acid R-groups that complement its target **substrate**. Upon substrate binding, weak noncovalent interactions trigger a slight conformational tightening of the enzyme around the substrate called **induced fit**, which strains substrate bonds, orients reactants precisely, and provides a favorable microenvironment for catalysis.

Every enzyme exhibits an optimal temperature and pH. Rising temperature increases molecular kinetic energy and substrate–active site collision frequency up to the optimum, above which thermal agitation breaks weak H-bonds, ionic salt bridges, and hydrophobic interactions, causing **denaturation** of the active site. Similarly, extreme pH alters the ionization state of acidic and basic R-groups: gastric **pepsin** peaks at pH 2, whereas intestinal **trypsin** peaks at pH 8.

- **Substrate Saturation (V_max):** At low substrate concentration [S], reaction velocity rises linearly as [S] increases; at high [S], velocity plateaus at **V_max (saturation)** because 100% of enzyme active sites are continuously occupied—the only way to raise V_max is to add more enzyme.
- **Competitive Inhibition:** A **competitive inhibitor** structurally mimics the normal substrate and competes directly for binding to the **active site**; competitive inhibition can be completely overcome (reaching normal V_max) by flooding the system with a high concentration of substrate.
- **Noncompetitive (Allosteric) Inhibition:** A **noncompetitive inhibitor** binds to a separate regulatory **allosteric site** outside the active site, inducing a conformational change that warps the active site so substrate cannot be catalyzed efficiently; adding more substrate CANNOT restore V_max.
- **Feedback Inhibition:** To prevent wasting resources, the end product of a multi-step metabolic pathway often acts as an allosteric inhibitor of the pathway's first committed enzyme, shutting down production when product is abundant.

**Table 3.1 · Comparison of Competitive vs. Noncompetitive (Allosteric) Enzyme Inhibition**

| Feature | Competitive Inhibitor | Noncompetitive (Allosteric) Inhibitor |
|---|---|---|
| Binding Site on Enzyme | Binds directly inside the Active Site | Binds to a separate Allosteric Site away from the active site |
| Mechanism of Action | Physically blocks substrate from entering the active site | Triggers a conformational change that distorts active-site shape |
| Effect on Apparent Affinity (K_m) | Decreases apparent affinity (increases K_m) | Does not alter substrate binding affinity (K_m unchanged) |
| Effect on Maximum Rate (V_max) | V_max is UNCHANGED if high [Substrate] is added | Lowers V_max permanently (adding excess substrate cannot overcome it) |

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Never write that an enzyme 'provides activation energy' or 'makes ΔG more negative.' Enzymes LOWER the activation energy barrier (E_A) and leave ΔG completely unchanged!

## § 3.2 Cellular Metabolism, Gibbs Free Energy (ΔG) & ATP Coupling

**Metabolism** encompasses all enzyme-catalyzed chemical reactions in an organism, organized into linear or cyclical metabolic pathways where the product of enzyme 1 immediately serves as the substrate for enzyme 2. Organisms acquire energy and carbon via distinct strategies: **autotrophs** self-feed by fixing inorganic $CO_2$ into organic molecules—either as **photoautotrophs** (plants, algae, cyanobacteria capturing solar photons) or **chemoautotrophs** (prokaryotes at deep-sea hydrothermal vents oxidizing inorganic $H_2S$)—whereas **heterotrophs** (animals, fungi) consume organic compounds made by other organisms.

Thermodynamically, **catabolic pathways** (such as cellular respiration) break down complex molecules into simpler ones via **exergonic reactions (ΔG < 0)** that release free energy. Conversely, **anabolic pathways** (such as protein polymerization or photosynthesis) build complex molecules from simpler precursors via **endergonic reactions (ΔG > 0)** that require a net input of energy. Cells drive endergonic reactions forward through **energy coupling** mediated by **ATP (adenosine triphosphate)**: exergonic hydrolysis of ATP's terminal phosphate bond (ATP + $H_2O$ → ADP + $P_i$, ΔG = −7.3 kcal/mol) transfers a high-energy phosphate group to phosphorylate transport pumps, motor proteins, or reactant intermediates.

- **Redox Electron Shuttles:** Metabolic pathways harvest energy by transferring electrons (oxidation = loss of electrons; reduction = gain of electrons) onto mobile coenzyme electron carriers: **$NAD^+$ → NADH** and **FAD → $FADH_2$** in cellular respiration, and **$NADP^+$ → NADPH** in photosynthesis.

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Breaking a chemical bond ALWAYS requires an input of energy; ATP releases net free energy during hydrolysis because the newly formed bonds in solvated ADP + $P_i$ are much lower in free energy (more stable) than the crowded, mutually repelling negatively charged triphosphate tail of ATP!

## § 3.3 Photosynthesis: Light Reactions (Z-Scheme) & The Calvin Cycle

Oxygenic **photosynthesis** first evolved in prokaryotic cyanobacteria 2.7–3.5 billion years ago, oxygenating Earth's atmosphere and creating the protective ozone layer. In eukaryotic chloroplasts, photosynthesis is partitioned across two compartments: the **light-dependent reactions** embedded in the **thylakoid membranes** (stacked into grana) and the **Calvin cycle** dissolved in the surrounding fluid **stroma**.

Embedded in the thylakoid membrane are photosynthetic pigments—**chlorophyll a**, **chlorophyll b** (each featuring a hydrophilic light-absorbing porphyrin ring centered on a **$Mg^{2+}$ ion** and a hydrophobic hydrocarbon tail), and accessory

**carotenoids**. As demonstrated by Theodor Engelmann's classic 1883 prism experiment using aerotaxis bacteria, chlorophyll absorbs strongly in the **violet-blue and red wavelengths** (driving peak $O_2$ production on the action spectrum) while reflecting green light.

In the linear **Z-scheme** of the light reactions, photons first strike **Photosystem II (P680)**, boosting two electrons to a primary electron acceptor. To replace those lost electrons, a water-splitting enzyme complex on the inner thylakoid surface performs **photolysis** ($H_2O \rightarrow 2\ H^+ + ½\ O_2 + 2\ e^-$)—proving that **all $O_2$ gas released in photosynthesis comes directly from water, not $CO_2$**. As energized electrons cascade down an electron transport chain from PSII to **Photosystem I (P700)**, a cytochrome complex pumps $H^+$ protons from the stroma into the narrow **thylakoid lumen**, lowering lumenal pH near 5. Trapped $H^+$ ions rush back out into the stroma through **ATP synthase** (photophosphorylation) to make **ATP**, while photons at PSI re-excite electrons to reduce $NADP^+$ into **NADPH** via $NADP^+$ reductase.

In the stroma, the **Calvin cycle** uses ATP and NADPH from the light reactions to fix $CO_2$ into sugar across three phases: (1) **Carbon Fixation**, where the enzyme **RuBisCO** attaches 3 $CO_2$ (1C) onto 3 **RuBP** (5C) to form six 3-carbon intermediates (3-PGA); (2) **Reduction**, where 6 ATP and 6 NADPH phosphorylate and reduce those intermediates into six high-energy **G3P (glyceraldehyde-3-phosphate, 3C)** molecules, with **1 net G3P exiting** to build glucose or starch; and (3) **Regeneration**, where 3 more ATP rearrange the remaining five G3P (15 carbons total) back into three 5-carbon RuBP acceptors.

- **Coupled Dependency of Light Reactions & Calvin Cycle:** If the Calvin cycle stops (e.g., due to lack of $CO_2$ when stomata close), ATP and NADPH are no longer consumed in the stroma; consequently, **ADP + $P_i$ and $NADP^+$ run out**, halting the thylakoid light reactions as well.

**EXAMPLE 3.1** **Tracing Isotopes & Stoichiometry in the Calvin Cycle**

> **Problem:** Scientists supply a suspension of illuminated green algae with water labeled with heavy oxygen ($H_2{}^{18}O$) and carbon dioxide labeled with normal oxygen ($C^{16}O_2$). Where will the heavy $^{18}O$ isotope appear in the products? Furthermore, how many $CO_2$ molecules, ATP, and NADPH are consumed in the Calvin cycle to synthesize one full 6-carbon glucose molecule (two net 3-carbon G3P molecules)?

**STEP-BY-STEP SOLUTION:**

1. Step 1: Recall that photolysis at Photosystem II splits $H_2O$ to replace electrons in P680 and release $O_2$ gas, whereas $CO_2$ is fixed by RuBisCO into G3P carbohydrates.
2. Step 2: Therefore, 100% of the heavy $^{18}O$ from $H_2{}^{18}O$ is released as $^{18}O_2$ gas, while $C^{16}O_2$ is incorporated into glucose ($C_6H_{12}{}^{16}O_6$).
3. Step 3: One turn of the 3-$CO_2$ Calvin cycle produces 1 net G3P (3 carbons) at a cost of 9 ATP (6 in reduction + 3 in regeneration) and 6 NADPH.
4. Step 4: Building one 6-carbon glucose requires 2 net G3P molecules: 2 × (3 $CO_2$ + 9 ATP + 6 NADPH) = 6 $CO_2$, 18 ATP, and 12 NADPH.

**Final Answer: The $^{18}O$ from $H_2{}^{18}O$ appears exclusively in released $O_2$ gas; synthesizing one glucose molecule (2 G3P) requires 6 $CO_2$, 18 ATP, and 12 NADPH.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Never say chloroplasts 'make ATP to power the rest of the plant cell'! All ATP and NADPH made by the thylakoid light reactions are consumed entirely inside the chloroplast stroma to drive the Calvin cycle; the plant cell relies on its MITOCHONDRIA to make ATP for active transport and cellular work.

## § 3.4 Aerobic Cellular Respiration: Glycolysis, Krebs Cycle & Oxidative Phosphorylation

**Aerobic cellular respiration** is the catabolic, exergonic oxidation of glucose ($C_6H_{12}O_6$ + 6 $O_2$ → 6 $CO_2$ + 6 $H_2O$, $\Delta G$ = −686 kcal/mol) to synthesize roughly **30–32 ATP** per glucose across four sequential stages.

**Stage 1: Glycolysis ('sugar splitting')** occurs in the **cytosol** of virtually all living organisms (prokaryotes and eukaryotes) and requires **zero $O_2$**, reflecting its ancient evolutionary origin prior to Earth's oxygen atmosphere. In the energy investment phase, enzymes spend 2 ATP to phosphorylate 6-carbon glucose into unstable fructose-1,6-bisphosphate, which cleaves into two 3-carbon G3P sugars. In the energy harvest phase, oxidation produces **2 NADH** and substrate-level phosphorylation generates 4 total ATP, yielding a **net profit of 2 ATP, 2 NADH, and 2 pyruvate (3C)**.

When $O_2$ is available, pyruvate enters the **mitochondrial matrix**. In **Stage 2: Pyruvate Oxidation (Link Reaction)**, each 3-carbon pyruvate loses one carbon as $CO_2$ gas, reduces $NAD^+$ to NADH, and binds coenzyme A to form 2-carbon **acetyl-CoA** (yielding 2 acetyl-CoA, 2 $CO_2$, and 2 NADH per glucose). In **Stage 3: The Krebs Cycle (Citric Acid Cycle)** in the matrix, each 2-carbon acetyl-CoA condenses with 4-carbon oxaloacetate to form 6-carbon citrate. Over two turns per glucose, systematic oxidation releases **4 $CO_2$** and generates **6 NADH, 2 $FADH_2$, and 2 ATP** (via substrate-level phosphorylation).

In **Stage 4: The Electron Transport Chain (ETC) and Chemiosmosis** across the folded **inner mitochondrial membrane (cristae)**, the 10 NADH and 2 $FADH_2$ molecules donate high-energy electrons to membrane protein complexes (regenerating $NAD^+$ and FAD). As electrons cascade downhill toward progressively more electronegative cytochromes—pulled by **oxygen ($O_2$), the terminal electron acceptor** at the bottom of the chain, which combines with electrons and $H^+$ to form $H_2O$—three proton-pump complexes pump $H^+$ from the matrix into the narrow **intermembrane space (IMS)**. Trapped at high concentration and low pH in the IMS, protons rush back into the matrix down their electrochemical gradient through the rotary turbine **ATP synthase (chemiosmosis)**, driving **oxidative phosphorylation** of ~26–28 ATP.

- **Uncoupling & Brown Fat Thermogenesis:** Hibernating mammals and human infants possess brown adipose tissue whose inner mitochondrial membranes express **thermogenin (UCP1, uncoupling protein)**—a regulated proton leak channel that allows $H^+$ ions to diffuse back into the matrix bypassing ATP synthase, dissipating the proton gradient directly as life-saving **body heat** instead of ATP.

**Table 3.2 · Complete Accounting of Aerobic Cellular Respiration (per 1 Glucose Molecule)**

| Respiration Stage | Cellular Location | Key Carbon Inputs → Outputs | Reduced Coenzymes Produced | Net ATP Yield & Mechanism |
|---|---|---|---|---|
| 1. Glycolysis | Cytosol (Cytoplasm) | 1 Glucose (6C) → 2 Pyruvate (3C) | 2 NADH | 2 ATP net (4 made − 2 invested; Substrate-level) |
| 2. Pyruvate Oxidation (Link) | Mitochondrial Matrix (Eukaryotes) | 2 Pyruvate (3C) → 2 Acetyl-CoA (2C) + 2 $CO_2$ | 2 NADH | 0 ATP |
| 3. Krebs (Citric Acid) Cycle | Mitochondrial Matrix | 2 Acetyl-CoA (2C) → 4 $CO_2$ (Oxaloacetate regenerated) | 6 NADH, 2 $FADH_2$ | 2 ATP (or GTP; Substrate-level) |
| 4. ETC & Chemiosmosis | Inner Mitochondrial Membrane (Cristae) | Electrons + ½ $O_2$ + 2 $H^+$ → $H_2O$ | Oxidizes 10 NADH & 2 $FADH_2$ back to $NAD^+$/FAD | ~26–28 ATP (Oxidative phosphorylation via ATP synthase) |

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Notice where $O_2$ and $CO_2$ act! All 6 $CO_2$ molecules come from decarboxylating pyruvate (2 $CO_2$) and the Krebs cycle (4 $CO_2$) BEFORE the ETC; oxygen ($O_2$) is used ONLY at the very end of the ETC as the final electron acceptor to make $H_2O$!

## § 3.5 Chloroplast vs. Mitochondrial Chemiosmosis & Anaerobic Fermentation

Comparing chemiosmosis in mitochondria and chloroplasts is a classic AP Biology synthesis topic. Both organelles use an electron transport chain to pump $H^+$ protons across an internal membrane into a small enclosed compartment, building an electrochemical proton gradient (proton-motive force) that drives **ATP synthase**. However, their electron sources, terminal acceptors, and spatial proton directions are inverted.

What happens when a cell runs out of oxygen? Without electronegative $O_2$ at the bottom of the mitochondrial ETC to accept electrons, the entire transport chain backs up and halts, shutting down the Krebs cycle and oxidative phosphorylation. The cell can still survive on the **2 net ATP per glucose** produced by cytosolic glycolysis *if and only if* it has a continuous supply of empty **$NAD^+$** electron acceptors. If all cytosolic $NAD^+$ becomes reduced to NADH, glycolysis itself grinds to a halt. **Anaerobic fermentation** solves this crisis by transferring electrons from NADH back onto pyruvate (or a pyruvate derivative) solely to **regenerate $NAD^+$** so glycolysis can continue.

- **Alcohol Fermentation (Yeast & Bacteria):** 3-carbon pyruvate is first decarboxylated into 2-carbon acetaldehyde plus **$CO_2$ gas** (which makes bread rise and beer carbonate); NADH then reduces acetaldehyde into 2-carbon **ethanol**, regenerating **$NAD^+$**.
- **Lactic Acid Fermentation (Human Muscle & Yogurt Bacteria):** During intense sprinting when $O_2$ delivery lags behind demand, NADH directly reduces 3-carbon pyruvate into 3-carbon **lactate (lactic acid)** with **zero $CO_2$ released**, regenerating **$NAD^+$** so glycolysis can keep supplying 2 ATP per glucose.

**Table 3.3 · Comparative Chemiosmosis in Mitochondria vs. Chloroplasts**

| Comparison Feature | Mitochondrion (Oxidative Phosphorylation) | Chloroplast (Photophosphorylation) |
|---|---|---|
| Ultimate Source of Electrons | Organic food molecules (Glucose via NADH and $FADH_2$) | Splitting of water (Photolysis of $H_2O$ at Photosystem II) |
| Terminal Electron Acceptor | Oxygen gas ($O_2$ → reduced to $H_2O$) | $NADP^+$ (reduced to NADPH by $NADP^+$ reductase) |
| Location of ETC Complexes | Inner mitochondrial membrane (Cristae) | Thylakoid membrane |
| Compartment Where $H^+$ Accumulates (Low pH) | Intermembrane Space (IMS, pumped outward from matrix) | Thylakoid Lumen (pumped inward from stroma) |
| Direction of $H^+$ Flow Through ATP Synthase | Flows inward from Intermembrane Space into Matrix | Flows outward from Thylakoid Lumen into Stroma |

**⚠ AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: The reaction steps that convert pyruvate into lactate or ethanol during fermentation produce ZERO additional ATP! Their ONLY biological purpose is to oxidize NADH back into $NAD^+$ so cytosolic glycolysis can continue netting 2 ATP per glucose.

### ✅ CHAPTER 3 MASTERY CHECKLIST (AP EXAM READINESS)

☑ Explain how enzymes lower activation energy ($E_A$) via induced fit without changing $\Delta G$, and distinguish competitive vs. allosteric (noncompetitive) inhibition on reaction rate curves.

☑ Describe how cells couple exergonic ATP hydrolysis ($\Delta G < 0$) to endergonic cellular processes ($\Delta G > 0$).

☑ Trace electron and proton flow in the chloroplast thylakoid light reactions (PSII photolysis → cytochrome $H^+$ pump → PSI → NADPH + ATP synthase) and connect them to the 3 phases of the Calvin cycle in the stroma.

☑ Account for the inputs, outputs, cellular locations, and ATP mechanisms across Glycolysis, Pyruvate Oxidation, the Krebs Cycle, and the Mitochondrial ETC / Chemiosmosis.

☑ Explain how brown-fat uncoupling proteins (UCP1) generate heat by bypassing ATP synthase, and why fermentation must regenerate $NAD^+$ when oxygen is absent.

CHAPTER 4 · CORE CURRICULUM

**AP Exam Weighting: 10–15%**

# Unit 4: Cell Communication and Cell Cycle

Multicellular and unicellular organisms coordinate physiological activities and cell division through precise chemical signaling pathways and feedback loops. This unit examines signal reception, second-messenger transduction cascades, homeostatic negative and positive feedback, the phases of mitosis, and how cyclin–CDK checkpoints and tumor suppressors prevent uncontrolled cancerous growth.

### CHAPTER 4 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Signal Transduction Pathway: Ligand Reception → Transduction (Second Messengers & Kinase Cascade) → Cellular Response | Amplifies a single extracellular ligand binding event into millions of activated intracellular proteins |
| cAMP Second-Messenger Synthesis: ATP —(Adenylyl Cyclase)→ cAMP + $PP_i$ ; cAMP —(Phosphodiesterase)→ AMP | Activated by GPCR → G-protein (GTP) signaling and terminated by phosphodiesterase |
| Mitotic Cell Division: 1 Diploid Somatic Cell (2n) —(S-phase Replication + Mitosis)→ 2 Identical Diploid Cells (2n) | Maintains exact chromosome number and genetic identity for growth and tissue repair |

## § 4.1 Modes of Cell Signaling, Quorum Sensing & Receptor Polarity

Cells communicate across three spatial scales: (1) **direct contact** via cytoplasmic channels—**plasmodesmata** perforating plant cell walls and protein-lined **gap junctions** connecting animal cells—or juxtacrine surface antigen binding between immune cells; (2) **local signaling** via secreted chemical messengers (**ligands**) diffusing to nearby neighbors, including **paracrine** growth factors and **synaptic** neurotransmitters crossing a neural cleft; and (3) **long-distance endocrine signaling** via hormones secreted into the bloodstream (or plant vascular sap) that travel throughout the body but elicit responses *only* in target cells expressing a matching receptor protein.

Even single-celled bacteria coordinate population-wide behavior through **quorum sensing**. Each bacterium continuously secretes small signaling ligands called **autoinducers**. At low cell density, autoinducers diffuse away; once population division reaches a critical threshold density (a *quorum*), extracellular autoinducers flood back into the cells, bind cytoplasmic receptors, and activate target genes simultaneously—coordinating **biofilm formation** (such as dental plaque), virulence factor secretion, or bioluminescence.

When a ligand reaches a target cell, signaling proceeds through three universal stages: **(1) Reception** (noncovalent ligand binding induces a conformational change in the receptor), **(2) Transduction** (conversion of the signal into an amplified intracellular relay via second messengers and protein kinases), and **(3) Response** (activation of cytoplasmic enzymes or nuclear transcription factors). Crucially, the cellular location of a receptor depends on the chemical polarity of its ligand.

- **Intracellular (Cytoplasmic/Nuclear) Receptors: Nonpolar, hydrophobic lipid ligands**—specifically steroid hormones (**estrogen, testosterone, aldosterone, cortisol**) and thyroid hormone, as well as dissolved NO gas—diffuse directly through the hydrophobic phospholipid bilayer to bind intracellular receptors; the hormone–receptor complex then enters the nucleus and acts directly as a **transcription factor** to turn on target genes.
- **Cell-Surface (Transmembrane) Receptors: Polar, hydrophilic water-soluble ligands**—specifically peptide and amine hormones (**epinephrine, insulin, glucagon**) and growth factors—cannot cross the hydrophobic core of the plasma membrane and must bind transmembrane receptors (such as GPCRs, RTKs, or ligand-gated ion channels) embedded on the cell surface.

**Table 4.1 · Comparison of Hydrophobic (Steroid) vs. Hydrophilic (Peptide) Hormone Signaling**

| Signaling Feature | Nonpolar / Hydrophobic Ligands (Steroids) | Polar / Hydrophilic Ligands (Peptides & Amines) |
|---|---|---|
| Representative Examples | Estrogen, Testosterone, Cortisol, Thyroid hormone | Insulin, Glucagon, Epinephrine (Adrenaline), Growth factors |
| Ability to Cross Lipid Bilayer | Diffuses directly across the hydrophobic membrane core | Cannot cross the hydrophobic core (repelled by fatty acid tails) |
| Receptor Location | Intracellular (in cytosol or inside the nucleus) | Transmembrane cell-surface protein (GPCR, RTK, Ion Channel) |
| Transduction & Primary Response | Hormone–receptor complex binds DNA directly as a transcription factor (slower, alters gene expression) | Activates second messengers (cAMP, $Ca^{2+}$) & phosphorylation cascades (rapid enzyme activation or gene regulation) |

⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: If an exam question introduces a newly discovered hormone that is a 'small peptide' or 'water-soluble glycoprotein,' its receptor MUST be embedded in the plasma membrane; if it is 'cholesterol-derived' or 'lipid-soluble,' its receptor is inside the cytoplasm or nucleus!

## § 4.2 GPCRs, cAMP Phosphorylation Cascades & Epinephrine Case Study

During the mammalian fight-or-flight response, the adrenal glands secrete the polar hormone **epinephrine (adrenaline)** into the bloodstream. Remarkably, this single identical ligand triggers completely different responses across different organs: liver cells hydrolyze glycogen into glucose, heart muscle contracts faster, bronchial smooth muscle relaxes to dilate airways, and digestive blood vessels constrict. This tissue specificity arises because different cell types express different receptor subtypes and different intracellular relay proteins.

In a liver cell, epinephrine activates a **G-protein coupled receptor (GPCR)** pathway across four transduction steps: (1) Epinephrine binds the extracellular pocket of the GPCR, inducing a conformational change on its cytoplasmic face; (2) the activated GPCR binds a membrane-anchored **G-protein**, causing it to release inactive GDP and bind active **GTP**; (3) the GTP-bound G-protein slides laterally to bind and activate the membrane enzyme **adenylyl cyclase**; and (4) adenylyl cyclase converts cytoplasmic ATP into the small non-protein **second messenger cyclic AMP (cAMP)**.

Cyclic AMP diffuses through the cytosol to bind and activate **Protein Kinase A (PKA)**, initiating a multi-step **phosphorylation cascade**. Recall that a **protein kinase** transfers a phosphate group from ATP onto a target protein (typically activating it), whereas a **protein phosphatase** removes phosphate groups via hydrolysis (dephosphorylation) to turn the pathway off. PKA phosphorylates downstream kinases that ultimately phosphorylate and activate **glycogen phosphorylase**, releasing millions of glucose molecules into the blood.

- **Two Evolutionary Advantages of a Multi-Step Cascade:** (1) **Massive Signal Amplification**: because each activated enzyme (adenylyl cyclase, PKA, phosphorylase kinase) catalyzes hundreds of reactions before inactivation, 1 epinephrine molecule binding 1 GPCR can mobilize $10^8$ glucose molecules; (2) **Multiple Control & Integration Points** for fine-tuning the cellular response.
- **Four-Step Pathway Termination (Shut-Off):** Once danger passes, the cascade is reset: (1) epinephrine unbinds from the GPCR; (2) the G-protein's built-in **GTPase** hydrolyzes bound GTP back to inactive GDP + $P_i$; (3) **phosphodiesterase (PDE)** converts cAMP into inactive AMP; and (4) **protein phosphatases** strip phosphate groups from activated kinases.

**EXAMPLE 4.1** **Predicting Effects of Toxin & Mutation Perturbations in GPCR Signaling**

> **Problem:** Cholera toxin (secreted by Vibrio cholerae) chemically modifies the G-protein in intestinal epithelial cells so that its intrinsic GTPase enzyme can no longer hydrolyze GTP into GDP. Conversely, caffeine inhibits the enzyme phosphodiesterase (PDE). Predict the intracellular effect of each substance on cAMP concentration and downstream PKA activity.

**STEP-BY-STEP SOLUTION:**

1. Step 1: Normally, G-protein GTPase hydrolyzes GTP → GDP to turn the G-protein OFF after transient signaling.
2. Step 2: When cholera toxin blocks GTP hydrolysis, the G-protein remains locked permanently in its active GTP-bound state, continuously stimulating adenylyl cyclase to overproduce cAMP and hyper-activate PKA (which opens $Cl^-$ channels, causing severe osmotic water loss into the gut).
3. Step 3: Normally, phosphodiesterase (PDE) degrades cAMP → AMP to terminate the second-messenger signal.
4. Step 4: When caffeine inhibits PDE, existing cAMP cannot be broken down, prolonging elevated [cAMP] and sustaining PKA activation even at low hormone levels.

**Final Answer: Both cholera toxin (by locking the G-protein in the active GTP state) and caffeine (by blocking cAMP degradation via PDE) cause sustained elevation of intracellular cAMP and prolonged activation of Protein Kinase A.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Adenylyl cyclase converts ATP into cAMP (NOT G-protein or PKA!), and Protein Kinases transfer phosphate groups from ATP (NOT from cAMP!). Cyclic AMP is an allosteric activator of PKA, not a phosphate donor.

## § 4.3 Homeostasis: Negative Feedback (Insulin/Glucagon) vs. Positive Feedback

**Homeostasis** is the active maintenance of stable internal physiological variables—such as human core body temperature near 37 °C, blood pH near 7.4, and blood glucose near **90 mg/dL**—around a target **set point** despite external environmental fluctuations. The primary mechanism preserving homeostasis is **negative feedback**, in which the physiological response counteracts or reduces the initial stimulus, returning the variable back toward its set point.

The premier AP Biology model of paired antagonistic negative feedback is blood glucose regulation by the pancreas and liver. When blood glucose rises above 90 mg/dL after a carbohydrate-rich meal, pancreatic **β-cells secrete insulin** into the blood; insulin binds receptors on liver, skeletal muscle, and adipose cells, triggering insertion of GLUT4 glucose channels into the plasma membrane so cells take up glucose and the liver polymerizes glucose into glycogen, lowering blood glucose back to the set point. Conversely, when blood glucose drops below 90 mg/dL during fasting or exercise, pancreatic **α-cells secrete glucagon**, which stimulates liver cells to hydrolyze glycogen into glucose and release it into the blood.

In contrast, **positive feedback** occurs when the output of a system **amplifies the initial stimulus**, driving a physiological process further from its starting state until a climactic completion event.

- **Type 1 vs. Type 2 Diabetes Mellitus:** In **Type 1 diabetes** (autoimmune destruction of pancreatic β-cells), the signaling **ligand (insulin) is missing**, so daily insulin injections restore signaling. In **Type 2 diabetes** (>90% of cases), insulin is present in the blood, but target cells exhibit **insulin resistance** due to a defect in **receptor binding or intracellular signal transduction**.
- **Positive Feedback Example 1 — Oxytocin & Childbirth:** Pressure of the baby's head against the cervix triggers nerve impulses to the mother's brain, stimulating pituitary release of the hormone **oxytocin**; oxytocin causes stronger uterine contractions, pushing the head harder against the cervix and triggering even more oxytocin release until delivery.

- **Positive Feedback Example 2 — Ethylene & Fruit Ripening:** One ripening fruit releases gaseous **ethylene** hormone, which binds receptors on neighboring fruits, stimulating them to ripen and release even more ethylene gas.

> ⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
> AP Exam Trap: Do not think 'negative feedback = bad for the organism' and 'positive feedback = good'! Negative feedback is stabilizing (subtracts from the stimulus to maintain homeostasis), whereas positive feedback is destabilizing/amplifying (adds to the stimulus to rush a process to completion).

## § 4.4 The Eukaryotic Cell Cycle, Mitosis & Cytokinesis

The eukaryotic **cell cycle** is the orderly sequence of events by which a somatic cell duplicates its genome and divides into two genetically identical daughter cells for organismal growth, tissue repair, and asexual reproduction. A dividing cell spends roughly 90% of its cycle in **Interphase**, subdivided into **$G_1$ (First Gap)**, where the cell grows larger, synthesizes proteins, and duplicates cytoplasmic organelles; **S Phase (Synthesis)**, where nuclear DNA is replicated so each chromosome consists of two identical **sister chromatids** joined at the centromere; and **$G_2$ (Second Gap)**, where the cell completes final growth and duplicates its centrosomes.

Following $G_2$ is **M Phase**, comprising nuclear division (**mitosis**) and cytoplasmic division (**cytokinesis**). Note that terminally differentiated cells such as mature neurons and skeletal muscle fibers exit $G_1$ into a non-dividing quiescent state called **$G_0$**.

- **Prophase & Prometaphase:** Diffuse chromatin condenses into discrete duplicated chromosomes (2 sister chromatids each); the nucleolus disappears, the nuclear envelope fragments, and mitotic spindle microtubules grow from opposite centrosomes to attach to protein **kinetochores** at each centromere.
- **Metaphase:** Kinetochore microtubules tug duplicated chromosomes into a single-file plane along the cell's equator called the **metaphase plate**.
- **Anaphase:** Enzymatic cleavage of **cohesin** proteins allows sister chromatids to separate into individual chromosomes; motor proteins walk along shortening kinetochore microtubules to pull chromosomes to opposite poles while non-kinetochore microtubules push poles apart to elongate the cell.
- **Telophase & Cytokinesis:** Two nuclear envelopes reassemble around the two identical diploid chromosome sets and chromatin decondenses. In **cytokinesis**, animal cells pinch in via a contractile ring of **actin microfilaments (cleavage furrow)**, whereas rigid plant cells fuse Golgi vesicles along the equator to build a **cell plate** from the inside out.

> ⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
> AP Exam Trap: DNA replication happens ONLY during S phase of Interphase—NEVER during prophase of mitosis! Also watch chromosome vs. chromatid counting in Anaphase: the instant sister chromatids separate in anaphase, each chromatid becomes an individual chromosome, temporarily doubling the chromosome count Inside the dividing cell until cytokinesis finishes.

## § 4.5 Cell Cycle Checkpoints, Cyclin–CDK Regulation & Cancer (RAS & p53)

Progression through the cell cycle is policed by three internal quality-control checkpoints—the **$G_1$, $G_2$, and M checkpoints**—driven by a molecular clock composed of two protein families: **cyclins** and **cyclin-dependent kinases (CDKs)**. CDKs are protein kinase enzymes present at a **constant concentration** throughout the cell cycle, but they are conformationally inactive on their own. To become active, a CDK must bind a regulatory **cyclin** protein whose concentration rises and falls rhythmically across the cycle.

For example, during S and $G_2$ phases, mitotic cyclin accumulates steadily until it reaches a critical threshold and binds CDK to form active **MPF (Maturation/M-phase Promoting Factor)** at the $G_2$ checkpoint. Active MPF phosphorylates nuclear lamins and condensins to fragment the nuclear envelope and condense chromosomes, driving the cell into mitosis.

During anaphase, proteolytic degradation destroys the cyclin subunit, switching MPF off so the cell can exit mitosis (while the CDK subunit remains behind for reuse).

When mutations disrupt cell-cycle regulation, cells divide uncontrollably to form tumors (**cancer**). Normal cells balance molecular accelerators—**proto-oncogenes** (like **RAS**) that stimulate appropriate division in response to growth factors—with molecular brakes—**tumor suppressor genes** (like **p53**) that halt division or trigger apoptosis when DNA is damaged.

- **The Three Checkpoints:** (1) **$G_1$ Checkpoint (Restriction Point)** verifies cell size, nutrient reserves, external growth factors, and undamaged DNA (if blocked, cell enters $G_0$); (2) **$G_2$ Checkpoint** verifies complete, accurate S-phase DNA replication; (3) **M-Spindle Checkpoint** (between metaphase and anaphase) ensures every kinetochore is attached to spindle microtubules from opposite poles before sister chromatids separate.
- **RAS Proto-Oncogene → Oncogene (Stuck Accelerator):** Normal **RAS** is a G-protein that binds GTP and activates a kinase cascade to synthesize $G_1$ cyclins *only* when an external growth factor binds its receptor. A **gain-of-function mutation** in just one allele converts RAS into a constitutively active **oncogene** locked permanently in the GTP 'ON' state even without growth factors, driving relentless division.
- **p53 Tumor Suppressor ('Guardian of the Genome' — Broken Brakes):** When UV light or carcinogens damage DNA, activated **p53** transcription factor halts the $G_1$ checkpoint (by transcribing a CDK inhibitor, p21) to allow DNA repair, or triggers **apoptosis** if damage is irreparable. **Loss-of-function mutations** knocking out both alleles of p53 allow cells with damaged DNA to divide unchecked into malignant tumors.

**Table 4.2 · Proto-Oncogenes (Accelerators) vs. Tumor Suppressor Genes (Brakes)**

| Feature | Proto-Oncogene (e.g., RAS) | Tumor Suppressor Gene (e.g., p53, BRCA1) |
|---|---|---|
| Normal Physiological Role | Stimulates cell division ONLY when external growth factors are present | Inhibits cell division, activates DNA repair, or triggers apoptosis when DNA is damaged |
| Cancer-Causing Mutation Type | Gain-of-function (hyperactive / constitutively ON oncogene) | Loss-of-function (inactivating / nonfunctional protein) |
| Genetic Dominance at Cellular Level | Dominant (mutating just 1 allele is sufficient to drive excess division) | Recessive (both alleles must be knocked out to completely cut the brakes) |
| Automobile Analogy | Gas pedal stuck to the floor (divides with zero growth factor) | Cut brake lines (fails to stop at $G_1$ checkpoint despite DNA damage) |

**⚠️ AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: CDK concentration stays CONSTANT throughout the entire cell cycle; it is CYCLIN concentration that fluctuates (synthesized during interphase, degraded in anaphase) to turn the Cyclin–CDK complex on and off!

**✅ CHAPTER 4 MASTERY CHECKLIST (AP EXAM READINESS)**

☑ Compare direct contact, paracrine, synaptic, endocrine, and bacterial quorum-sensing signaling, and predict receptor location (intracellular vs. transmembrane) from ligand polarity.

☑ Trace the GPCR → G-protein (GTP) → Adenylyl Cyclase → cAMP → Protein Kinase A phosphorylation cascade and its 4-step termination mechanism.

☑ Contrast negative feedback (insulin and glucagon maintaining blood glucose at 90 mg/dL; Type 1 vs. Type 2 diabetes) with positive feedback (oxytocin in childbirth, ethylene in fruit ripening).

☑ Describe chromosomal and cytoskeletal events across Interphase ($G_1$, S, $G_2$), Mitosis (Prophase, Metaphase, Anaphase, Telophase), and Cytokinesis (cleavage furrow vs. cell plate).

☑ Explain how fluctuating cyclins activate constant CDKs (MPF) at cell-cycle checkpoints, and contrast gain-of-function RAS oncogene mutations with loss-of-function p53 tumor suppressor mutations.

CHAPTER 5 · CORE CURRICULUM

**AP Exam Weighting: 8–11%**

# Unit 5: Heredity

Heredity explains how genetic information is transmitted from one generation to the next while generating the variation upon which natural selection acts. This unit examines meiotic reduction division, crossing over, independent assortment, Mendelian probability laws, Chi-Square statistical analysis, non-Mendelian inheritance patterns, sex linkage, genetic recombination mapping, and environmental phenotypic plasticity.

### CHAPTER 5 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Independent Assortment Gamete Combinations = $2^n$ (where n = haploid chromosome number) | In humans (n = 23), $2^{23}$ = 8,388,608 distinct gametes per parent before crossing over |
| Probability Laws: P(A and B) = P(A) × P(B) \| P(A or B) = P(A) + P(B) | Multiplication rule for independent simultaneous events; Addition rule for mutually exclusive outcomes |
| Chi-Square Goodness-of-Fit: $\chi^2 = \sum [ (O - E)^2 / E ]$, df = n − 1 | If $\chi^2$ > critical value (p < 0.05), reject the null hypothesis ($H_0$) |
| Recombination Frequency (RF) = (Total Recombinant Offspring / Total Offspring) × 100% | 1% RF = 1 map unit (m.u.) = 1 centiMorgan (cM); maximum RF = 50% (unlinked) |

## § 5.1 Diploid vs. Haploid Life Cycles, Meiosis I & II & Genetic Variation

In sexually reproducing species, somatic body cells are **diploid (2n)**—in humans, **2n = 46**, comprising two complete sets of 23 chromosomes (one maternal set inherited from the egg and one paternal set from the sperm). Matching maternal and paternal chromosomes are **homologous chromosomes (homologs)**: they share identical length, centromere position, and gene loci, though they may carry different versions of those genes called **alleles**. By contrast, gametes (sperm and egg cells produced in the gonads) are **haploid (n = 23)**, containing a single set of unpaired chromosomes. Alternating between **meiosis** (which halves ploidy from 2n → n) and **fertilization / syngamy** (which restores diploidy from n + n → 2n) prevents chromosome number from doubling every generation.

Following a single round of S-phase DNA replication, **meiosis** executes two consecutive nuclear divisions. **Meiosis I (the reduction division)** separates homologous chromosome pairs to reduce ploidy from 2n to n: during **Prophase I**, replicated homologs pair up gene-for-gene in **synapsis** (held by the synaptonemal complex) to form four-chromatid **tetrads (bivalents)**, and non-sister chromatids exchange DNA segments at X-shaped **chiasmata** via **crossing over**; during **Metaphase I**, homologous pairs line up in *double file* along the metaphase plate; and during **Anaphase I**, homologous chromosomes are pulled to opposite poles while sister chromatids remain joined at their centromeres.

Immediately after Telophase I/Cytokinesis, the two haploid (n) cells enter **Meiosis II (the equational division)** with **zero further DNA replication**. In Metaphase II, chromosomes align in *single file* at the metaphase plate, and in Anaphase II cohesin is cleaved so sister chromatids finally separate to opposite poles, yielding **four genetically unique haploid (n) gametes**.

- **Mechanism 1 — Crossing Over (Prophase I):** Homologous recombination between **non-sister chromatids** at chiasmata creates brand-new **recombinant chromatids** combining maternal and paternal alleles on the same chromosome.
- **Mechanism 2 — Independent Assortment (Metaphase I):** Each homologous pair orients randomly left-or-right along the metaphase plate independently of every other pair, generating **$2^n$** possible chromosome combinations in gametes ($2^{23}$ ≈ 8.4 million in humans).

- **Mechanism 3 — Random Fertilization:** Any of ~8.4 million genetically distinct sperm can fertilize any of ~8.4 million distinct eggs, producing $(2^{23})^2 \approx 70$ trillion diploid zygote combinations even before crossing over.

**Table 5.1 · Comprehensive Comparison of Mitosis vs. Meiosis**

| Feature | Mitosis (Somatic Division) | Meiosis (Gametogenesis) |
|---|---|---|
| Cellular Location | Somatic (body) cells throughout the organism | Germ cells in gonads (ovaries, testes, anthers, ovules) |
| DNA Replication & Divisions | 1 S-phase replication followed by 1 nuclear division | 1 S-phase replication followed by 2 nuclear divisions (Meiosis I & II) |
| Synapsis & Crossing Over | Does NOT occur (homologs never pair up) | Occurs during Prophase I (tetrads form; crossing over at chiasmata) |
| Metaphase Alignment | Individual duplicated chromosomes line up in SINGLE file | Metaphase I: Homologous pairs line up in DOUBLE file (Metaphase II: single file) |
| Anaphase Separation | Sister chromatids separate in Anaphase | Anaphase I: Homologous chromosomes separate; Anaphase II: Sister chromatids separate |
| Daughter Cell Outcome | 2 genetically identical diploid (2n) somatic cells | 4 genetically unique haploid (n) gametes or spores |

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Crossing over occurs strictly between NON-SISTER chromatids of homologous chromosomes during Prophase I! Exchanging segments between identical sister chromatids produces zero new genetic variation.

## § 5.2 Nondisjunction, Karyotypes & Diverse Sex-Determination Systems

When chromosomes fail to separate properly during meiosis, the error is termed **nondisjunction**. If homologous chromosomes fail to separate during **Anaphase I**, *100% (all 4) of the resulting gametes are abnormal*: two gametes carry an extra chromosome (**n + 1**) and two are missing a chromosome (**n − 1**). By contrast, if sister chromatids fail to separate during **Anaphase II**, *50% (2 of 4) of the gametes are normal haploid (n)*, while one is **n + 1** and one is **n − 1**.

Fertilization of an abnormal gamete by a normal gamete produces **aneuploidy**—an abnormal chromosome number diagnosed clinically by preparing a **karyotype** (an ordered photograph of condensed metaphase chromosomes stained for banding patterns). Across the tree of life, organisms utilize diverse chromosomal and environmental mechanisms to determine biological sex.

- **Human Aneuploidies: Trisomy 21 (2n + 1 = 47)** causes Down syndrome; sex-chromosome aneuploidies include Klinefelter syndrome (47,XXY) and **Monosomy X / Turner syndrome (2n − 1 = 45,XO)**.
- **XY System (Mammals & Drosophila):** Females are homogametic (**XX**, producing only X eggs) and males are heterogametic (**XY**, producing 50% X and 50% Y sperm); in mammals, the **SRY gene** on the Y chromosome triggers testis development.
- **ZW System (Birds, Butterflies & Some Fishes):** Males are homogametic (**ZZ**) and females are heterogametic (**ZW**), so the female's ovum determines offspring sex.
- **Haplodiploidy (Bees, Wasps & Ants) & Temperature-Dependent Sex:** In hymenopterans, fertilized diploid (**2n**) eggs develop into females while unfertilized haploid (**n**) eggs develop directly into males. In many reptiles (sea turtles, alligators), egg incubation temperature during embryonic development determines sex.

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Always check whether a nondisjunction question specifies Meiosis I (0% normal gametes: two n+1, two n−1) or Meiosis II (50% normal n gametes, one n+1, one n−1)!

## § 5.3 Mendelian Genetics, Probability Laws & Chi-Square ($\chi^2$) Analysis

In the 1860s, Gregor Mendel refuted the 'blending hypothesis' of inheritance by demonstrating the **particulate model** in garden peas (*Pisum sativum*). A diploid individual carries two alleles for each gene: if identical (**PP** or **pp**), the genotype is **homozygous**; if different (**Pp**), it is **heterozygous**, where the **dominant allele** encodes a functional protein that masks the phenotypic expression of the **recessive allele**. Mendel's First Law, the **Law of Segregation**, states that the two alleles for a gene separate during Anaphase I of meiosis so each haploid gamete receives only one allele.

In a **monohybrid cross** between true-breeding parents (PP × pp), 100% of the $F_1$ hybrids are heterozygous (Pp). Self-crossing two $F_1$ heterozygotes (**Pp × Pp**) yields the classic $F_2$ **genotypic ratio of 1 PP : 2 Pp : 1 pp** and **phenotypic ratio of 3 dominant : 1 recessive**. To determine whether an organism displaying a dominant phenotype is homozygous (BB) or heterozygous (Bb), breeders perform a **test cross** with a homozygous recessive tester (**bb**): if all offspring show the dominant trait, the unknown parent is BB; if a 1:1 ratio (50% recessive) appears, the unknown parent is Bb.

Mendel's Second Law, the **Law of Independent Assortment**, applies to two genes located on *different (non-homologous) chromosomes*. In a **dihybrid cross** between two $F_1$ dihybrids (**YyRr × YyRr**), each parent produces four gamete types in equal 25% frequencies (YR, Yr, yR, yr), yielding a **9 : 3 : 3 : 1 $F_2$ phenotypic ratio** (9/16 yellow round : 3/16 yellow wrinkled : 3/16 green round : 1/16 green wrinkled). For multi-gene crosses (such as trihybrids, AaBbCc × AaBbCc), we solve each gene separately and apply the **Rule of Multiplication** and **Rule of Addition**.

- **Chi-Square ($\chi^2$) Goodness-of-Fit Test:** Tests whether observed experimental offspring counts (O) deviate significantly from expected Mendelian predictions (E). The **null hypothesis ($H_0$)** always states that there is NO statistically significant difference between observed and expected counts (any deviation is due purely to random chance). Degrees of freedom equal **df = n − 1** (where n = number of phenotypic categories).

### EXAMPLE 5.1 Solving Trihybrid Cross Probabilities Without a 64-Box Punnett Square

> **Problem:** Two parent plants with genotypes AaBbCc and AaBbcc are crossed (where A, B, and C assort independently). What fraction of the offspring is expected to have the genotype AabbCc, and what fraction will display the dominant phenotype for all three traits (A_B_C_)?

**STEP-BY-STEP SOLUTION:**

1. Step 1: Break the trihybrid cross into three independent monohybrid crosses: (1) Aa × Aa, (2) Bb × Bb, and (3) Cc × cc.
2. Step 2: For genotype AabbCc: from Aa × Aa, P(Aa) = 1/2; from Bb × Bb, P(bb) = 1/4; from Cc × cc, P(Cc) = 1/2. Multiply independent probabilities: (1/2) × (1/4) × (1/2) = 1/16.
3. Step 3: For phenotype A_B_C_: from Aa × Aa, P(A_) = 3/4; from Bb × Bb, P(B_) = 3/4; from Cc × cc, P(C_) = 1/2. Multiply: (3/4) × (3/4) × (1/2) = 9/32.

**Final Answer: P(genotype AabbCc) = 1/16; P(dominant phenotype A_B_C_) = 9/32.**

**EXAMPLE 5.2** **Chi-Square ($\chi^2$) Test for Independent Assortment vs. Genetic Linkage**

**Problem:** A geneticist performs a dihybrid test cross (BbVv × bbvv) in fruit flies and observes 400 total offspring across 4 phenotypic classes: 165 Gray-Normal, 155 Black-Vestigial, 42 Gray-Vestigial, and 38 Black-Normal. Assuming a null hypothesis ($H_0$) of independent assortment (1:1:1:1 ratio), calculate $\chi^2$, determine the degrees of freedom, and evaluate $H_0$ at $p = 0.05$ (critical value for df = 3 is 7.81).

**STEP-BY-STEP SOLUTION:**

1. Step 1: Under $H_0$ (independent assortment in a dihybrid test cross, 1:1:1:1), the expected count (E) for each of the 4 categories out of 400 offspring is $E = 400 / 4 = 100$.
2. Step 2: Compute $(O - E)^2 / E$ for each class: Class 1: $(165 - 100)^2 / 100 = 65^2 / 100 = 42.25$; Class 2: $(155 - 100)^2 / 100 = 55^2 / 100 = 30.25$; Class 3: $(42 - 100)^2 / 100 = (-58)^2 / 100 = 33.64$; Class 4: $(38 - 100)^2 / 100 = (-62)^2 / 100 = 38.44$.
3. Step 3: Sum the values: $\chi^2 = 42.25 + 30.25 + 33.64 + 38.44 = 144.58$. Degrees of freedom $df = n - 1 = 4 - 1 = 3$.
4. Step 4: Compare $\chi^2$ (144.58) to the $p = 0.05$ critical value for df = 3 (7.81). Because $144.58 > 7.81$, we REJECT the null hypothesis ($H_0$); the two genes do NOT assort independently and are linked on the same chromosome.

**Final Answer: $\chi^2 = 144.58$ (df = 3). Because $144.58 > 7.81$, we reject $H_0$ and conclude that the genes are syntenic (linked on the same chromosome).**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Degrees of freedom ($df = n - 1$) in a Chi-Square genetics problem is the number of PHENOTYPIC CATEGORIES minus 1—NEVER the number of individual organisms minus 1! And if $\chi^2$ < critical value, you FAIL TO REJECT $H_0$ (deviations are due to random chance).

## § 5.4 Non-Mendelian Inheritance, Sex Linkage & Genetic Recombination Maps

Many inheritance patterns deviate from simple Mendelian dominance. In **incomplete dominance** (e.g., snapdragon flower color), the heterozygote (**$C^RC^W$**, pink) exhibits an intermediate phenotype between the two homozygotes ($C^RC^R$ red and $C^WC^W$ white) because one functional allele synthesizes only half as much red pigment, making the $F_2$ phenotypic ratio (**1 : 2 : 1**) identical to the genotypic ratio. In **codominance** and **multiple alleles**, illustrated by human **ABO blood groups** (alleles **$I^A$, $I^B$, and i**), both $I^A$ and $I^B$ are fully and simultaneously expressed as distinct A and B surface carbohydrates on red blood cells in an **$I^AI^B$** heterozygote.

Beyond single-gene interactions, **pleiotropy** occurs when one gene affects multiple traits (such as the sickle-cell β-globin allele), **epistasis** occurs when the expression of one gene masks or modifies a second gene at a different locus (such as the *E/e* pigment-deposition gene masking the *B/b* black/brown melanin gene in Labrador retrievers, yielding a **9 : 3 : 4** $F_2$ ratio), and **polygenic inheritance** occurs when multiple genes have additive effects on a continuous quantitative trait (such as human height or skin tone, producing a bell-shaped normal curve).

Thomas Hunt Morgan discovered **X-linked inheritance** in *Drosophila* white-eyed mutants. Because males are **XY (hemizygous)**, they carry only one X chromosome and express any X-linked recessive allele (color blindness, hemophilia, Duchenne muscular dystrophy) with a single copy inherited from their mother, whereas females (XX) require two recessive copies. Furthermore, Morgan and his student Alfred Sturtevant showed that **linked genes** located on the same chromosome violate independent assortment: parental phenotypes appear in high frequency (>50%), while **recombinant offspring** arise strictly via **crossing over in Prophase I**. Because the probability of a crossover increases proportionally with physical distance along a chromosome, **1% recombination frequency equals 1 map unit (centiMorgan, cM)**.

- **Father-to-Son Rule in X-Linkage:** Because a father always passes his **Y chromosome** to his sons and his **X chromosome** to his daughters, a father can NEVER transmit an X-linked trait to his sons.
- **Maximum 50% Recombination Frequency:** Genes located ≥50 map units apart on the same chromosome exhibit a 50% recombination frequency and behave genetically just like unlinked genes on separate chromosomes.

**Table 5.2 · Summary of Non-Mendelian & Chromosomal Inheritance Patterns**

| Inheritance Pattern | Genetic Mechanism | Diagnostic Ratio / Pedigree Clue | Classic Biological Example |
|---|---|---|---|
| Incomplete Dominance | Heterozygote makes 50% functional pigment (intermediate blend) | 1 : 2 : 1 $F_2$ phenotypic & genotypic ratio | Snapdragon flowers (Red × White → Pink) |
| Codominance & Multiple Alleles | Both alleles fully expressed side-by-side on cell surface | Distinct AB phenotype in $I^AI^B$ heterozygotes | Human ABO blood group antigens ($I^A$, $I^B$, i) |
| Epistasis | One gene locus masks phenotypic expression of a second locus | Modified 9 : 3 : 4 or 9 : 7 $F_2$ dihybrid ratio | Labrador retriever coat color (B/b and E/e loci) |
| Polygenic Inheritance | Additive effect of many genes on a single quantitative trait | Continuous bell-shaped normal distribution | Human height, skin pigmentation, wheat kernel color |
| X-Linked Recessive | Gene on X chromosome; males (XY) are hemizygous | Mostly affects males; skips generations via carrier mothers; no father-to-son transmission | Red-green color blindness, Hemophilia A, white-eyed Drosophila |
| Autosomal Genetic Linkage | Two genes located close together on the same autosome | Test cross yields >50% parental and <50% recombinant offspring | Drosophila body color (b) and wing shape (vg) (17% RF) |

**EXAMPLE 5.3** **Constructing a Linear Chromosome Linkage Map from Recombination Frequencies**

> **Problem:** In Example 5.2, a Drosophila test cross (BbVv × bbvv) produced 400 total offspring: 165 Gray-Normal (parental), 155 Black-Vestigial (parental), 42 Gray-Vestigial (recombinant), and 38 Black-Normal (recombinant). Calculate the recombination frequency (RF) and map distance between genes b and vg. Then, given that a third gene cn (cinnabar eyes) has RF(b–cn) = 9% and RF(cn–vg) = 9.5%, determine the exact linear order of the three genes along the chromosome.

**STEP-BY-STEP SOLUTION:**

1. Step 1: Identify recombinant offspring in the b–vg test cross: 42 + 38 = 80 recombinants out of 400 total offspring.
2. Step 2: Calculate Recombination Frequency: RF = (80 / 400) × 100% = 20.0%, corresponding to a genetic distance of 20 map units (cM) between b and vg (or 18.5 m.u. when double crossovers are accounted for).
3. Step 3: Compare pairwise distances for the three genes b, cn, and vg: b–cn = 9.0 m.u., cn–vg = 9.5 m.u., and b–vg = 9.0 + 9.5 = 18.5 m.u.
4. Step 4: Because b–vg is the largest distance (18.5 m.u.) and equals the sum of b–cn (9.0) + cn–vg (9.5), gene cn must lie in the middle between b and vg.

**Final Answer: RF = 20% (20 map units); the linear gene order along the chromosome is b — (9.0 cM) — cn — (9.5 cM) — vg (or vg–cn–b).**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Do not confuse Incomplete Dominance (an intermediate blended phenotype like pink flowers from 1 gene) with Polygenic Inheritance (a continuous bell-curve gradient like human height controlled by 3+ separate genes)!

## § 5.5 Non-Nuclear (Maternal) Inheritance & Phenotypic Plasticity

Not all eukaryotic genes reside on nuclear chromosomes. Because **mitochondria and chloroplasts** evolved from endosymbiotic bacteria, they retain their own circular DNA genomes (**mtDNA and cpDNA**) encoding essential subunits for oxidative phosphorylation and photosynthesis. Because these cytoplasmic organelles do notsegregate on the meiotic spindle, organelle-encoded traits exhibit strict **maternal inheritance**: during fertilization, the large egg contributes virtually 100% of the zygote's cytoplasm and mitochondria, whereas the tiny sperm contributes only a haploid nucleus.

Finally, an organism's observable phenotype is not rigidly fixed by genotype alone; rather, phenotype emerges from the interaction of genotype with the environment. The capacity of a single genotype to produce different phenotypes in response to environmental cues—without any change in DNA sequence—is termed **phenotypic plasticity**.

- **Pedigree Signature of Mitochondrial Inheritance:** An affected mother passes a mitochondrial DNA disorder (such as Leber hereditary optic neuropathy or mitochondrial myopathy) to **100% of her offspring (both sons and daughters)**, whereas an affected father passes it to **0% of his offspring**.
- **Soil pH & Hydrangea Flower Color:** Cloned *Hydrangea* plants with the exact same genotype produce **blue flowers in acidic soil** (where $Al^{3+}$ ions are soluble and absorbed by roots to complex with anthocyanin pigments) but produce **pink flowers in alkaline soil** (where aluminum is insoluble).
- **Temperature-Sensitive Tyrosinase in Himalayan Rabbits & Siamese Cats:** A homozygous allele encodes a heat-sensitive version of the melanin-synthesizing enzyme **tyrosinase** that folds and produces dark black fur *only* in cool extremities (ears, nose, paws, tail) while denaturing into an inactive conformation across the warm core of the body.
- **UV Light & Human Melanin / Arctic Fox Coat Color:** Increased UV exposure stimulates melanocyte transcription of melanin genes (tanning), and seasonal photoperiod/temperature shifts regulate pigment enzymes in arctic animals.

> ⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
>
> AP Exam Trap: When environmental changes alter phenotype via phenotypic plasticity (like soil pH changing hydrangea color or ice packs darkening rabbit fur), the underlying DNA nucleotide sequence is 100% UNCHANGED—only enzyme activity or gene transcription is modulated!

> ✅ **CHAPTER 5 MASTERY CHECKLIST (AP EXAM READINESS)**
>
> ☑ Contrast chromosome behavior in Mitosis vs. Meiosis I & II, and explain how Prophase I crossing over, Metaphase I independent assortment ($2^n$), and random fertilization generate genetic variation.
>
> ☑ Predict gamete ploidies resulting from nondisjunction in Anaphase I vs. Anaphase II, and compare XY, ZW, haplodiploid, and temperature-dependent sex determination.
>
> ☑ Apply the Multiplication and Addition probability rules to multi-gene crosses and execute a Chi-Square ($\chi^2$) goodness-of-fit test with df = n − 1.
>
> ☑ Distinguish incomplete dominance, codominance/multiple alleles (ABO), pleiotropy, epistasis, polygenic inheritance, X-linked recessive pedigrees, and autosomal linkage mapping (1% RF = 1 cM).
>
> ☑ Identify maternal mitochondrial/chloroplast inheritance on pedigrees and explain how environmental factors drive phenotypic plasticity without altering DNA sequence.

CHAPTER 6 · CORE CURRICULUM

**AP Exam Weighting: 12–16%**

# Unit 6: Gene Expression and Regulation

Molecular genetics elucidates how hereditary information encoded in DNA is replicated with high fidelity, transcribed into RNA, spliced and translated into functional polypeptides, and dynamically regulated in response to cellular and environmental signals. This unit also covers mutations, horizontal gene transfer, and modern molecular biotechnology including PCR, gel electrophoresis, and CRISPR-Cas9.

### CHAPTER 6 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Central Dogma of Molecular Biology: DNA —(Transcription)→ mRNA —(Translation)→ Polypeptide | Retroviruses (HIV) reverse transcription: Viral RNA —(Reverse Transcriptase)→ cDNA → Host DNA |
| Universal Synthesis Directionality: 5' → 3' (Nucleophilic attack by 3'-OH on incoming 5'-dNTP/NTP) | Applies to all DNA Polymerases (leading & lagging strands) and RNA Polymerases |
| PCR Exponential Amplification: Total DNA Copies = $2^n$ (after n thermal cycles) | 30 cycles of Denaturation (95 °C) → Annealing (55 °C) → Taq Extension (72 °C) yields $>10^9$ copies |

## § 6.1 Classic DNA Discovery Experiments & Semiconservative DNA Replication

Three landmark 20th-century experiments established that **DNA—not protein—is the universal molecule of heredity**. In 1928, **Frederick Griffith** discovered *transformation* when heat-killed pathogenic S-strain *Streptococcus pneumoniae* transformed harmless living R-strain bacteria into virulent cells. In 1944, **Oswald Avery, Colin MacLeod, and Maclyn McCarty** treated heat-killed S-strain extracts with proteases, RNase, or DNase, proving that transformation halted *only* when DNase destroyed DNA. In 1952, **Alfred Hershey and Martha Chase** used T2 bacteriophages labeled with radioactive **$^{35}$S in proteins** (cysteine/methionine) or **$^{32}$P in DNA** (sugar–phosphate backbone) to infect *E. coli*; after blending and centrifugation, $^{35}$S remained outside in the liquid supernatant while **$^{32}$P entered the bacterial pellet**, sealing the proof that DNA carries genetic instructions.

Building on **Rosalind Franklin's** X-ray diffraction crystallography and Erwin Chargaff's base ratios (%A = %T, %G = %C), **James Watson and Francis Crick** (1953) deduced DNA's double-helix structure: two antiparallel sugar–phosphate backbones (**5' → 3'** and **3' → 5'**) with a uniform **2 nm diameter** maintained by pairing a double-ring **purine (A, G)** with a single-ring **pyrimidine (T, C)**—specifically **A=T (2 H-bonds)** and **G≡C (3 H-bonds**, giving high-GC DNA a higher thermal melting temperature).

In 1958, **Matthew Meselson and Franklin Stahl** grew *E. coli* in heavy nitrogen ($^{15}$N) and shifted them to light nitrogen ($^{14}$N), proving that DNA replication is **semiconservative**: each parental strand separates and serves as a direct template to build a new complementary strand, so every daughter helix contains one old strand and one newly synthesized strand. Replication initiates at **origins of replication** (a single origin on a circular prokaryotic chromosome vs. hundreds of replication bubbles on linear eukaryotic chromosomes) and proceeds bidirectionally at each **replication fork**.

- **Helicase, SSBPs & Topoisomerase: Helicase** unwinds the double helix at the replication fork by breaking hydrogen bonds between bases; **single-strand binding proteins (SSBPs)** prevent template strands from re-annealing; and **topoisomerase (gyrase)** relieves torsional supercoiling ahead of the fork.
- **Primase & The 3'–OH Requirement:** Because **DNA Polymerase III** cannot initiate a strand de novo and can ONLY add nucleotides to an existing free **3' –OH group** in the **5' → 3' direction**, the RNA polymerase enzyme **primase** must first lay down a short complementary **RNA primer**.

- **Leading vs. Lagging Strand (Okazaki Fragments):** Along the **3' → 5' template strand**, DNA Pol III synthesizes the **leading strand** continuously (5' → 3') toward the opening fork. Along the antiparallel **5' → 3' template strand**, DNA Pol III must synthesize the **lagging strand** discontinuously (5' → 3') away from the fork as short **Okazaki fragments**.
- **DNA Polymerase I & DNA Ligase: DNA Polymerase I** excises the RNA primers and replaces them with DNA nucleotides; finally, **DNA ligase** seals the remaining nicks in the sugar–phosphate backbone by catalyzing covalent **phosphodiester bonds**.

**Table 6.1 · Essential Enzymes & Proteins of the DNA Replication Fork**

| Replication Enzyme / Protein | Specific Biochemical Function at the Fork | Effect if Mutated / Inhibited |
|---|---|---|
| Topoisomerase (Gyrase) | Cuts and rejoins DNA ahead of fork to relieve supercoiling tension | Torsional strain builds up ahead of fork, halting unwinding |
| Helicase | Unwinds double helix at replication fork by breaking H-bonds between bases | Double helix cannot separate into single-stranded templates |
| Single-Strand Binding Proteins | Coat separated template strands to prevent re-pairing or nuclease cleavage | Template strands snap back together into double-stranded DNA |
| Primase | Synthesizes short complementary RNA primer providing a free 3'-OH group | DNA Polymerase III cannot initiate synthesis on either strand |
| DNA Polymerase III | Elongates new DNA strands 5' → 3' by adding dNTPs to 3'-OH; proofreads | No new leading or lagging DNA strands are synthesized |
| DNA Polymerase I | Removes RNA primers (5' → 3' exonuclease) and replaces them with DNA | RNA segments remain embedded in daughter strands |
| DNA Ligase | Seals nicks in sugar–phosphate backbone via covalent phosphodiester bonds | Okazaki fragments on lagging strand remain unjoined fragments |

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: DNA Polymerase III synthesizes BOTH the leading strand AND the lagging strand strictly in the 5' → 3' direction! Never write that the lagging strand is synthesized 3' → 5'—it is synthesized 5' → 3' in short discontinuous Okazaki fragments moving away from the replication fork.

## § 6.2 Transcription & Eukaryotic Post-Transcriptional mRNA Processing

According to the **Central Dogma**, genetic information flows from DNA → RNA via **transcription** and from RNA → protein via **translation** (with a notable exception in retroviruses like **HIV**, which use the enzyme **reverse transcriptase** to copy their single-stranded RNA genome backward into complementary DNA that integrates into the host genome). Protein synthesis requires three collaborating RNA classes: **messenger RNA (mRNA)** carrying three-base **codons**, **transfer RNA (tRNA)** folding into a cloverleaf with a complementary **anticodon** and a 3' amino acid attachment site, and **ribosomal RNA (rRNA)** forming the catalytic core (ribozyme) of the ribosome.

During **transcription initiation**, **RNA polymerase** binds to an upstream control sequence called the **promoter** (in eukaryotes, general **transcription factors** must first bind the **TATA box** within the promoter to recruit RNA Polymerase II). Unlike DNA polymerase, RNA polymerase requires **no primer** and unwinds the DNA strands itself. During **elongation**, RNA polymerase reads *only* the **3' → 5' template strand** (also called the noncoding, minus, or antisense strand) and synthesizes a complementary single-stranded RNA molecule in the **5' → 3' direction**, pairing **Uracil (U)** opposite Adenine (A). Consequently, the new 5' → 3' RNA transcript has the exact same sequence as the opposite **5' → 3' coding (sense) DNA strand**, except with U in place of T.

In prokaryotes, which lack a nuclear envelope, ribosomes attach to the mRNA and begin translation in the cytoplasm *simultaneously while transcription is still occurring* (coupled transcription–translation). In eukaryotes, the primary transcript

(**pre-mRNA**) must undergo three **post-transcriptional modifications** inside the nucleus before export through nuclear pores.

- **1. 5' Methyl-Guanosine (5' GTP) Cap:** Added to the 5' end of pre-mRNA; protects the transcript from hydrolytic exonucleases, aids nuclear pore export, and serves as the recognition site for the small ribosomal subunit.
- **2. 3' Poly-A Tail (50–250 Adenines):** Added to the 3' end; protects mRNA from cytosolic degradation (longer poly-A tails increase mRNA lifespan and total protein output) and facilitates nuclear export.
- **3. RNA Splicing & Alternative Splicing (Spliceosome):** Eukaryotic genes contain noncoding intervening sequences called **introns** interspersed between coding sequences called **exons** (**EX**ons are **EX**pressed). The **spliceosome** (a complex of snRNPs and proteins) excises introns and splices exons together. Through **alternative RNA splicing**, different subsets of exons can be joined from the same pre-mRNA in different tissues, enabling **one eukaryotic gene to encode multiple distinct protein isoforms**.

**EXAMPLE 6.1** **Decoding Template vs. Coding DNA Strands, mRNA Codons & tRNA Anticodons**

> **Problem:** A short segment of a eukaryotic gene has the following double-stranded DNA sequence: Strand X: 3' – T A C G G C A T T A C T – 5' Strand Y: 5' – A T G C C G T A A T G A – 3' Given that Strand X serves as the transcription template strand, write the 5' → 3' mRNA sequence, the 3' → 5' tRNA anticodons, and the resulting polypeptide sequence (using standard codons: AUG = Met/Start, CCG = Pro, UAA = Stop, UGA = Stop).

**STEP-BY-STEP SOLUTION:**

1. Step 1: RNA Polymerase reads the 3' → 5' template strand (Strand X) and synthesizes mRNA in the 5' → 3' direction using A→U, T→A, G→C, C→G.
2. Step 2: Transcribing Strand X (3'–TAC GGC ATT ACT–5') yields mRNA: 5' – A U G C C G U A A U G A – 3'. (Notice this matches Coding Strand Y 5'→3' with U replacing T!).
3. Step 3: Translate the mRNA codons 5' → 3': Codon 1 = AUG (Methionine, Start); Codon 2 = CCG (Proline); Codon 3 = UAA (Stop codon — release factor binds, terminating translation before UGA is reached).
4. Step 4: Find the complementary 3' → 5' tRNA anticodons for the translated codons: for mRNA 5'-AUG-3', tRNA anticodon is 3'-UAC-5'; for mRNA 5'-CCG-3', tRNA anticodon is 3'-GGC-5' (stop codon UAA has no tRNA).

**Final Answer: mRNA: 5'–AUG CCG UAA UGA–3'; Polypeptide: N-Met–Pro-C (2 amino acids; UAA terminates translation); tRNA anticodons: 3'–UAC–5' and 3'–GGC–5'.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Introns and exons are transcribed into pre-mRNA and spliced by the spliceosome BEFORE translation; do not confuse promoters/enhancers (untranscribed regulatory DNA sequences) with exons/introns (transcribed RNA regions)!

## § 6.3 Translation at the Ribosome (A–P–E Sites) & Point vs. Frameshift Mutations

During **translation**, the ribosome decodes the mRNA nucleotide sequence in non-overlapping three-base triplets called **codons** in the **5' → 3' direction**. With 4 RNA bases read 3 at a time, there are **$4^3$ = 64 codons**: **AUG** is the universal start codon (specifying Methionine and establishing the reading frame), 60 more codons specify amino acids, and three codons (**UAA, UAG, UGA**) are **stop codons** that bind a protein release factor. The genetic code exhibits two vital properties: (1) it is **redundant (degenerate)**—multiple codons specify the same amino acid due to 3rd-base wobble, buffering against silent mutations—and (2) it is **nearly universal** across all living domains, allowing human insulin genes to be expressed in transgenic bacteria.

In the cytosol, **aminoacyl-tRNA synthetase** enzymes hydrolyze ATP to covalently attach each specific amino acid to the 3' end of its matching tRNA. The ribosome coordinates translation across three tRNA binding pockets—the **A site (Aminoacyl)**, **P site (Peptidyl)**, and **E site (Exit)**—through three stages: (1) **Initiation**, where the small subunit binds the 5' cap/leader, scans to the **AUG** start codon, pairs initiator tRNA (Met) via its 3'-UAC-5' anticodon, and recruits the large

subunit with Met-tRNA in the **P site**; (2) **Elongation** (driven by GTP hydrolysis), where an incoming charged tRNA binds the **A site**, large-subunit **rRNA (a ribozyme)** catalyzes peptide bond formation by transferring the growing polypeptide from the P-site tRNA onto the A-site amino acid, and the ribosome translocates one codon 5' → 3' (shifting the empty tRNA to the **E site** to exit); and (3) **Termination**, where a stop codon (UAA, UAG, UGA) enters the A site and binds a **release factor** that hydrolyzes the finished polypeptide free.

**Mutations**—permanent changes in DNA nucleotide sequence—are the ultimate source of all new alleles and evolutionary variation.

- **Silent Point Substitution:** Changes a nucleotide (usually in the 3rd codon position) to a synonymous codon that specifies the **exact same amino acid** due to genetic code redundancy; has zero effect on protein structure.
- **Missense Point Substitution:** Changes one codon into a codon specifying a **different amino acid** (e.g., hydrophilic Glu → hydrophobic Val in sickle-cell hemoglobin); effect depends on whether the R-group chemical property changes.
- **Nonsense Point Substitution:** Changes an amino-acid codon into a **premature stop codon (UAA, UAG, UGA)**, producing a truncated, almost always nonfunctional polypeptide.
- **Frameshift Mutation (Insertion or Deletion):** Inserting or deleting a number of nucleotides **not divisible by 3** shifts the triplet reading frame for *every single downstream codon*, scrambling the amino acid sequence and usually introducing an early stop codon.

> ⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
>
> AP Exam Trap: Mutations in DNA are ALWAYS random—organisms cannot mutate purposefully to adapt! Also remember that somatic mutations (in skin or liver cells) are NOT passed to sexually produced offspring; only germline mutations (in gametes) are heritable.

## § 6.4 Gene Regulation: Bacterial Operons (lac vs. trp) & Eukaryotic Epigenetics

Cells conserve ATP and amino acids by expressing genes only when needed. In bacteria, genes encoding enzymes for a single metabolic pathway are clustered together under the control of one **promoter** and one **operator** (an on/off DNA switch site) and transcribed together as a single polycistronic mRNA—a functional unit called an **operon** (discovered by François Jacob and Jacques Monod). Upstream, a separate **regulatory gene** constitutively encodes an allosteric **repressor protein** that can bind the operator to physically block RNA polymerase.

In multicellular eukaryotes, every somatic cell descends by mitosis from a single zygote and contains the **exact same DNA genome**; a liver cell differs from a neuron strictly because of **differential gene expression** driven by cell-type-specific combinations of transcription factors. Eukaryotic expression is regulated at multiple levels: (1) **epigenetic chromatin remodeling** (histone acetylation vs. DNA methylation), (2) **transcriptional control** via distal **enhancers** and **activators** (which bend DNA via mediator proteins to recruit RNA Pol II at the promoter), (3) **post-transcriptional alternative splicing**, (4) **translational RNA interference** via small noncoding **microRNAs (miRNAs)** and **siRNAs** that bind complementary mRNAs to degrade them or block ribosome translation, and (5) **post-translational** ubiquitin tagging for proteasome degradation.

- **Inducible Catabolic Operon — The E. coli lac Operon (Normally OFF):** Encodes enzymes (β-galactosidase/lactase) that break down lactose. When lactose is **absent**, the *lac* repressor is synthesized in an **active conformation** that binds the operator and blocks transcription. When lactose is **present**, its isomer **allolactose acts as an inducer**: it binds allosterically to the repressor, inactivating it so it releases the operator and RNA polymerase transcribes the lactose-digesting genes (further boosted by high cAMP–CAP when glucose is scarce).
- **Repressible Anabolic Operon — The E. coli trp Operon (Normally ON):** Encodes enzymes that synthesize the amino acid tryptophan. When tryptophan is **absent**, the *trp* repressor is synthesized in an **inactive conformation**, so RNA polymerase continuously transcribes the operon. When tryptophan accumulates to **high levels**, **tryptophan itself acts as a corepressor**, binding the repressor to switch it into its active operator-binding shape and turning transcription **OFF**.

- **Histone Acetylation vs. DNA Methylation:** Adding **acetyl groups** to positively charged histone tails neutralizes their positive charge, loosening DNA–histone packing into open **euchromatin** to turn transcription **ON**. Conversely, adding **methyl groups** directly to cytosine bases (**DNA methylation**) or removing acetyl groups condenses chromatin into tightly packed **heterochromatin**, silencing transcription **OFF**.

**Table 6.2 · Contrast Between the Inducible lac Operon and Repressible trp Operon in E. coli**

| Operon Feature | lac Operon (Inducible) | trp Operon (Repressible) |
|---|---|---|
| Metabolic Pathway Type | Catabolic (breaks down environmental lactose sugar) | Anabolic (synthesizes essential amino acid tryptophan) |
| Default Baseline State | Normally OFF (active repressor bound to operator) | Normally ON (repressor synthesized in inactive form) |
| Allosteric Effector Molecule | Allolactose (isomer of lactose) acts as an INDUCER | Tryptophan itself acts as a COREPRESSOR |
| Effect of Ligand Binding Repressor | Inactivates repressor → falls off operator → turns operon ON | Activates repressor → binds operator → turns operon OFF |
| Biological Logic for the Cell | Only waste ATP making lactase when lactose is available to eat | Stop wasting ATP making tryptophan when external supply is already high |

> ⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
> AP Exam Trap: If a mutation disables the regulatory gene ($lacI^-$) or mutates the operator DNA sequence so the repressor cannot bind, the lac operon becomes CONSTITUTIVELY ON (transcribed continuously even when lactose is absent)!

## § 6.5 Horizontal Gene Transfer & Modern Biotechnology (Cloning, PCR, Gel, CRISPR)

Although prokaryotes reproduce asexually by binary fission, they rapidly acquire novel genetic variation (such as multidrug antibiotic resistance) via three mechanisms of **horizontal gene transfer**: (1) **Transformation**, uptake of naked foreign DNA or plasmids from the environment; (2) **Transduction**, accidental transfer of bacterial DNA from one host cell to another by a bacteriophage virus; and (3) **Conjugation**, direct one-way transfer of a plasmid (such as an F-plasmid or resistance R-plasmid) through a hollow protein **sex pilus**.

Modern molecular biotechnology harnesses bacterial and viral enzymes to manipulate DNA with pinpoint precision.

- **Recombinant Plasmid Cloning & Bacterial Transformation:** To produce human insulin in *E. coli*, scientists cut both a bacterial plasmid vector (carrying an **ampicillin resistance gene, $amp^R$**, and a reporter gene like **GFP**) and human insulin cDNA (lacking introns!) with the **exact same restriction endonuclease** to generate complementary single-stranded **sticky ends**, seal them with **DNA ligase**, and heat-shock transform bacteria. Only transformed bacteria survive on **ampicillin agar plates**.
- **Polymerase Chain Reaction (PCR):** Amplifies a specific target DNA segment billions of times in vitro across a 3-step thermal cycle: (1) **Denaturation (95 °C)** breaks H-bonds to separate DNA strands; (2) **Annealing (55 °C)** allows forward and reverse DNA primers to base-pair flanking the target; and (3) **Extension (72 °C)** uses heat-stable **Taq DNA polymerase** (from thermophilic bacteria) to synthesize new DNA.
- **Agarose Gel Electrophoresis:** Separates DNA fragments by length. Because phosphate groups give DNA a uniform **negative charge**, samples loaded into wells near the **negative cathode (−)** migrate through the porous gel matrix toward the **positive anode (+)**; **shorter DNA fragments** snake through pores faster and travel **farther down the gel** than longer fragments.
- **CRISPR-Cas9 Genome Editing:** Adapted from a bacterial adaptive immune system against phages, a synthetic single **guide RNA (sgRNA)** directs the **Cas9 endonuclease** to base-pair with any matching 20-bp target genomic sequence (adjacent to a PAM sequence) and make a double-stranded DNA cut to knock out or edit a gene.

### EXAMPLE 6.2 Interpreting Restriction Digests & Plasmid vs. Linear DNA on Gel Electrophoresis

**Problem:** A scientist digests two 10,000-bp (10 kb) DNA molecules—Molecule A (a circular bacterial plasmid) and Molecule B (a linear eukaryotic DNA fragment)—with the restriction enzyme EcoRI. Each DNA molecule contains exactly TWO EcoRI recognition sites located 3 kb apart along one side. Predict the number and sizes (in kb) of DNA bands observed for Molecule A and Molecule B after agarose gel electrophoresis, and identify which band migrates farthest toward the positive (+) electrode.

**STEP-BY-STEP SOLUTION:**

1. Step 1: Recall geometry: cutting a CLOSED CIRCLE (plasmid) n times yields n fragments; cutting a LINEAR strand n times yields (n + 1) fragments.
2. Step 2: For circular Plasmid A (10 kb total) cut at 2 sites separated by 3 kb: 2 cuts produce 2 bands—one fragment of 3 kb and the remaining arc of 10 − 3 = 7 kb.
3. Step 3: For linear DNA Molecule B (10 kb total) cut at 2 internal sites separated by 3 kb (say at positions 2 kb and 5 kb): 2 cuts produce 2 + 1 = 3 bands (e.g., 2 kb, 3 kb, and 5 kb totaling 10 kb).
4. Step 4: Because DNA is negatively charged ($PO_4^{3-}$ backbone) and shorter fragments experience less friction through agarose pores, the smallest fragment (2 kb from Molecule B, or 3 kb from Plasmid A) migrates farthest toward the positive anode (+).

**Final Answer: Circular Plasmid A yields 2 bands (3 kb and 7 kb); linear DNA B yields 3 bands (e.g., 2 kb, 3 kb, and 5 kb). The shortest fragment migrates fastest and farthest toward the positive (+) pole.**

### ⚠ AP EXAM TRAP & FRQ SCORING GUIDELINE

AP Exam Trap: When cloning a human eukaryotic gene into bacteria to manufacture a protein like insulin, you MUST insert reverse-transcribed cDNA (made from mature spliced mRNA) rather than genomic DNA—because bacteria lack spliceosomes and cannot remove eukaryotic introns!

### ✅ CHAPTER 6 MASTERY CHECKLIST (AP EXAM READINESS)

☑ Summarize how Griffith, Avery–MacLeod–McCarty, and Hershey–Chase ($^{35}S$ vs. $^{32}P$) proved DNA is the genetic material, and how Meselson–Stahl ($^{15}N/^{14}N$) proved semiconservative replication.

☑ State the exact role of helicase, topoisomerase, SSBPs, primase, DNA Pol III, DNA Pol I, and DNA ligase on the leading and lagging (Okazaki) strands.

☑ Trace eukaryotic transcription (promoter/TATA box, 3' → 5' template reading) and nuclear pre-mRNA processing (5' GTP cap, 3' poly-A tail, alternative splicing of exons).

☑ Decode mRNA codons at the ribosome (A–P–E sites) and predict the effects of silent, missense, nonsense, and frameshift mutations on protein structure.

☑ Contrast inducible (lac) vs. repressible (trp) bacterial operons, eukaryotic histone acetylation vs. DNA methylation, and analyze PCR, gel electrophoresis, plasmid transformation, and CRISPR-Cas9 experiments.

CHAPTER 7 · CORE CURRICULUM

**AP Exam Weighting: 13–20%**

# Unit 7: Natural Selection

Evolution—descent with modification, or change in the allele frequencies of a population over generations—is the overarching unifying theme of biology and the highest-weighted unit on the AP Exam. This unit covers Darwinian natural selection, population genetics (Hardy–Weinberg equilibrium and genetic drift), anatomical and molecular evidence for common ancestry, phylogenetic cladistics, reproductive isolation, speciation, and the RNA World origin of life.

### CHAPTER 7 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Hardy–Weinberg Allele Frequencies: $p + q = 1$ | p = frequency of dominant allele (A); q = frequency of recessive allele (a) |
| Hardy–Weinberg Genotype Frequencies: $p^2 + 2pq + q^2 = 1$ | $p^2$ = homozygous dominant (AA), 2pq = heterozygous carriers (Aa), $q^2$ = homozygous recessive (aa) |
| Always Solve From Recessive Phenotype First: $q = \sqrt{(q^2)} \rightarrow p = 1 - q \rightarrow 2pq$ | Never take the square root of the dominant phenotype frequency (which equals $p^2$ + 2pq)! |

## § 7.1 Darwinian Natural Selection, Evolutionary Fitness & Modes of Selection

Charles Darwin's mechanism of **natural selection** operates through four logical steps: (1) **Overproduction of offspring** creates competition for limited environmental resources (food, water, shelter, mates); (2) **Heritable phenotypic variation** exists among individuals in a population due to pre-existing random mutations and sexual recombination; (3) **Differential survival and reproduction** ensures that individuals whose inherited traits best suit the local environment survive and leave more offspring; and (4) **Adaptation** occurs over generations as advantageous alleles increase in frequency in the population while unfavorable alleles decline.

On the AP Biology Exam, **biological fitness** is defined strictly as an individual's **relative reproductive success**—its ability to survive and contribute fertile offspring to the next generation in a specific environment. Because selective pressures shift across space and time, fitness depends entirely on environmental context: in the American Southwest, light-furred **rock pocket mice** have high fitness on light sandy granite, whereas a random *Mc1r* gene mutation producing dark melanic fur confers high fitness on dark basalt lava flows (just as soot-darkened birch trees during the Industrial Revolution favored dark **peppered moths** over light speckled moths).

When natural selection acts on a continuous polygenic trait, it reshapes the population's bell curve in one of three modes: **directional, stabilizing, or disruptive selection**. Humans also drive evolution via **artificial selection** (selective breeding of wild mustard *Brassica oleracea* into cabbage, broccoli, kale, and Brussels sprouts, or wolves into domestic dog breeds), while **sexual selection** favors traits that maximize mating success via intrasexual male combat or intersexual female mate choice.

- **Golden Rule of Evolution: Individuals do NOT evolve**—natural selection acts on individual phenotypes, but only **populations evolve** as allele frequencies change across generations!
- **Pre-Existing Random Mutations (Antibiotic Resistance):** Antibiotics, pesticides, or herbicides NEVER 'cause' resistance mutations to appear on demand. Rather, a rare random mutation or R-plasmid is **already present** in a few individuals *before* the drug is applied; the drug kills 99.9% of susceptible cells, allowing the resistant survivors to reproduce without competition.
- **Three Modes of Natural Selection:** (1) **Directional Selection** shifts the mean toward one extreme (e.g., deeper Galápagos finch beaks during drought); (2) **Stabilizing Selection** favors intermediate phenotypes and culls both

extremes (e.g., human birth weight ~7 lbs); (3) **Disruptive (Diversifying) Selection** favors both extremes over intermediates, splitting the curve into a bimodal distribution (e.g., small vs. large beaks in African seedcrackers).

> ⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
>
> AP Exam Trap: Automatically eliminate any answer choice claiming an organism 'mutated in order to survive,' 'learned to adapt its genes,' or 'needed to evolve resistance.' Selection only edits variation that was ALREADY generated by random mutation!

## § 7.2 Population Genetics, Hardy–Weinberg Equilibrium & Genetic Drift

**Population genetics** defines microevolution as a change in allele frequencies within a population's **gene pool** over generations. As a baseline null model, **Hardy–Weinberg Equilibrium (HWE)** describes a theoretical *non-evolving population* in which allele frequencies (**$p + q = 1$**) and genotype frequencies (**$p^2 + 2pq + q^2 = 1$**) remain constant from generation to generation.

For a population to remain in Hardy–Weinberg Equilibrium, **five strict conditions** must be met simultaneously: (1) **No natural selection** (all genotypes have equal fitness), (2) **No mutations**, (3) **No gene flow** (no migration of individuals, pollen, or gametes in or out), (4) **Extremely large population size** (no random genetic drift), and (5) **Random mating** (no sexual selection or inbreeding). If allele frequencies shift over time, at least one condition is violated and evolution is occurring.

In small populations, chance sampling error causes random, non-adaptive fluctuations in allele frequencies called **genetic drift**, which reduces genetic variation and can fix harmful alleles. Meanwhile, **gene flow** (migration between populations) homogenizes allele frequencies between neighboring populations, and **heterozygote advantage** (balancing selection) maintains harmful recessive alleles in a gene pool—most famously the **sickle-cell allele (HbS)** in equatorial Africa, where **HbA/HbS heterozygotes** enjoy the highest fitness because they neither suffer fatal sickle-cell anemia (HbS/HbS) nor die from *Plasmodium falciparum* malaria (HbA/HbA).

- **The Bottleneck Effect (Genetic Drift):** A sudden catastrophe (volcanic eruption, severe overhunting as in northern elephant seals or cheetahs) randomly slashes a large population down to a tiny surviving remnant whose allele frequencies no longer reflect the original gene pool.
- **The Founder Effect (Genetic Drift):** A small handful of individuals colonizes a new isolated habitat (e.g., Galápagos finches blown to an island, or the Amish population in Pennsylvania with high Ellis–van Creveld polydactyly frequency), carrying an unrepresentative sample of alleles.

**EXAMPLE 7.1** **Complete Hardy–Weinberg Equilibrium Calculation (PKU Recessive Disorder)**

**Problem:** Phenylketonuria (PKU) is an autosomal recessive metabolic disorder (aa). In a population of 10,000 newborns assumed to be in Hardy–Weinberg equilibrium, 16 babies are born with PKU. Calculate the frequencies of the recessive allele (q) and dominant allele (p), the frequencies of all three genotypes ($p^2$, 2pq, $q^2$), and the exact number of heterozygous carrier individuals in this population of 10,000.

**STEP-BY-STEP SOLUTION:**

1. Step 1: ALWAYS start with the homozygous recessive phenotype (aa = $q^2$): 16 out of 10,000 individuals have PKU → $q^2$ = 16 / 10,000 = 0.0016.
2. Step 2: Take the square root of $q^2$ to find the recessive allele frequency q: q = √(0.0016) = 0.04 (4%).
3. Step 3: Use p + q = 1 to find the dominant allele frequency p: p = 1 − 0.04 = 0.96 (96%).
4. Step 4: Calculate the remaining genotype frequencies: Homozygous dominant (AA) = $p^2$ = $(0.96)^2$ = 0.9216 (92.16%); Heterozygous carriers (Aa) = 2pq = 2(0.96)(0.04) = 0.0768 (7.68%).
5. Step 5: Multiply 2pq by the total population size N = 10,000 to find the number of carriers: 0.0768 × 10,000 = 768 heterozygous carriers.

**Final Answer: q = 0.04, p = 0.96; $q^2$ (aa) = 0.0016, $p^2$ (AA) = 0.9216, 2pq (Aa) = 0.0768; there are 768 heterozygous carriers in the population.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: If a problem gives you the percentage of individuals with the DOMINANT phenotype (say 84%), that number equals ($p^2$ + 2pq), NOT $p^2$! Never take the square root of 0.84; instead, subtract from 1 first to get $q^2$ = 1 − 0.84 = 0.16, then take √(0.16) to get q = 0.4!

## § 7.3 Evidence for Evolution: Homologous vs. Analogous Structures & Molecular Clocks

Multiple independent lines of paleontological, biogeographical, anatomical, embryological, and molecular evidence confirm descent with modification from common ancestors. The **fossil record** (dated via relative rock stratigraphy and absolute **radiometric isotope decay** such as $^{14}C$ and $^{238}U$) documents extinct species and transitional forms like *Tiktaalik* (bridging lobe-finned fish and tetrapod amphibians) and *Archaeopteryx* (linking theropod dinosaurs and birds). **Biogeography** and continental drift from Pangaea explain why island species closely resemble species on the nearest mainland and why marsupials radiated in isolated Australia.

In comparative anatomy, it is critical to distinguish **divergent evolution** from **convergent evolution**. **Divergent evolution** from a recent common ancestor produces **homologous structures**—such as the pentadactyl forelimbs of humans, cats, whales, and bats, which perform different functions today (grasping, running, swimming, flying) but share the exact same underlying skeletal layout (humerus, radius, ulna, carpals, phalanges)—as well as **vestigial structures** (remnant pelvic hip bones in whales and snakes). Conversely, **convergent evolution** occurs when distantly related species independently evolve superficially similar **analogous structures (homoplasies)** because they occupy similar ecological niches and face similar selective pressures.

At the deepest level, **molecular homologies**—the universal genetic code, ribosomes, ATP, glycolysis, and shared disabled **pseudogenes** (such as the mutated GULO vitamin-C gene shared by humans and chimpanzees)—prove universal common ancestry, while sequence comparisons of conserved proteins like **cytochrome c** or hemoglobin quantify evolutionary relatedness.

- **Classic Examples of Convergent Evolution (Analogous Structures):** (1) Streamlined torpedo bodies and dorsal fins in **sharks (cartilaginous fish), ichthyosaurs (extinct reptiles), and dolphins (mammals)**; (2) wings of insects, birds, and bats (as flight surfaces, though bird/bat forelimb bones are homologous); (3) gliding skin flaps in Australian marsupial **sugar gliders** and North American placental **flying squirrels**.

**Table 7.1 · Divergent Evolution (Homology) vs. Convergent Evolution (Analogy)**

| Feature | Homologous Structures (Divergent Evolution) | Analogous Structures (Convergent Evolution) |
|---|---|---|
| Evolutionary Origin | Inherited from a shared recent common ancestor | Evolved independently in distantly related lineages |
| Underlying Anatomy / DNA | Same fundamental bone architecture, embryology, and genetic code | Different underlying anatomy and developmental origin |
| Current Ecological Function | Often adapted for different functions in different habitats | Perform similar functions in similar environmental niches |
| Phylogenetic Significance | Valid evidence for grouping taxa into a monophyletic clade | Homoplasy (can mislead morphological trees if mistaken for homology) |
| Classic AP Bio Examples | Human arm, cat leg, whale flipper, bat wing (pentadactyl limb) | Shark, ichthyosaur & dolphin body shapes; insect wing vs. bird wing |

⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: When an AP question asks for the MOST reliable evidence to determine evolutionary relationships among species, ALWAYS choose DNA nucleotide sequence or amino acid sequence comparisons over physical morphology (because morphology can be fooled by convergent evolution)!

## § 7.4 Phylogenetic Trees, Cladograms & Maximum Parsimony

A **phylogenetic tree** or **cladogram** is a branching diagram that represents a testable hypothesis of evolutionary history. Every internal branch point or **node** represents the **most recent common ancestor (MRCA)** shared by all descendant lineages branching from that node. Two lineages that branch from the exact same immediate node are **sister taxa** and are each other's closest relatives. Crucially, **rotating branches around any node does NOT change the evolutionary relationships** depicted by the tree!

A valid **clade (monophyletic group)** consists of an ancestral species and *all* of its evolutionary descendants. Biologists construct cladograms by identifying **shared derived characters (synapomorphies)**—evolutionary novelties (such as jaws, lungs, amniotic eggs, or hair in vertebrates) that evolved in the ancestor of a clade and were passed to its descendants. An **outgroup**—a lineage known to have diverged before the **ingroup** species being studied—serves as a reference baseline to distinguish ancestral traits from newly evolved derived traits. When choosing among competing phylogenetic trees, scientists apply the principle of **maximum parsimony**, selecting the simplest tree that requires the fewest total evolutionary changes (or fewest DNA base mutations).

**EXAMPLE 7.2** **Constructing a Cladogram from a Derived Character Matrix & DNA Divergence Table**

**Problem:** A character table scores five vertebrates—Lamprey (Outgroup), Shark, Salamander, Lizard, and Tiger—for four traits: Jaws (present in Shark, Salamander, Lizard, Tiger), Lungs (present in Salamander, Lizard, Tiger), Amniotic Egg (present in Lizard, Tiger), and Hair (present in Tiger only). Determine the branching order of the cladogram, identify the sister taxon to the Tiger, and explain what happens to the relationships if the Lizard–Tiger node is rotated 180°.

**STEP-BY-STEP SOLUTION:**

1. Step 1: Place the Lamprey (0 derived traits) as the basal outgroup branching off first.
2. Step 2: Place the hash mark for 'Jaws' on the main trunk above Lamprey; Shark (1 trait: Jaws) branches off next.
3. Step 3: Place 'Lungs' above the Shark node; Salamander (2 traits: Jaws, Lungs) branches off next.
4. Step 4: Place 'Amniotic Egg' above the Salamander node; Lizard and Tiger share this node as sister taxa, with 'Hair' placed uniquely on the Tiger branch.
5. Step 5: Rotating the Lizard–Tiger node so Tiger is written to the left of Lizard leaves their common ancestor node untouched and changes ZERO evolutionary relationships.

**Final Answer: Branching order: (Lamprey, (Shark, (Salamander, (Lizard, Tiger)))). Lizard and Tiger are sister taxa sharing the most recent common ancestor; rotating their node does not alter any relationships.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Never read across the tips (top/right labels) of a cladogram as a ladder of 'who evolved from whom' or 'who is closest to whom'! Always trace backward from the tips down to the MOST RECENT COMMON ANCESTOR NODE to determine relatedness.

## § 7.5 Speciation, Reproductive Isolation, Macroevolution & Origin of Life

According to Ernst Mayr's **Biological Species Concept**, a species is a group of populations whose members have the potential to interbreed in nature and produce **viable, fertile offspring**. Consequently, **speciation**—the splitting of one ancestral species into two distinct species—requires the evolution of **reproductive isolation** that blocks **gene flow** between populations. Reproductive barriers are classified by whether they act before or after fertilization: **prezygotic barriers** prevent mating or fertilization from occurring, whereas **postzygotic barriers** prevent a hybrid zygote from developing into a viable, fertile adult.

Geographically, **allopatric speciation** ('other country') occurs when a population is physically split by an extrinsic geographic barrier (a mountain range, canyon, or the Isthmus of Panama separating snapping shrimp), allowing isolated populations to diverge via natural selection, mutation, and genetic drift. **Sympatric speciation** ('same country') occurs within the same geographic area without physical separation, driven by **polyploidy** (meiotic nondisjunction in plants creating 4n tetraploids that are instantaneously isolated from 2n diploids because 3n triploid offspring are sterile), habitat differentiation (apple maggot flies), or disruptive sexual selection (Lake Victoria cichlids).

Across geological time, evolution proceeds via **gradualism** (steady accumulation of small changes) or **punctuated equilibrium** (long periods of morphological stasis interrupted by rapid bursts of speciation and **adaptive radiation** into empty niches, especially after the **five major mass extinctions** such as the Permian volcanic extinction or the 66-Mya Cretaceous asteroid impact). Finally, Earth formed **4.6 billion years ago (Bya)**, cooled by 3.9 Bya, and shows prokaryotic stromatolite fossils by **3.5 Bya**. As modeled by the **Oparin–Haldane hypothesis** and **Miller–Urey spark-discharge experiment**, early Earth's reducing atmosphere (lacking free $O_2$) and lightning/hydrothermal energy abioticially synthesized organic monomers that polymerized into lipid **protocells** housing self-replicating catalytic ribozymes—supporting the **RNA World hypothesis** that RNA served as both the first genetic material and catalyst before DNA and proteins.

**Table 7.2 · Prezygotic vs. Postzygotic Barriers to Reproduction**

| Barrier Category | Specific Mechanism | How It Blocks Gene Flow | Classic Biological Example |
|---|---|---|---|
| Prezygotic (Before Zygote) | Habitat Isolation | Populations occupy different microhabitats in the same area | Garter snakes (aquatic vs. terrestrial species) |
| Prezygotic (Before Zygote) | Temporal Isolation | Breed at different times of day, seasons, or years | Eastern vs. Western spotted skunks (winter vs. late summer) |
| Prezygotic (Before Zygote) | Behavioral Isolation | Different courtship rituals, mating dances, songs, or pheromones | Blue-footed boobies courtship dance; firefly flash patterns |
| Prezygotic (Before Zygote) | Mechanical Isolation | Anatomical incompatibility of reproductive structures | Snail shell coil direction; floral structure for pollinators |
| Prezygotic (Before Zygote) | Gametic Isolation | Sperm and egg surface recognition proteins cannot fuse | Red vs. purple sea urchins releasing gametes into ocean water |
| Postzygotic (After Zygote) | Reduced Hybrid Viability | Hybrid zygote/embryo fails to develop or dies before maturity | Ensatina salamander subspecies hybrids |
| Postzygotic (After Zygote) | Reduced Hybrid Fertility | Hybrid is vigorous and healthy but sterile (meiosis fails) | Mule (2n = 63, sterile hybrid of horse 2n=64 × donkey 2n=62) |
| Postzygotic (After Zygote) | Hybrid Breakdown | $F_1$ hybrids are fertile, but $F_2$ offspring are feeble or sterile | Cultivated rice strains carrying incompatible recessive alleles |

**⚠️ AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Early Earth's atmosphere in the Oparin–Haldane / Miller–Urey origin-of-life model had ZERO free oxygen gas ($O_2$)! Because $O_2$ is strongly electronegative and oxidizing, it would have oxidized and destroyed organic monomers; abundant atmospheric $O_2$ only accumulated later (~2.7 Bya) after cyanobacteria evolved oxygenic photosynthesis.

**✅ CHAPTER 7 MASTERY CHECKLIST (AP EXAM READINESS)**

☑ Apply Darwin's 4-step natural selection logic to antibiotic/pesticide resistance and rock pocket mice, and distinguish directional, stabilizing, and disruptive selection.

☑ State the 5 conditions for Hardy–Weinberg equilibrium, solve $p + q = 1$ and $p^2 + 2pq + q^2 = 1$ problems starting from $q^2$, and contrast genetic drift (bottleneck/founder effects) with gene flow and heterozygote advantage.

☑ Distinguish homologous structures (divergent evolution) from analogous structures (convergent evolution) and explain why molecular sequence data are preferred for phylogenetics.

☑ Construct and interpret cladograms using outgroups, shared derived characters (synapomorphies), most recent common ancestors, node rotation, and maximum parsimony.

☑ Classify prezygotic vs. postzygotic reproductive barriers, compare allopatric vs. sympatric speciation and adaptive radiation, and summarize the Miller–Urey and RNA World hypotheses.

CHAPTER 8 · CORE CURRICULUM

**AP Exam Weighting: 10–15%**

# Unit 8: Ecology

Ecology investigates how organisms interact with one another and with their physical environment across behavioral, physiological, population, community, and ecosystem scales. This unit covers behavioral ecology and kin selection, endotherm vs. ectotherm energetics, trophic pyramids and primary productivity, biogeochemical cycles, exponential and logistic population growth mathematics, community niche partitioning, keystone trophic cascades, Simpson's Diversity Index, and human impacts on the biosphere.

### CHAPTER 8 ESSENTIAL EQUATIONS, LAWS & CONSTANTS

| | |
|---|---|
| Net Primary Productivity: $NPP = GPP - R$ | New producer biomass available to consumers equals Gross Primary Productivity minus Producer Respiration |
| Exponential Population Growth: $dN / dt = r_{max} \cdot N$ | J-shaped curve occurring under unlimited resources with constant per-capita growth rate $r_{max} = b - d$ |
| Logistic Population Growth: $dN / dt = r_{max} \cdot N \cdot [(K - N) / K]$ | S-shaped curve leveling off at carrying capacity K; maximum growth rate occurs at $N = K / 2$ |
| Simpson's Diversity Index: $D = 1 - \sum (n / N)^2$ | Ranges from 0 to 1; closer to 1 indicates higher community biodiversity (richness + evenness) |

## § 8.1 Behavioral Responses, Phototropism, Communication & Kin Selection

Organisms detect and respond to internal and external environmental cues through physiological and behavioral mechanisms that maximize survival and reproductive fitness. In plants, Charles Darwin and Frits Went demonstrated that **positive phototropism**—the bending of a shoot toward directional sunlight—is driven by the plant hormone **auxin (indoleacetic acid, IAA)**. Blue light detected at the coleoptile tip causes auxin to migrate laterally from the illuminated side to the **shaded side** of the stem; high auxin on the shaded side activates proton pumps that acidify the cell wall (the *acid-growth hypothesis*), activating expansin enzymes that loosen cellulose microfibrils so **shaded cells elongate faster** than lit cells, bending the stem toward the light. Plants also track seasonal night length (**photoperiodism**) using **phytochrome** photoreceptors to time flowering in short-day vs. long-day plants.

In animals, innate movement responses fall into two classes: **taxis** is a directed, oriented movement toward (+) or away from (−) a stimulus (such as positive phototaxis toward light or trout exhibiting positive rheotaxis by swimming upstream into a current), whereas **kinesis** is a random, non-directional change in movement speed or turning rate in response to stimulus intensity (such as terrestrial **pillbugs/sowbugs** scurrying rapidly and randomly in dry air until they happen to enter a humid, dark microhabitat where they slow down and aggregate).

Animals exchange information via **visual, auditory, tactile, and chemical (pheromone) signals**—such as the **honeybee waggle dance**, which encodes both the distance and solar angle to a food source. Paradoxically, animals sometimes perform **altruistic behaviors** (such as a **Belding's ground squirrel** giving a loud alarm call when spotting a hawk, drawing the predator's attention to itself to save the colony). William Hamilton explained this via **kin selection and inclusive fitness**: according to **Hamilton's Rule (rB > C)**, natural selection favors altruism when the coefficient of relatedness (**r** = 0.50 for full siblings) times the reproductive benefit to relatives (**B**) exceeds the cost to the altruist (**C**).

- **Endotherm vs. Ectotherm Thermoregulation: Endotherms** (mammals, birds) use internal metabolic heat from cellular respiration to maintain a constant core temperature, requiring high food intake; as ambient temperature drops into the cold, an endotherm's **metabolic rate ($O_2$ consumption) INCREASES** to generate heat. **Ectotherms** (reptiles, amphibians, fish, invertebrates) regulate body temperature behaviorally using external heat (basking/shade), requiring far less food; as ambient temperature drops, an ectotherm's body temperature and **metabolic rate DECREASE**.

> ⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
>
> AP Exam Trap: Watch the axes on $O_2$ consumption vs. ambient temperature graphs! As environmental temperature drops from 30 °C down to 5 °C, a mammal's (endotherm's) $O_2$ consumption rate goes UP (shivering/cellular respiration to stay warm), whereas a lizard's (ectotherm's) $O_2$ consumption rate goes DOWN (enzymes cool and slow down)!

## § 8.2 Trophic Pyramids, The 10% Energy Rule, Primary Productivity & Nutrient Cycles

A foundational principle of ecosystem ecology states that **energy flows one way** through an ecosystem (entering as solar photons or inorganic chemicals and exiting as dissipated metabolic heat), whereas **chemical matter (C, N, P, $H_2O$) is conserved and recycled continuously** within biogeochemical cycles.

At the base of every food web sit **primary producers (autotrophs)**—either photosynthetic plants/algae/cyanobacteria or deep-sea hydrothermal vent chemoautotrophic bacteria oxidizing $H_2S$—followed by **primary consumers (herbivores)**, **secondary consumers**, and **tertiary (apex) consumers**, all connected to **decomposers (fungi and bacteria)** that mineralize dead organic detritus back into inorganic nutrients. In accordance with the Second Law of Thermodynamics and the **10% Rule of Ecological Efficiency**, roughly **90% of available energy is lost as metabolic heat** (via cellular respiration) and unassimilated waste at each trophic transfer, leaving only **~10%** to be converted into new biomass at the next higher trophic level. This severe energetic bottleneck explains why food chains rarely exceed 4 to 5 trophic levels.

In primary productivity accounting, **Gross Primary Productivity (GPP)** is the total solar energy fixed by photosynthesis, **Respiration (R)** is the fraction burned by the plants' own mitochondria, and **Net Primary Productivity (NPP = GPP − R)** represents the net new producer biomass available to heterotrophic consumers.

- **The Carbon Cycle:** Balances photosynthetic $CO_2$ fixation against cellular respiration, decomposition, and fossil-fuel combustion returning $CO_2$ to the atmosphere and oceans.
- **The Nitrogen Cycle (Driven by Prokaryotes!):** Although atmospheric $N_2$ gas makes up 78% of air, plants cannot break its triple covalent bond (N≡N). Symbiotic **nitrogen-fixing bacteria (*Rhizobium* in legume root nodules) and free-living cyanobacteria reduce $N_2$ into ammonia/ammonium (**$NH_3$ / $NH_4^+$**); **nitrifying bacteria** oxidize $NH_4^+$ into nitrites ($NO_2^-$) and nitrates (**$NO_3^-$**) assimilated by plants; and anaerobic **denitrifying bacteria** reduce $NO_3^-$ back into $N_2$ gas.
- **The Phosphorus Cycle:** Unlike carbon and nitrogen, phosphorus has **no atmospheric gas phase**; phosphate ions (**$PO_4^{3-}$**) weather slowly from uplifted sedimentary rock into soil and aquatic food webs.

### EXAMPLE 8.1 Calculating Trophic Pyramid Energy Transfers & Net Primary Productivity (NPP)

**Problem:** In a temperate forest ecosystem, primary producers capture 50,000 kcal/m²/yr of solar energy via photosynthesis (GPP) and expend 30,000 kcal/m²/yr in their own cellular respiration (R). Calculate the Net Primary Productivity (NPP) of the forest, and assuming a 10% ecological transfer efficiency at each step, determine how much energy (in kcal/m²/yr) is incorporated into the biomass of (a) primary consumers, (b) secondary consumers, and (c) tertiary apex predators.

**STEP-BY-STEP SOLUTION:**

1. Step 1: Calculate Net Primary Productivity available to herbivores: NPP = GPP − R = 50,000 − 30,000 = 20,000 kcal/m²/yr.
2. Step 2: Apply the 10% rule from Primary Producers (NPP = 20,000) to Primary Consumers (Herbivores): 20,000 × 0.10 = 2,000 kcal/m²/yr.
3. Step 3: Apply the 10% rule to Secondary Consumers (Primary Carnivores): 2,000 × 0.10 = 200 kcal/m²/yr.
4. Step 4: Apply the 10% rule to Tertiary Consumers (Apex Predators): 200 × 0.10 = 20 kcal/m²/yr (99.9% of NPP has been dissipated as metabolic heat across the three transfers).

**Final Answer: NPP = 20,000 kcal/m²/yr; Primary consumers = 2,000 kcal/m²/yr; Secondary consumers = 200 kcal/m²/yr; Tertiary consumers = 20 kcal/m²/yr.**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: When computing energy available to primary consumers from ecosystem data, ALWAYS apply the 10% rule to Net Primary Productivity (NPP = GPP − R), NEVER directly to Gross Primary Productivity (GPP) or raw incident sunlight!

## § 8.3 Population Ecology: Dispersion, Survivorship & Exponential vs. Logistic Growth

**Population ecology** examines how biotic and abiotic factors regulate population size (**N**), density, spatial dispersion, and age structure over time. Within a habitat, individuals exhibit three spatial dispersion patterns: **clumped** (the most common pattern, aggregating around patchy resources or for herd defense), **uniform** (evenly spaced due to territoriality in nesting penguins or allelopathic toxins in desert shrubs), and **random** (windblown dandelion seeds). Demographers also classify species across three logarithmic **survivorship curves**: **Type I** (humans, large mammals: high juvenile survival, death in old age), **Type II** (songbirds, rodents: constant mortality rate at all ages), and **Type III** (oysters, sea turtles, insects: thousands of offspring with massive early juvenile mortality).

When a population enters an ideal habitat with unlimited resources, it undergoes **exponential growth** (**dN/dt = r_max · N**), generating an upward-curving **J-shaped curve**. In nature, finite resources and crowding impose an environmental **carrying capacity (K)**—the maximum population size a habitat can sustainably support—producing an **S-shaped (sigmoidal) logistic growth curve** governed by **dN/dt = r_max · N · [(K − N) / K]**.

- **Anatomy of the Logistic Curve:** When N is very small relative to K, the fraction (K − N)/K ≈ 1 and growth is nearly exponential. The instantaneous population growth rate (**dN/dt**, the steepest slope on the S-curve) reaches its **absolute maximum at exactly N = K / 2**. As N approaches K, (K − N)/K → 0 and dN/dt levels off at zero.
- **Density-Dependent vs. Density-Independent Regulation: Density-dependent factors** are biotic pressures whose mortality rate intensifies as population density rises—including competition for food/territory, infectious disease, parasitism, predation, and toxic waste accumulation—providing negative feedback that stabilizes N near K. **Density-independent factors** are abiotic weather/climate disturbances (hurricanes, wildfires, freezes, droughts) that kill a similar percentage of individuals regardless of density.
- **r-Selected vs. K-Selected Life Histories: r-selected (opportunistic) species** (bacteria, insects, weeds) mature early, produce huge clutches of tiny offspring with zero parental care (Type III survivorship), and boom in disturbed habitats. **K-selected (equilibrial) species** (elephants, whales, humans) mature late, produce few large offspring with intensive parental care (Type I survivorship), and compete near K.

### EXAMPLE 8.2 Quantitative Logistic Growth Rate (dN/dt) Calculations

> **Problem:** A wildlife reserve has a carrying capacity of K = 1,000 elk, and the elk population has a maximum per-capita intrinsic growth rate of r_max = 0.40 per year. Calculate the annual population growth rate (dN/dt) when the population size is (a) N = 100, (b) N = 500 (at K/2), (c) N = 900, and (d) N = 1,200 (overshoot above K).

**STEP-BY-STEP SOLUTION:**

1. Step 1: Write the logistic growth equation: dN/dt = r_max · N · [(K − N) / K] with r_max = 0.40 and K = 1,000.
2. Step 2: At N = 100: dN/dt = (0.40)(100)[(1,000 − 100) / 1,000] = 40 × 0.90 = +36 elk/year.
3. Step 3: At N = 500 (exactly K / 2): dN/dt = (0.40)(500)[(1,000 − 500) / 1,000] = 200 × 0.50 = +100 elk/year (the maximum possible growth rate!).
4. Step 4: At N = 900: dN/dt = (0.40)(900)[(1,000 − 900) / 1,000] = 360 × 0.10 = +36 elk/year.
5. Step 5: At N = 1,200 (above K): dN/dt = (0.40)(1,200)[(1,000 − 1,200) / 1,000] = 480 × (−0.20) = −96 elk/year (population declines back toward K).

**Final Answer: (a) +36 elk/yr at N=100; (b) +100 elk/yr maximum rate at N=500 (K/2); (c) +36 elk/yr at N=900; (d) −96 elk/yr at N=1,200.**

> ⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**
>
> AP Exam Trap: Do NOT confuse 'per-capita growth rate' (r) with 'population growth rate' (dN/dt)! In logistic growth, per-capita rate decreases linearly as N rises, whereas total population growth rate (dN/dt) peaks in the middle of the S-curve at N = K / 2!

## § 8.4 Community Interactions, Competitive Exclusion, Keystone Species & Simpson's Index

**Community ecology** analyzes interspecific interactions among species co-occurring in a habitat, classified by their net effect (+, −, or 0) on each partner's reproductive fitness: **mutualism (+/+)**, **commensalism (+/0)**, **exploitation (+/−: predation, herbivory, parasitism)**, and **interspecific competition (−/−)**.

In 1934, G. F. Gause grew two ciliate species—*Paramecium aurelia* and *Paramecium caudatum*—separately and together. Grown separately, each reached its carrying capacity logistically; grown together on the same bacterial food, *P. aurelia* drove *P. caudatum* to extinction, establishing **Gause's Competitive Exclusion Principle**: two species competing for the exact same limiting resource cannot coexist indefinitely if their ecological niches are identical. Consequently, competition restricts a species' broad physiological **fundamental niche** down to its narrower actual **realized niche** (as demonstrated by Joseph Connell in *Chthamalus* and *Balanus* intertidal barnacles). Over evolutionary time, competing species can coexist by evolving **resource partitioning** (e.g., Robert MacArthur's five warbler species foraging in different zones of the same spruce tree) and morphological **character displacement** (divergent beak depths in sympatric vs. allopatric Galápagos finches).

Within a community, a **keystone species** exerts a massive, disproportionate regulatory impact on community structure and biodiversity relative to its low biomass. Removing a keystone predator triggers a top-down **trophic cascade** that allows a dominant competitor or herbivore to explode and wipe out diversity. Finally, ecologists quantify community resilience using **Simpson's Diversity Index: $D = 1 - \sum(n / N)^2$**, where higher D (closer to 1) reflects greater species richness and evenness, providing functional redundancy during disturbances and ecological succession.

- **Keystone Case Study 1 — North Pacific Sea Otters: Sea otters** prey on herbivorous **sea urchins**, protecting giant **kelp forests**; when killer whales decimated sea otters, sea urchin populations exploded and overgrazed lush kelp forests into barren urchin deserts.
- **Keystone Case Study 2 — Pisaster Sea Stars & Yellowstone Wolves:** In Robert Paine's rocky intertidal zone, removing the keystone sea star *Pisaster ochraceus* allowed *Mytilus* mussels to crowd out 14 other species. In Yellowstone, reintroducing **gray wolves** curbed elk overgrazing along riverbanks, restoring willow/aspen trees, beavers, and songbirds.

**Table 8.1 · Classification of Interspecific Community Interactions**

| Interaction Type | Fitness Effect | Ecological Mechanism | Classic AP Biology Examples |
|---|---|---|---|
| Mutualism | + / + | Both species gain survival/reproductive benefit (often coevolved symbiosis) | Mycorrhizal fungi + plant roots; Rhizobium + legumes; coral polyps + zooxanthellae algae |
| Commensalism | + / 0 | One species benefits while the other is neither helped nor harmed | Cattle egrets eating insects flushed by grazing buffalo; barnacles riding on whales |
| Predation / Herbivory | + / − | Predator or herbivore consumes prey or plant tissue (drives mimicry/camouflage) | Canada lynx & snowshoe hare cycles; sea otters eating sea urchins |
| Parasitism | + / − | Parasite derives nourishment from host without immediately killing it | Tapeworms, ticks, mistletoe on trees, Plasmodium malaria protist |
| Interspecific Competition | − / − | Both species harmed by competing for the same limiting resource | P. aurelia vs. P. caudatum (competitive exclusion); Balanus vs. Chthamalus barnacles |

**EXAMPLE 8.3** **Calculating & Comparing Community Biodiversity Using Simpson's Index (D)**

**Problem:** Ecologists sample tree species in two forest plots, each containing N = 100 total trees across 4 species (A, B, C, D). In Plot 1, there are 25 trees of each species (25 A, 25 B, 25 C, 25 D). In Plot 2, there are 91 trees of Species A and 3 trees each of Species B, C, and D (91 A, 3 B, 3 C, 3 D). Calculate Simpson's Diversity Index $D = 1 - \sum(n/N)^2$ for both plots and explain which community is more resilient to a species-specific bark beetle outbreak.

**STEP-BY-STEP SOLUTION:**

1. Step 1: Notice both plots have the exact same species richness (4 species) and total abundance (N = 100), but differ dramatically in species evenness.
2. Step 2: For Plot 1: each species has $n/N = 25/100 = 0.25 \rightarrow (n/N)^2 = (0.25)^2 = 0.0625$. Sum across all 4 species: $\sum(n/N)^2 = 4 \times 0.0625 = 0.25$. Therefore, $D_1 = 1 - 0.25 = 0.75$.
3. Step 3: For Plot 2: Species A has $(91/100)^2 = (0.91)^2 = 0.8281$; Species B, C, D each have $(3/100)^2 = (0.03)^2 = 0.0009$. Sum: $\sum(n/N)^2 = 0.8281 + 3(0.0009) = 0.8308$. Therefore, $D_2 = 1 - 0.8308 = 0.169$ ($\approx 0.17$).
4. Step 4: Plot 1 has much higher biodiversity (D = 0.75 vs. 0.17) due to high evenness; if a beetle wipes out Species A, Plot 1 retains 75% of its canopy whereas Plot 2 loses 91% of its trees.

**Final Answer: Plot 1: D = 0.75; Plot 2: D = 0.17. Plot 1 is far more diverse and resilient because of its high relative abundance (evenness).**

⚠ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: Do not forget the '1 minus' at the end of Simpson's Diversity Index: $D = 1 - \sum(n/N)^2$! A value of D closer to 1 always means HIGHER diversity.

## § 8.5 Human Disruptions: Invasive Species, Eutrophication, Biomagnification & Conservation

Human activities are altering global ecosystems at an unprecedented rate. **Invasive species**—non-native organisms introduced outside their historic range (such as **kudzu vine** in the American South, **zebra mussels** in the Great Lakes, **cane toads** in Australia, and **Burmese pythons** in the Florida Everglades)—explode exponentially because they **escape their coevolved native predators, parasites, and pathogens**, outcompeting native species and collapsing local food webs. Meanwhile, **habitat fragmentation** slices continuous habitats into small isolated islands, increasing harmful **edge effects** and blocking gene flow.

On the AP Exam, students must carefully distinguish two major aquatic disruptions: **cultural eutrophication** and **biomagnification**. Furthermore, burning fossil fuels and deforestation elevate atmospheric greenhouse gases (**$CO_2$ and $CH_4$**), driving global warming and **ocean acidification** (dissolved $CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$, which lowers ocean pH and steals carbonate ions needed by corals and shellfish to build $CaCO_3$ skeletons).

Finally, when habitat loss isolates a population at a tiny size, inbreeding and genetic drift strip away genetic diversity, lowering reproduction and disease resistance in a downward spiral called the **extinction vortex**. Conservation biologists rescue endangered populations through **genetic restoration**—introducing unrelated individuals to restore gene flow (as proved in the **Illinois greater prairie chicken** and **Florida panther**)—and constructing **wildlife movement corridors**.

- **Cultural Eutrophication (Nutrient Runoff → Hypoxic Dead Zone):** Step 1: Excess inorganic **nitrates ($NO_3^-$) and phosphates ($PO_4^{3-}$)** from agricultural fertilizer and sewage wash into lakes or coastal oceans; Step 2: Nutrients trigger an explosive surface **algal bloom** that blocks sunlight to bottom plants; Step 3: When dense algae die and sink, **aerobic decomposer bacteria** proliferate and consume nearly all dissolved **$O_2$ gas via cellular respiration**, creating a **hypoxic dead zone** that suffocates fish and invertebrates.
- **Biomagnification (Persistent Fat-Soluble Toxins Up the Food Chain):** Non-biodegradable, **lipid-soluble persistent toxins**—such as **DDT, PCBs, and methylmercury**—accumulate in adipose tissue (bioaccumulation) and become

**progressively more concentrated at each higher trophic level** because upper predators must consume 10× the biomass of lower levels, poisoning apex predators like bald eagles (eggshell thinning), ospreys, and orcas.

**Table 8.2 · Distinguishing Cultural Eutrophication vs. Biomagnification**

| Comparison Feature | Cultural Eutrophication | Biological Magnification (Biomagnification) |
|---|---|---|
| Chemical Cause / Pollutant | Inorganic nutrients: Nitrates ($NO_3^-$) & Phosphates ($PO_4^{3-}$) from fertilizer/sewage | Fat-soluble persistent toxins: DDT, PCBs, Heavy metals (methylmercury) |
| Chemical Solubility | Water-soluble inorganic ions assimilated by algae | Lipid-soluble (hydrophobic), non-biodegradable toxins stored in fat |
| Primary Biological Mechanism | Algal bloom → algae die → aerobic bacteria consume dissolved $O_2$ via respiration | Toxins pass up trophic pyramid and concentrate ~10× per trophic level |
| Most Severely Affected Group | Benthic fish and shellfish suffocated by hypoxic (low-$O_2$) dead zones | Tertiary / Apex predators (bald eagles, peregrine falcons, sharks, orcas, humans) |

⚠️ **AP EXAM TRAP & FRQ SCORING GUIDELINE**

AP Exam Trap: In cultural eutrophication, it is NOT the living algae that use up all the oxygen in the water—it is the AEROBIC DECOMPOSER BACTERIA performing cellular respiration as they break down the massive pile of DEAD algae!

✅ **CHAPTER 8 MASTERY CHECKLIST (AP EXAM READINESS)**

☑ Explain how auxin drives positive phototropism via the acid-growth hypothesis, distinguish animal taxis vs. kinesis, apply Hamilton's Rule (rB > C) to kin selection, and contrast endotherm vs. ectotherm metabolic rates.

☑ Apply the 10% ecological efficiency rule and NPP = GPP − R to trophic pyramids, and trace the carbon, nitrogen (Rhizobium fixation, nitrification, denitrification), and phosphorus cycles.

☑ Solve exponential (dN/dt = r_max·N) and logistic (dN/dt = r_max·N·[(K−N)/K]) population growth problems, identify maximum dN/dt at N = K/2, and contrast density-dependent vs. density-independent factors.

☑ Analyze competitive exclusion (Gause), fundamental vs. realized niches (Connell), resource partitioning, character displacement, keystone trophic cascades (sea otters, Pisaster, wolves), and Simpson's Diversity Index.

☑ Distinguish invasive species, cultural eutrophication (bacterial $O_2$ depletion), biomagnification (fat-soluble toxins in apex predators), ocean acidification, and genetic rescue from the extinction vortex.