Chapter 8:
An Introduction to Metabolism

1. Energy & Chemical Reactions
2. ATP
3. Enzymes & Metabolic Pathways
1. Energy & Chemical Reactions

Chapter Reading – pp. 142-148
2 Basic Forms of Energy

Kinetic Energy (KE)

• energy in motion or “released” energy:
  • heat (molecular motion)
  • electric current* (flow of charged particles)
  • light energy* (radiation of photons)
  • mechanical energy* (structural movement)
  • chemical energy* (breaking covalent bonds, flow from high to low concentration)

*forms of KE cells use to “do things”
Potential Energy (PE)

- stored energy (i.e., not yet released):
  - gravitational potential
  - chemical bonds*
  - chemical gradients*, charge gradients*

A diver has more potential energy on the platform than in the water. Diving converts potential energy to kinetic energy.

Climbing up converts the kinetic energy of muscle movement to potential energy. A diver has less potential energy in the water than on the platform.

*sources of PE cells rely on
Illustration of Kinetic & Potential Energy

KE highest at b, lowest at a & c

PE highest at a & c, lowest at b
Laws of Energy Transformation

1\textsuperscript{st} Law of Thermodynamics

Principle of Conservation of Energy:

“Energy is neither created nor destroyed, but may be converted to other forms.”

(a) First law of thermodynamics

(b) Second law of thermodynamics

2\textsuperscript{nd} Law of Thermodynamics

- every energy conversion results in a loss of usable energy as HEAT

“Every energy transfer or transformation increases the entropy of the universe.”
Chemical Free Energy

Gibb’s Free Energy \( (G) = \text{“chemical PE”} \)

\[ \Delta G = G_{\text{products}} - G_{\text{reactants}} \]

Negative \( \Delta G \):
- “loss” of chemical PE (e.g., respiration)
- net release of KE (for work or to raise temperature)

Positive \( \Delta G \):
- “gain” of chemical PE (e.g., photosynthesis)
- requires input of KE (e.g., sunlight)

\( \Delta G = 0 \):
- system is at equilibrium
More free energy (higher $G$)
Less stable
Greater work capacity

In a spontaneous change
• The free energy of the system decreases ($\Delta G < 0$)
• The system becomes more stable
• The released free energy can be harnessed to do work

Less free energy (lower $G$)
More stable
Less work capacity

• in each case $\Delta G$ is negative and PE decreases

Examples of Spontaneous Changes in Free Energy

(a) Gravitational motion
(b) Diffusion
(c) Chemical reaction
**Exergonic Reactions**

- net *release* of energy ($\Delta G$ is negative)
- loss of PE

**Endergonic Reactions**

- net *consumption* of energy ($\Delta G$ is positive)
- gain of PE
Whether endergonic or exergonic, all chemical reactions require some energy input for the reaction to proceed – the activation energy ($E_A$).

- all reactions require some sort of “spark”
- this is why sources of chemical PE are “stable”
The upright bottle falling over is analogous to an exergonic reaction, yet it still requires some energy input for the bottle to tip over.
2. ATP

Chapter Reading – pp. 148-151
ATP – an Ideal Cellular Fuel

- useable amount of energy ($\Delta G -7.3 \text{ kcal/mole}$)
- stable, soluble in water (negatively charged)

- terminal phospho-anhydride bond easily broken
ATP Hydrolysis

- exergonic cleavage of terminal phospho-anhydride bond

\[ \text{ATP} \rightarrow \text{ADP} + \text{P}_i + \text{H}_2\text{O} \]

\[ \Delta G = -7.3 \text{ kcal/mole} \]

Inorganic phosphate + Adenosine diphosphate (ADP) + Energy
Exergonic processes (e.g., cellular respiration) provide energy for the endergonic synthesis of ATP, whereas ATP hydrolysis releases energy that can be used for other endergonic activities...
(b) Mechanical work: ATP binds noncovalently to motor proteins, then is hydrolyzed
**Coupling of Biochemical Reactions**

*Exergonic* reactions fuel (provide energy for) *endergonic* reactions in cells (i.e., they are “coupled”)

- Breakdown of glucose fuels ATP production
- ATP hydrolysis fuels most cellular activities
Example of Coupling w/ ATP Hydrolysis

(a) Glutamic acid conversion to glutamine

\[
\text{Glu} + \text{NH}_3 \rightarrow \text{Glu} \quad \Delta G_{\text{Glu}} = +3.4 \text{ kcal/mol}
\]

(b) Conversion reaction coupled with ATP hydrolysis

\[
\text{Glu} + \text{ATP} \rightarrow \text{Glu} \quad \Delta G_{\text{Glu}} = +3.4 \text{ kcal/mol}
\]

\[
\text{Glu} \rightarrow \text{Glu} + \text{ADP} + \text{P}_i 
\]

\[
\Delta G_{\text{ATP}} = -7.3 \text{ kcal/mol}
\]

(c) Free-energy change for coupled reaction

\[
\text{Glu} + \text{NH}_3 + \text{ATP} \rightarrow \text{Glu} \quad \Delta G = -3.9 \text{ kcal/mol}
\]

\[
\Delta G_{\text{Glu}} = +3.4 \text{ kcal/mol}
\]

\[
+ \Delta G_{\text{ATP}} = -7.3 \text{ kcal/mol}
\]

\[
\text{Net } \Delta G = -3.9 \text{ kcal/mol}
\]
3. Enzymes & Metabolic Pathways

Chapter Reading – pp. 142, 151-159
Enzymes are Biological Catalysts

Biochemical reactions such as the one below will not occur spontaneously without a catalyst:

Enzymes are biological catalysts made of protein or RNA that determine when reactions occur.

- the production and regulation of enzymes give a cell complete control over all of the biochemical reactions that occur within the cell
Enzymes Lower Activation Energy

Course of reaction without enzyme

Course of reaction with enzyme

$E_A$ without enzyme

$E_A$ with enzyme is lower

$\Delta G$ is unaffected by enzyme

Reactants

Products

Progress of the reaction

Free energy
Enzymes physically bind Substrates

The “fit” of substrate into active site is highly specific and due to molecular complementarity

- complementary in physical shape ("hand in glove")
- complementary in chemical properties (attraction between opposite charges, hydrophobic regions)
The Catalytic Cycle of Enzymes

1. Enzyme available with empty active site
   - Active site

2. Substrate binds to enzyme with induced fit
   - Substrate (sucrose)

3. Substrate is converted to products
   - Glucose, Fructose

4. Products are released
   - H₂O

- Every enzyme has a unique substrate & thus catalyzes a specific reaction
- Cells produce 1000s of different enzymes, all of which are proteins encoded by a particular gene
Factors effecting Enzyme Activity

Optimal temperature and pH for a given enzyme depend on the environment in which it normally functions.

Deviation from the optimal conditions can result in denaturation and loss of enzyme activity.

(a) Optimal temperature for two enzymes

(b) Optimal pH for two enzymes
Enzymes can be regulated by inhibitors in two general ways:

1) *Competition* between inhibitor & substrate for active site
2) *Remotely* inducing the active site to *change shape*
Competitive Enzyme Inhibition

(a) Competitive inhibition involves binding of an inhibitor to the active site.

(b) Reversible competitive inhibitors are reversible to regulate in response to concentration.

- inhibitor must be reversible to be able to regulate in response to concentration.

irreversible inhibitors essentially poison the enzyme.
Allosteric Enzyme Regulation

Allosteric regulation involves the binding of a substance to an enzyme outside the active site.

- induces change in shape of active site
- must be reversible

(a) Allosteric inhibition
(b) Allosteric activation
Cooperativity

With many multimeric enzymes, the binding of substrate to one active site can stabilize the “active conformation” of other active sites, thus increasing the frequency with which they bind substrate.

- this is a type of allosteric regulation since active sites are regulated in a non-competitive manner

(b) Cooperativity: another type of allosteric activation
Most biological processes, whether anabolic (building) or catabolic (breaking down), require a series of chemical reactions (i.e., a pathway).

- Each step in a metabolic pathway is catalyzed by a specific enzyme.
- A missing or inactive enzyme can prematurely shut down a metabolic pathway, leading to the accumulation of potentially dangerous intermediates.
**Feedback Inhibition**

The end-products of metabolic pathways can be important *reversible* enzyme inhibitors

- inhibit 1\textsuperscript{st} enzyme, turn pathway “off”
  - low [inhibitor] = pathway ON
  - high [inhibitor] = pathway OFF
- can be competitive or allosteric inhibition
- important way of regulating end-product levels
Key Terms for Chapter 8

- kinetic, potential energy, free energy
- endergonic, exergonic, coupling of reactions
- activation energy
- enzyme, catalyst
- substrate, active site, molecular complementarity
- competitive, noncompetitive, feedback inhibition
- allosteric, cooperative regulation
- reversible vs irreversible

Relevant Chapter Questions 1-7