



RIDLEY COLLEGE

Biology 12 (SBI4U) Course

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class notes

Metabolism - An Introduction

An Introduction to Metabolism

I. Metabolism, Energy and Life

A. The chemistry of life is organized into metabolic pathways

Metabolism = totality of an organism's chemical processes

- organized into pathways that are orderly series of enzymatically controlled reactions
- metabolic pathways are generally of two types:
 1. **Catabolic** pathways = pathways that release energy by breaking down complex molecules to simpler compounds (e.g. cellular respiration)
 2. **Anabolic** pathways = pathways that consume energy to build complicated molecules from simpler compounds (e.g. photosynthesis)
- metabolic reactions may be coupled, so that energy released from a catabolic reaction can be used to drive an anabolic one

B. Organisms transform energy

energy = the capacity to do work

Kinetic energy = energy in the process of doing work (energy of motion)

For example,

- heat (thermal energy) is kinetic energy expressed in random movement of molecules.
- light (solar energy) is kinetic energy which powers photosynthesis

Potential energy = energy that matter possess because of its location or arrangement (energy of position). For example,

- in the earth's gravitational field, an object on a hill or water behind a dam have potential energy
- chemical energy is potential energy stored in molecules because of the arrangement of nuclei and electrons in its atoms

Energy can be transformed from one form to another

- kinetic energy of sunlight can be transformed into the potential energy of chemical bonds during photosynthesis

- potential energy in the chemical bonds of ATP (cellular energy) can be transformed into kinetic energy which drives biological processes

C. The energy transformations of life are subject to two laws of thermodynamics

thermodynamics = study of energy transformations

First Law of Thermodynamics = energy can be transferred and transformed, but it cannot be created or destroyed (energy of the universe is constant)

Second Law of Thermodynamics = every energy transfer or transformation makes the universe more disordered (every process increases the **entropy** of the universe)

Entropy = quantitative measure of disorder that is proportional to randomness (designated by the letter S)

Closed systems = collection of matter under study which is isolated from its surroundings

Open Systems = system in which energy can be transferred between the system and its surroundings

The entropy of a system may decrease, but the entropy of the system **plus** its surroundings must always increase. Highly ordered living organisms do not violate the second law because they are always open systems. For example, animals:

- maintain highly ordered structure at the expense of increased entropy of their surroundings
- take in complex high energy molecules as food and extract chemical energy to create and maintain order
- return the surroundings simpler low energy molecules (CO₂ and water) and heat

Energy can be transformed, but part of it is dissipated as heat, which is largely unavailable to do work. Heat energy can [perform work if there is a heat gradient resulting in heat flow from warmer to cooler.

Combining the first and second laws; the *quantity* of energy in the universe is constant but its *quality* is not.

D. Organisms live at the expense of free energy

1. Free energy: a criterion for spontaneous change

Free energy (G) = the system's energy available to do work
Free energy is related to the system's total energy, **enthalpy** (H) and its entropy (S) in the following way:

$$G = H - TS$$

where:

G = Gibbs free energy (energy available to do work)

H = enthalpy or total energy

T = temperature in °K

S = entropy

Free energy (G) = portion of a system's energy available to do work; is the difference between the total energy (enthalpy) and the energy **not** available for doing work (TS)

The maximum amount of usable energy that can be harvested from a particular reaction is the system's free energy change from the initial to the final state. This change in free energy (ΔG) is given by the Gibbs-Helmholtz equation at constant temperature and pressure:

$$\Delta G = \Delta H - T\Delta S$$

where:

ΔG = change in free energy

ΔH = change in total energy (enthalpy)

ΔS = change in entropy

T = absolute temperature in °K (which is °C + 273)

Let's put these thermodynamic concepts into the context of the Gibbs-Helmholtz equation: ΔH or change in total energy (enthalpy) is measured as the *heat of reaction* . You must understand that during a chemical

reaction, reactant molecules must absorb energy for their bonds to break, and that energy is released when bonds form between the rearranged atoms of the products. Consequently, the net energy consumed or released when reactants are converted to products is the *net difference* between the energy consumed to break the chemical bonds of reactants and the energy released from the formation of the products.

Significance of free energy:

- ☑ indicates the maximum amount of a system's energy which is available to do work
- ☑ indicates whether a reaction will occur spontaneously or not
- a spontaneous reaction is one that will occur without additional energy
- in a spontaneous process, ΔG or free energy of a system **decreases** ($\Delta G < 0$)
- a decrease in enthalpy ($-\Delta H$) and an increase in entropy ($+\Delta S$) reduce the free energy of a system and contribute to the spontaneity of a process
- a higher temperature enhances the effect of an entropy change. Greater kinetic energy of molecules tends to disrupt order as the chances for random collisions increase
- when enthalpy and entropy changes in a system have an opposite effect on free energy, temperature may determine whether the reaction will be spontaneous or not (e.g. protein denaturation by increased temperature)
- high energy systems, including high energy chemical systems, are unstable and tend to change to a more stable state with a lower free energy

2. Free Energy and equilibrium

There is a relationship between chemical equilibrium and the free energy change (ΔG) of a reaction:

- as a reaction approaches equilibrium, the free energy of the system decreases (spontaneous and exergonic reaction)
- when a reaction is pushed away from equilibrium, the free energy of the system increases (non-spontaneous and endergonic reaction)
- when a reaction reaches equilibrium, $\Delta G = 0$, because there is no net

change in the system

3. Free energy and metabolism

a. reactions can be classified based upon their free energy changes:

Exergonic reaction = a reaction that proceeds with a net loss of free energy

Endergonic reaction = an energy-requiring reaction that proceeds with a net gain in free energy; a reaction that absorbs free energy from its surroundings

Exergonic Reaction	Endergonic Reaction
chemical products have less free energy than the reactant molecules	products store more free energy than reactants
Reaction is energetically downhill	Reaction is energetically uphill
delta G is negative	delta G is positive

b. Metabolic disequilibrium

Since metabolic reactions are reversible, they have the potential to reach equilibrium.

- at equilibrium, $\Delta G=0$, so the system can do no work
- metabolic disequilibrium is a necessity for life; a cell at equilibrium is dead
- in the cell, these potentially reversible reactions are pulled forward away from equilibrium, because the products of some reactions become the reactants for the next reaction in the metabolic pathway

E. ATP powers cellular work by coupling exergonic and endergonic reactions

ATP is the immediate source of energy that drives most cellular work, which includes:

- **mechanical work** such as beating of cilia, muscle contraction, cytoplasmic flow, and chromosome movement during mitosis and meiosis
- **transport work** such as pumping substances across membranes
- **chemical work** such as the endergonic process of polymerization

1. The structure and hydrolysis of ATP

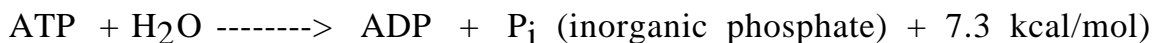
ATP (adenosine triphosphate) = nucleotide with unstable phosphate bonds that the cell hydrolyzes for energy to drive endergonic reactions.

ATP consists of:

- adenine, a nitrogenous base
- ribose, a five-carbon sugar
- chain of three phosphate groups

Unstable bonds between the phosphate groups can be hydrolyzed in an exergonic reaction that releases energy.

- when the terminal phosphate bond is hydrolyzed, a phosphate group is removed producing ADP (adenosine diphosphate)



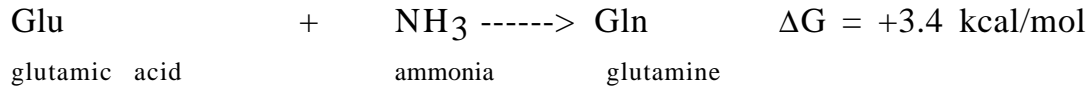
The terminal phosphate bonds of ATP are unstable, so:

- the products of the hydrolysis reactions are more stable than the reactant
- hydrolysis of the phosphate bonds is thus exergonic as the system shifts to a more stable state

2. How ATP performs work

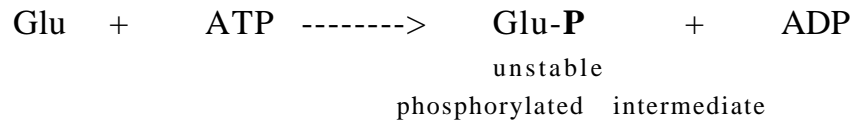
Exergonic hydrolysis of ATP is coupled with endergonic processes by transferring a phosphate group, and its 7.3 kcal/mol of energy to another molecule

- phosphate transfer is enzymatically controlled
- the molecule acquiring the phosphate (phosphorylated or activated intermediate) becomes more reactive

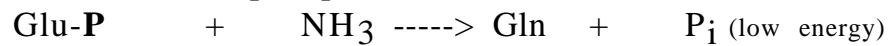


Two step process of energy coupling with ATP hydrolysis:

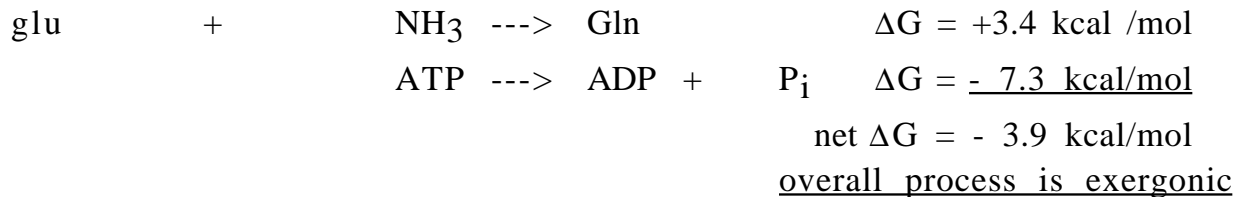
1. hydrolysis of ATP and phosphorylation of glutamic acid:



2. replacement of the phosphate with the reactant ammonia



overall ΔG :



3. The regeneration of ATP

ATP is continually regenerated by the cell.

- process is rapid (10^7 molecules used and regenerated/sec/cell)
 - reaction is endergonic.
- $$\text{ADP} + \text{P} + \text{ENERGY} \text{---} > \text{ATP} \quad \Delta G = +7.3 \text{ kcal/mol}$$
- energy to drive the endergonic regeneration of ATP comes from the exergonic process of cellular respiration

II. Enzymes

A. Enzymes speed up metabolic reactions by lowering energy barriers

Free energy change indicates whether a reaction will occur spontaneously, but does not give information about the speed of reaction.

- A chemical reaction will occur spontaneously if it releases free energy ($-\Delta G$), but it may occur too slowly to be effective in living cells.
- biochemical reactions require enzymes to speed up and control reaction rates

catalyst = chemical agent that accelerates a reaction without being permanently changed in the process, so it can be used over and over.

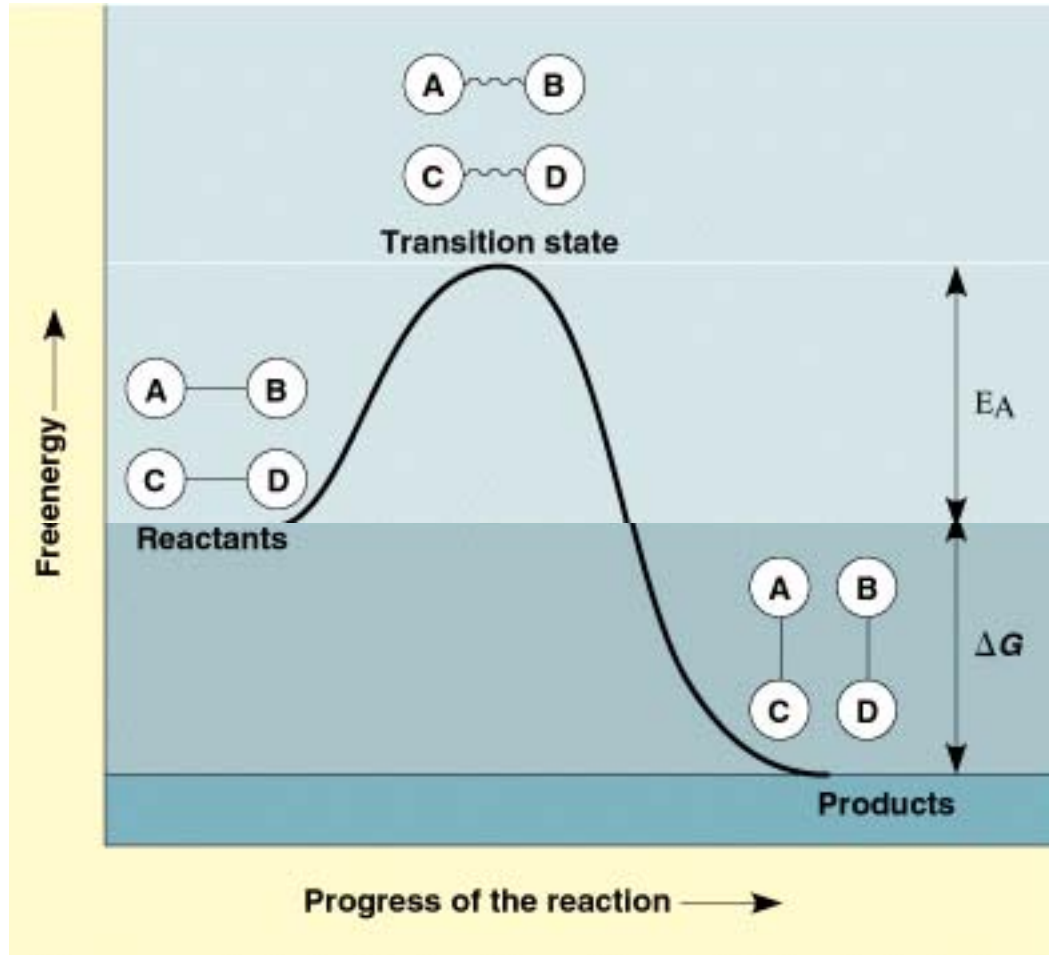
enzymes = biological (organic) catalysts made of proteins

Before a reaction can occur, the reactants must absorb energy to break chemical bonds. This initial energy investment is the activation energy.

Free energy of activation = amount of energy that reactant molecules must absorb to start a reaction (E_A)

Transition state = unstable condition of reactant molecules that have absorbed sufficient energy to react.

Energy Profile of an Exergonic Reaction:



1. Reactants must absorb enough energy (E_A) to reach the transition state (uphill portion of the curve). Usually the absorption of thermal energy from the surroundings is enough to break chemical bonds.
2. Reaction occurs and energy is released as new bonds form (downhill portion of the curve).
3. ΔG for the overall reaction is the difference in free energy between products and reactants. In an exergonic reaction the free energy of the products is less than reactants.

Even though a reaction is energetically favorable, there must be an initial investment of activation energy (E_A).

The breakdown of biological macromolecules is exergonic. However, these molecules react very slowly at cellular temperatures because they cannot absorb enough thermal energy to reach transition state.

In order to make these molecules reactive when necessary, cells use biological catalysts called enzymes, which:

- are proteins
- lower E_A , so the transition state can be reached at cellular temperatures
- do not change the nature of the reaction (ΔG), but only speed up a reaction that would have occurred anyway
- are very selective for which reaction they will catalyze

B. Enzymes are substrate-specific

Enzymes are specific for a particular substrate, and that specificity depends upon the enzyme's three-dimensional shape.

substrate = the substance an enzyme acts on and makes more reactive

- an enzyme binds to its substrate and catalyzes its conversion to product. The enzyme is released in original form

substrate + enzyme \rightarrow enzyme-substrate complex \rightarrow product + enzyme

- the substrate binds to the enzyme's **active site**

Active site = restricted region of an enzyme molecule which binds to the substrate

- is usually a pocket or groove on the protein's surface
- formed with only a few of the enzyme's amino acids
- determines enzyme specificity which is based upon a compatible fit between the shape of an enzyme's active site and the shape of the substrate

- changes its shape in response to the substrate
 - as substrate binds to the active site, it **induces** the enzyme to change its shape
 - this brings its chemical groups into positions that enhance their ability to interact with the substrate and catalyze the reaction

Induced fit = change in the shape of an enzyme's active site, which is induced by the substrate.

C. The active site is an enzyme's catalytic center

The entire enzymatic cycle is quite rapid. Steps in the catalytic cycle of enzymes:

1. substrate binds to the active site forming an ***enzyme-substrate complex***. Substrate is held in the active site by weak interactions (e.g. hydrogen bonds and ionic bonds)
2. ***induced fit*** of the active site around the substrate. Side chains of a few amino acids in the active site catalyze the conversion of substrate to product
3. product departs active site and the enzyme emerges in its original form. Since enzymes are used over and over, they can be effective in very small amounts

Enzymes lower activation energy and speed up reactions by several mechanisms:

- active site can hold two or more reactants in the proper position so they may react
- induced fit of the enzyme's active site may distort the substrate's chemical bonds, so less thermal energy (lower ΔG) is needed to break them during the reaction
- active site might provide a micro-environment conducive to a particular type of reaction (e.g. localized regions of low pH caused by acidic side chains on amino acids at the active site)
- side chains of amino acids in the active site may participate directly in the reaction

The initial substrate concentration partly determines the rate of an enzyme controlled reaction.

- the higher the substrate concentration, the faster the reaction-up to a

limit

- if substrate concentration is high enough, the enzyme becomes ***saturated*** with substrate (the active sites of all enzymes molecules are engaged)
- when an enzyme is saturated, the reaction rate depends upon how fast the active sites can convert substrate to product
- when enzyme is saturated, reaction rate may be increased by adding more enzyme

D. A cell's physical and chemical environment affects enzyme activity

Each enzyme has optimal environmental conditions that favor the most active enzyme conformation

1. Effects of temperature and pH

Optimal temperature allows the greatest number of molecular collisions without denaturing the enzyme

- enzyme reaction rate increases with increasing temperature. Kinetic energy of reactant molecules increases with rising temperature, which increases substrate collisions with active sites
- beyond the optimal temperature, reaction rate slows. The enzyme denatures when increased thermal agitation of molecules disrupts weak bonds that stabilize the active conformation
- optimal temperature range of most human enzymes is 35^o-40^oC

Optimal pH range for most enzymes is pH 6-8

- some enzymes operate best at more extreme pH
- for example, the digestive enzyme, pepsin, found in the acid environment of the stomach has an optimal pH of 2

2. Cofactors

cofactor = small nonprotein molecules that are required for proper enzyme catalysis

- may bind tightly to active site
- may bind loosely to both active site and substrate
- some are inorganic (e.g. metal atoms of zinc, iron or copper)
- some are organic and are called ***coenzymes*** (e.g. vitamins)

3. Enzyme inhibitors

Certain chemicals can selectively inhibit enzyme activity

- inhibition can be irreversible if the inhibitor attaches by covalent bonds
- inhibition can be reversible if the inhibitor attaches weak bonds

Competitive inhibitors = chemicals that resemble an enzyme's normal substrate and compete with it for the active site

- block the active site from the substrate
- if reversible, the effect of these inhibitors can be overcome by increased substrate concentration

Noncompetitive inhibitors = enzyme inhibitors that do not enter the enzyme's active site, but bind to another part of the enzyme molecule

- causes enzyme to change shape so the active site cannot bind substrate
- may act as metabolic poisons (e.g. DDT, many antibiotics)
- selective enzyme inhibition is an essential mechanism in the cell for regulating metabolic reactions

III. The Control of Metabolism

A. Metabolic pathways are regulated by controlling enzyme activity

Metabolic control often depends on allosteric regulation

1. Allosteric regulation

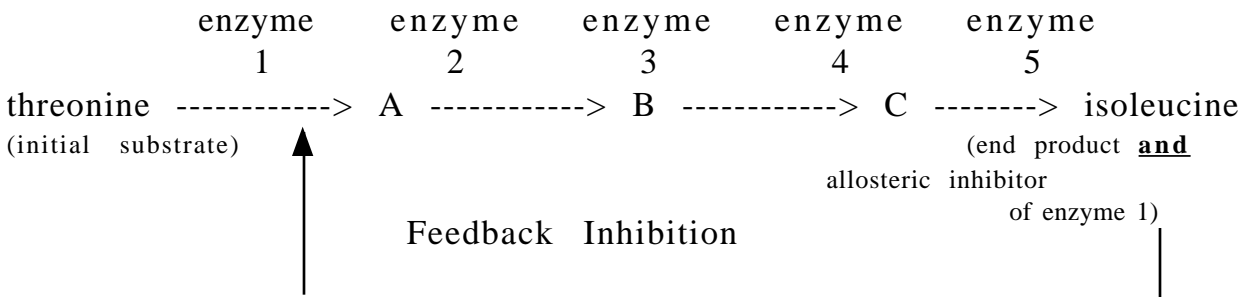
allosteric site = specific receptor site on some part of the enzyme molecule other than the active site

- most enzymes with allosteric sites have two or more polypeptide chains, each with its own active site. Allosteric sites are often located where the subunits join
- allosteric enzymes have two conformations, one catalytically active and the other inactive
- binding of an activator to an allosteric site stabilizes the active conformation

- binding of the *inhibitor* (noncompetitive inhibitor) to an allosteric site stabilizes the inactive conformation
- enzyme activity changes continually in response to changes in the relative proportions of activators and inhibitors (e.g. ATP/ADP)
- subunits may interact so that a single activator or inhibitor at one allosteric site will affect the active sites of the other subunits

2. Feedback inhibition

feedback inhibition = regulation of a metabolic pathway by its end product, which inhibits an enzyme within the pathway. For example:



Prevents the cell from wasting chemical resources by synthesizing more product than is necessary.

3. Cooperativity

Substrate molecules themselves may enhance enzyme activity
cooperativity = the phenomenon where substrate binding to the active site of one subunit induces a conformational change that enhances substrate binding at the active sites of the other subunits.

B. The localization of enzymes within the cell helps order metabolism

Cellular structure orders and compartmentalizes metabolic pathways.

- some enzymes and enzyme complexes have fixed locations in the cell because they are incorporated into a membrane
- other enzymes and their substrates may be localized within

membrane-enclosed eukaryotic organelles (e.g. chloroplasts and mitochondria)