An Introduction to Metabolism

Chapter 8
METABOLISM

• I. Introduction
• All of an organism’s chemical reactions
• Thousands of reactions in a cell

• Example: digest starch → use sugar for energy and to build new molecules
II. Metabolic Pathways

• starting molecule $\rightarrow$ chemical reactions $\rightarrow$ product(s)

• Each step catalyzed by specific enzyme

![Diagram showing metabolic pathways with starting molecule A, Enzyme 1, Enzyme 2, Enzyme 3, and product D.]
• **Catabolic pathways** -
  – break down complex molecules into simpler compounds
  – release **energy** for cells to use

• Ex. Glucose metabolism yeilds ATP
• **Anabolic pathways** use energy to build complex molecules from simpler ones

• Ex. Protein synthesis from amino acids
III. Energy

- Energy
  - capacity of a system to do work
  - can be converted from one form to another

- 1. Kinetic energy  = energy of motion
  - Due to vibration of atoms /molecules
• Kinetic energy examples:
  – **LIGHT Energy** -electromagnetic energy includes visible light, x-rays, gamma rays and radio waves.
  – **MOTION** energy in the movement of objects. The faster they move, the more energy. Wind is motion energy. When a car comes to a total stop, releases all motion energy in uncontrolled instant.
  – **SOUND** -movement of energy through substances in longitudinal waves. Sound produced when force causes object or substance to vibrate —energy is transferred through the substance in a wave. Far less than other forms of energy.
  – **HEAT** – average total kinetic energy of molecules
2. Potential energy = energy stored within system
   Ex. rubberband

- Chemical energy = PE available for release in chemical reaction
- Ex. Glucose has high CE
IV. The Laws of Energy Transformation

• **Thermodynamics** – study of energy transformation

• In open system energy and matter can be transferred between system and surroundings

• Why are organisms/cells open systems?
First Law of Thermodynamics

• The energy of universe is constant:
  • *Energy can be transferred and transformed, but it cannot be created or destroyed.*

• This is the **principle of conservation of energy**
Second Law of Thermodynamics

- *Every energy transfer or transformation increases entropy (disorder) of the universe*

- Living systems (open) increase entropy in environment

- During E transfer some E is released as heat (unusable)
First Law: chemical E in food converted to kinetic E

Second Law: disorder is entered into environment as heat, CO$_2$
Cells create ordered structures from less ordered materials

- Ex. proteins built from amino acids

Amino acids in cell -----------------------------Growth hormone
Organisms replace ordered forms of matter and energy with less ordered

• break down molecules, releases heat

• Energy flows into ecosystem as ____ and leaves as ______
VI. Free-energy (G)

- $G =$ amt. of energy available to do work in biochemical reaction
- $\Delta G =$ change in free energy
- unstable systems move towards stable (equilibrium)
- System at equilibrium does no work
Equilibrium and Metabolism

• Reactions in closed system eventually reach equilibrium and then do no work

(a) An isolated hydroelectric system

\( \Delta G < 0 \)

\( \Delta G = 0 \)

It’s a positive free energy change for the surroundings, negative for the system
Equilibrium and Metabolism

• Cells are open systems
  – constant flow of materials
  – not in equilibrium

(b) An open hydroelectric system

$\Delta G < 0$
Equilibrium and Metabolism

• catabolic pathway releases free energy in series of reactions

(c) A multistep open hydroelectric system
Spontaneous processes

1. occur without (additional) energy input
   – explosion, rusting (slow!)
2. release energy, usually heat
3. Gives up energy \(-\Delta G\)
4. Exergonic

The Gibbs free energy equation does depend on T, increasing T may increase reaction rate
Exergonic reaction

- $\Delta G = \text{exergonic reaction}$
  - releases energy
  - Spontaneous
  - “downhill”
  - Products have less $G$ than reactants

(a) Exergonic reaction:
   - energy released

Amount of energy released ($\Delta G < 0$)
Exergonic reaction

- **Cellular respiration**

\[ \text{C}_6\text{H}_{12}\text{O}_6 + 6 \text{O}_2 \rightarrow 6 \text{CO}_2 + 6 \text{H}_2\text{O} \]

\[ \Delta G = -686 \text{kcal/mol} \quad \text{available for work} \]

- **ATP + H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i \] (hydrolysis)

\[ \Delta G = -7.3 \text{ kcal/mol} \]
• $+\Delta G = \text{endergonic rxn}$
  - Absorbs free energy from surroundings.
  - Non-spontaneous
Endergonic

• Photosynthesis

$$6\text{CO}_2 + 6\text{H}_2\text{O} (+ \text{light energy}) \rightarrow \text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2$$

686 kcal/mol
(b) Endergonic reaction: energy required

Free energy

Reactants

Energy

Products

Amount of energy required ($\Delta G > 0$)

Progress of the reaction

(b) Endergonic reaction: energy required
VI. ATP powers cellular work

ATP

– High stored chemical potential energy
– drives cell activities
ATP

- ATP = adenosine triphosphate

Energy released when terminal phosphate bond broken by hydrolysis
ATP $\rightarrow$ ADP + P

$\Delta G = -7.3\text{ kcal/mol}$
• **Phosphorylation**

• Transfer P from ATP to other molecule to *phosphorylate* it.

• The phosphorylated molecule is

  Phosphorylation opens an aquaporin (spinach)

• Coupling = Use exergonic reactions to drive endergonic rxns (overall exergonic)
• **Regeneration of ATP**
  
  – Add phosphate group to ADP

  \[ \text{ADP} + \text{P} \rightarrow \text{ATP} \text{ is this } + \text{ or } - \Delta G? \]

  \[ \Delta G = 7.3 \text{kcal/mol} \]
Coupled reactions

Energy from catabolism (exergonic, energy-releasing processes)

ATP + H₂O

Energy for cellular work (endergonic, energy-consuming processes)

ADP + Pᵢ
VIII. ENZYMES
A. Enzymes speed up metabolic reactions

- **catalyst** = chemical agent that speeds up a reaction
  - Unchanged by reaction

- **enzyme** = catalytic protein (organic)

- Ex. Hydrolysis of sucrose by sucrase
B. Enzymes lower activation energy barrier

- chemical reaction = bonds broken/formed

- free energy of activation = activation energy ($E_a$)
  = energy to start chemical reaction

- $E_a$ contorts molecule $\rightarrow$ makes bonds unstable

- No change in $\Delta G$ (doesn’t affect reactants or product energy)
Progress of the reaction

Products

Reactants

Free energy

Course of reaction without enzyme

E_A without enzyme

Course of reaction with enzyme

E_A with enzyme is lower

ΔG is unaffected by enzyme

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C. How Enzymes Lower the $E_A$

- $37^\circ\text{C} \rightarrow$ reactants do not reach $E_A$ (transition state)
- Enzymes speed rate to transition state
- Reactants most unstable
- Does not affect $\Delta G$ of rxn. Why?
D. Substrate **Specificity** of enzymes

- \( S = \text{Substrate} = \) reactant
- \( ES = \text{Enzyme-substrate complex} \)
- \( P = \text{Product(s)} \)

Sucrose + **Sucrase** → E-S complex → Fructose + Glucose + ?

substrate  enzyme  products
• **Active site** region on enzyme where substrate binds

• **Induced fit** - enzyme shape changes to fit to substrate
E. Catalysis in Active Site

1000 – 1,000,000 rxns/sec

• Induced fit by:
  – Hydrogen bonds
  – Ionic bonds
  – Hydrophobic interactions

• Enzyme can catalyze forward or reverse rxn
  – Always in direction of equilibrium

• Active site can lower $E_a$
  – Orient substrates
  – Contort bonds
  – Provide microenvironment
  – Covalently bond to substrate
Substrates enter active site; enzyme changes shape such that its active site enfolds the substrates (induced fit).

- Substrates held in active site by weak interactions, such as hydrogen bonds and ionic bonds.
- Active site can lower $E_A$ and speed up a reaction.

- Substrates are converted to products.
- Products are released.
- Enzyme-substrate complex

Substrates held in active site by weak interactions, such as hydrogen bonds and ionic bonds.
F. Local Conditions

• activity affected by
  – temperature, pH (each has optimal)
  – chemicals
Temperature influences the rate of enzyme-catalyzed reactions.
Rate of reaction

Optimal temperature for typical human enzyme
Optimal temperature for enzyme of thermophilic (heat-tolerant) bacteria

(a) Optimal temperature for two enzymes

Temperature (°C)

0 10 20 30 40 50 60 70 80 90 100

Rate of reaction

(pH)

5 4 3 2 1 0 6 7 8 9 10

0 20 40 80 60 100

Optimal pH for pepsin (stomach enzyme)
Optimal pH for trypsin (intestinal enzyme)

(b) Optimal pH for two enzymes

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G. Cofactor assists enzyme

- Non-protein
- inorganic cofactor
  - Metal ion
- organic cofactor is a coenzyme
  - Vitamins
  - Bind to active site
H. Enzyme Inhibitors

- **Competitive inhibitors**
  - bind to active site of enzyme
  - compete with substrate at active site

Alcohol dehydrogenase enzyme
• Noncompetitive inhibitors
  – bind to another part of enzyme
  – change shape of active site
  – May not be reversible

• toxins, poisons, pesticides, antibiotics
(a) Normal binding  
(b) Competitive inhibition  
(c) Noncompetitive inhibition
9. Regulation of enzyme activity helps control metabolism

• metabolic pathways are tightly regulated
Allosteric Regulation (normal in cells)

- Regulatory molecule binds to enzyme but not at the active sites! (note: each subunit has its own active site)

- Most enzymes have inactive and active forms – shape changers!
A. Allosteric inhibition → molecule binds to stabilize inactive state → blocks substrate

- Binding is reversible
B. Allosteric cooperativity boosts enzyme activity

- Regulatory molecule binds to one site
- stabilizes favorable shape changes at other subunits
IX. Feedback Inhibition

• End product of metabolic pathway turns off pathway

• No wasting chemical resources by synthesizing more product than is needed
Isoleucine used up by cell

Active site available

Threonine in active site

Enzyme 1 (threonine deaminase)

Intermediate A

Enzyme 2

Intermediate B

Enzyme 3

Intermediate C

Enzyme 4

Intermediate D

Enzyme 5

End product (isoleucine)

Feedback inhibition

Active site of enzyme 1 no longer binds threonine; pathway is switched off.

Isoleucine binds to allosteric site

Initial substrate (threonine)