Energy, Enzymes & Metabolism

LIFE Ch. 8

Some definitions

- Energy: ability to carry out work
- Enzymes: Protein molecules that function as catalysts
- Metabolism: All chemical transformations in an organism

Energy - the ability to carry out work

- Energy can be converted from one form to another

- Potential energy can be stored or released
- In biochemistry: energy can be released in the form of e.g. nerve impulses, muscle contraction, heat

chemical energy = potential energy
Metabolism

- Chemical transformations = catabolism + anabolism

Anabolism: building up
Catabolism: breaking down

Anabolism

- Synthesis of biomolecules
  - Lipids
  - Amino acids/proteins
  - Nucleic acids
  - Carbohydrates

Catabolism

- Molecules are broken down to smaller molecules
- Often releases chemical energy

Anabolism pathways

Catabolic pathways

Building blocks for biosynthesis

Catabolism thermodynamics

- Energy can be converted between different forms
- Energy is conserved
  First law of thermodynamics
- Not all energy can be used for work
  Second law of thermodynamics
  Entropy increases: $\Delta S > 0$
Free Energy

All energy  unusable energy

\[ H = G + TS \]
Gibbs Free energy

During a chemical transformation:

\[ \Delta G = \Delta H - T\Delta S \]

Spontaneous chemical reactions release chemical energy (are exergonic)

ie \( \Delta G \) is negative

Chemical Equilibrium

Exergonic reaction

\[ \Delta G < 0 \]

Chemical reactions are reversible

\[ A \Leftrightarrow B \]

Endergonic reaction

\[ \Delta G > 0 \]

At equilibrium:

\[ \Delta G = 0 \]

Chemical equilibrium is determined by \( \Delta G \)

\( \Delta G \) depends on:

- the characteristic \( \Delta G^0 \) for the reaction
- concentrations of reactant and product

The reaction can run in either direction

The reaction continues until equilibrium, \( \Delta G = 0 \)

Adenosine triphosphate is the “energy currency” of the cell

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

\[ \Delta G = -30 \text{ kJ mol}^{-1} \]
Endergonic and exergonic reactions can be coupled

An energy barrier must be overcome, before a reaction can run

Enzymes catalyse reactions by lowering the activation energy

Activation energy $E_a$ is independent of $\Delta G$
Activation energy is lowered by bringing reactants close to each other.

**Catalytic mechanisms**

Substrate is bound and orientated correctly.

Stretching of chemical bonds may be induced by conformational changes in the protein.

Transient modifications of the substrate: acid-base, covalent, redox.

Many enzymes need cofactors, coenzymes or prosthetic groups for activity.

**Induced fit**

Change in conformation of the enzyme induced by substrate binding.

In hexokinase, water is excluded from the active site by a conformational change. This prevents water from acting as a phosphate acceptor instead of glucose.

\[
\text{Glucose} + \text{ATP} \rightarrow \text{Glucose-6-phosphate} + \text{ADP}
\]

\[
\text{Glucose} + \text{ATP} + \text{H}_2\text{O} \rightarrow \text{Glucose} + \text{ADP} + \text{P}_i
\]
Rate of reaction is dependent on substrate concentration

The enzyme is saturated with substrate

Concentration of substrate

**Turnover number** is a measure of enzyme effectiveness:
Lysozyme: transforms 0.5 substrate molecules per second
Catalase: transforms 40,000,000 substrate molecules per second

Enzyme activity can be described by the Michaelis-Menten model

\[
V = \frac{1}{2} V_{\text{max}} \quad \text{at} \quad [S] = K_m
\]

Concentration of substrate \([S]\)

Regulation of enzyme activity

**Homeostasis:** Maintenance of constant conditions

Inhibitors
Allosteric regulation
Environment

Irreversible inhibition

The enzyme is irreversibly inhibited and becomes catalytically inactive

Irreversible inhibition often involves covalent modification of amino acid side chains

DIPF reacts with a OH-group of a serine in trypsin's active site
Reversible inhibition can be competitive or non-competitive

(A) Competitive inhibition

The inhibitor competes with the substrate for binding to the active site

(B) Noncompetitive inhibition

The inhibitor binds to a site elsewhere on the enzyme, preventing catalysis

Allosteric regulation

Allosteric enzymes can switch between an active and an inactive form

The inactive form is stabilised by allosteric inhibitors
The active form is stabilised by allosteric activators

Allosteric inhibitors and activators bind to a regulatory site away from the active site

Allosteric enzymes show S-shaped (sigmoid) reaction curves (ie they DO NOT conform to the Michaelis-Menten model)

Consequence: The rate of reaction is extremely sensitive to changes in substrate concentrations. Allosteric enzymes are often important regulators of metabolic pathways
Feedback inhibition

The typical point at which metabolic pathways are regulated is the **commitment step**.

The end product of the pathway inhibits the enzyme at the commitment step of the pathway.

Effect of pH on enzyme activity

The pH optimum for different enzymes:
- Salivary amylase
- Pepsin
- Arginase

Effect of temperature

The optimal temperature for the reaction rate:
- Maximum rate
- Optimal temperature

Temperature vs. Reaction rate graph.