Biology 112 – Chapter 8: Energy, Enzymes, and Catalysis

Metabolism can be divided into two types of activities:

- **Anabolic** reactions link simple molecules together to make complex ones; these are energy-storing reactions → they require energy
- **Catabolic** reactions breaks down complex molecules into simpler ones → they release energy

→ Cells must constantly acquire energy from their environment; energy released by the breakdown of catabolic reactions is used to drive anabolic reactions

What drives energy conversions?

Not the energy content because:

→ First Law of Thermodynamics: during any conversion of energy, the total initial energy equals the total final energy → energy is neither created nor destroyed

But the drive of energy to become evenly distributed or dispersed

Second Law of Thermodynamics: Energy spontaneously disperses from being localized to become spread out if it is not hindered from doing so (entropy increases)

→ Energy conversions, e.g. chemical reactions only occur if energy disperses in the universe - **dispersing energy is the driving force for energy conversions**

→ Another way to put it: energy transformations always result in a state of higher probability (**a more disordered state)**

To judge biochemical reactions, we need an equation that gives us the amount of energy released to drive a reaction (change in entropy or free energy) → the total energy is called **enthalpy** and the useable energy that can do work is called **free energy**. The unusable energy is called **entropy**

How can a cell release free energy (drive a chemical reaction)?

→ By dispersing energy/increasing entropy; how?

1) With a chemical reactions creating disorder in the cell (digesting a polymer)
2) With a chemical reaction releasing hear with generates disorder/disperses energy in the surrounding (environment)
   → Both reactions require the constant uptake of energy-rich molecules

Total Free Energy G = H – TS

(H = enthalpy = **heat**; S = entropy = **disorder**; T = absolute temperature)

→ We don't want to know the total free energy of a molecule, but the change associated with a specific chemical reaction. This change can be measured in calories or joules

Free energy change $\Delta G = \Delta H - T\Delta S$

If the change in G is negative, **energy is released/dispersed** → disorder is created

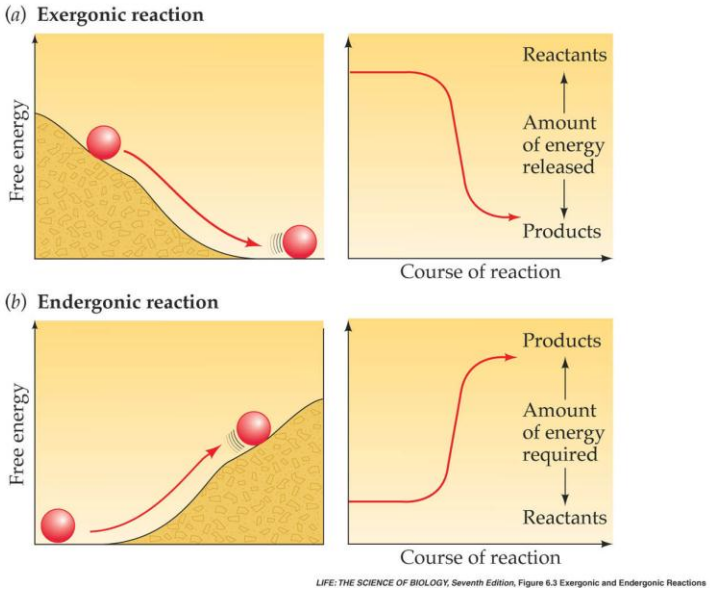
If the change in G is positive, **energy is required**

Only four types of reactions:

1) Heat is released and disorder is increased → ALWAYS SPONTANEOUS (**exergonic**)
   i. Most catabolic reactions

   ii. The change in G is the actual amount of energy dispersed during a chemical reaction
2) Heat is released, but disorder decreased → only spontaneous below a certain temperature; e.g. denatured/native protein, lipid bilayers vs. individual lipids
   i. This reaction occurs only (-ΔG) if the heat released is greater than the increase in order

3) Heat is used, but disorder increases → spontaneous above a certain temperature; e.g. dissolving NaCl in water
4) Heat is used and disorder decreases → NEVER SPONTANEOUS (**endergonic**)
    i. Most anabolic reactions
    ii. Basically, the ΔG calculations are good for finding out which reactions can occur and which cannot
    iii. How do endergonic (anabolic) reactions occur? ➔ by coupling endergonic and exergonic reactions



LIFE: THE SCIENCE OF BIOLOGY, Seventh Edition, Figure 6.3 Exergonic and Endergonic Reactions

Two more complications of thermodynamics

- In principle, all reactions are reversible
- Adding more A speeds up the forward reactions; adding more B speeds up the reverse reaction (A ↔ B)
- At the point of chemical equilibrium, the relative concentrations of A and B are such that **forward and reverse reactions take place at the same rate** → ΔG = 0

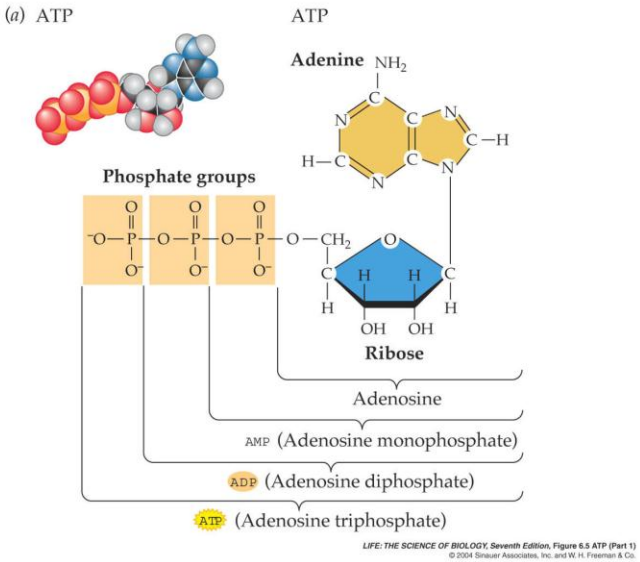
At equilibrium: ΔG = 0

The standard free energy (ΔG°) applies to 25°C and 1M concentration of all reactants and products. Therefore, **the concentrations have to be taken into account in most cases to calculate the actual ΔG**

➔ The change in free energy for a reaction is related directly to its point of equilibrium → the further toward completion the point of equilibrium lies, the more free energy is released

Transferring Energy in Cells

- All living cells use adenosine triphosphate (ATP) for capture, transfer, and storage of energy; ATP is a also a nucleotide that can be converted into a building block for nucleic acids
- Some of the free energy released by exergonic reactions is captured in ATP from ADP and inorganic phosphate → the ATP can than be hydrolyzed at other sites in the cell to release free energy to drive endergonic reactions



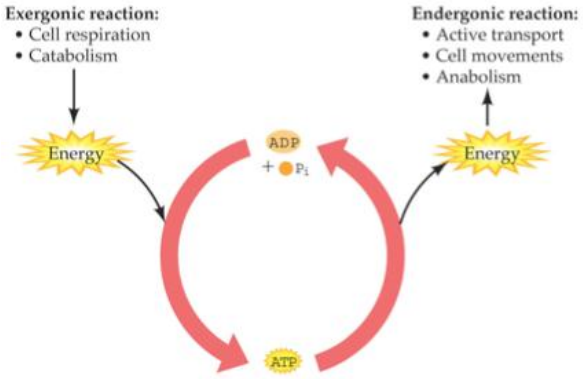
ATP can hydrolyze to yield ADP and an inorganic phosphate ion (P_i) → **exergonic**

$ATP + H_2O \rightarrow ATP + P_i$ + free energy

The reaction is exergonic (ΔG = -12kcal/mole) for two reasons:

- The energy of the P-O bond is much higher than the H-O bond that forms after hydrolysis
- Because the phosphates are negatively charged and so repel each other, energy is required to get them near each other to bond; some of this energy is conserved when the third phosphate is attached

ADP is constantly removed either by reforming ATP or by hydrolysis to AMP (ΔG = -7.3kcal/mole)

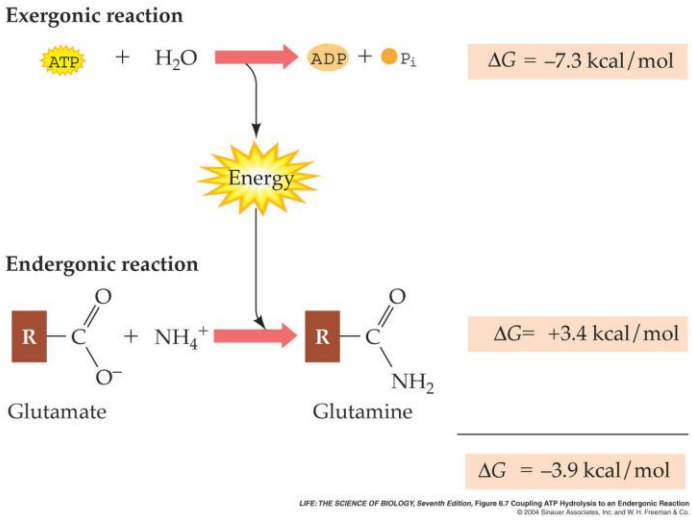


Coupled Reactions

→ ATP is so particularly useful as the energy current because its ΔG is intermediate between what you gain in respiration and what you expend in anabolism

Coupling of exergonic and endergonic reactions is very common in metabolism:

- Free energy is captured and retained in the P-O bonds of ATP
- ATP then diffuses to another site in the cell, where its hydrolysis releases the free energy to rive an endergonic reaction



Two more complications of thermodynamics

- The direction of a reaction can be predicted if ΔG is known, but not the rate of the reaction. Many exergonic reactions occur immeasurably slow
- Exergonic reactions proceed only after the addition of a small amount of added energy, called the **activation energy**
    - In a chemical reaction, activation energy is the energy need to put molecules into a transition state

Catalysis

- A **catalyst** is any substance that speeds up a chemical reaction without itself being used up
- Most biological catalysts are proteins called enzymes
- Exergonic reactions often are initiated by the addition of heat, which increases the average kinetic energy of molecules
- **Enzymes solve the problem by lowering the activation energy**
    - Enzymes bind to specific reactant molecules called substrates
    - Substrates bind to a particular site on the enzyme surface called the active site, where catalysis takes places
    - Enzymes are highly specific
    - In an enzyme catalyzed reaction, the reactants = **substrates** → molecules bind to a particular site on the enzyme, called the activation site, where catalysis takes place
    - Enzymes catalyze reactions by using one or of the following mechanisms:
        - Orienting substrates: substrates may not be oriented properly to interact when they collide; bring together specific atoms so that the bonds can form
        - Inducing strain in the substrates: cause bonds in the substrate to stretch, putting it in an unstable transition state = more reactive
        - Adding charges to substrates: makes the substrate more chemically reactive
    - Some enzymes require **cofactors** in order to function → these can be:
        - Metal ions (zinc, copper)
        - Small organic molecules temporarily binding → *coenzyme*
        - Small organic molecules that are permanently bound to the protein (heme) → *prosthetic group*
    - Enzymes are saturated when all binding sites are occupied; maximum rate = turnover from 1 molecule/second to lysosome to 40 million/second for catalase

Regulation of metabolic pathways → end product or **feedback inhibition** regulates the whole pathway

Principles governing metabolic pathways:

- Each reaction in the pathway is catalyzed by a specific enzyme
- The operation of each metabolic pathway can be regulated by the activities of key enzymes

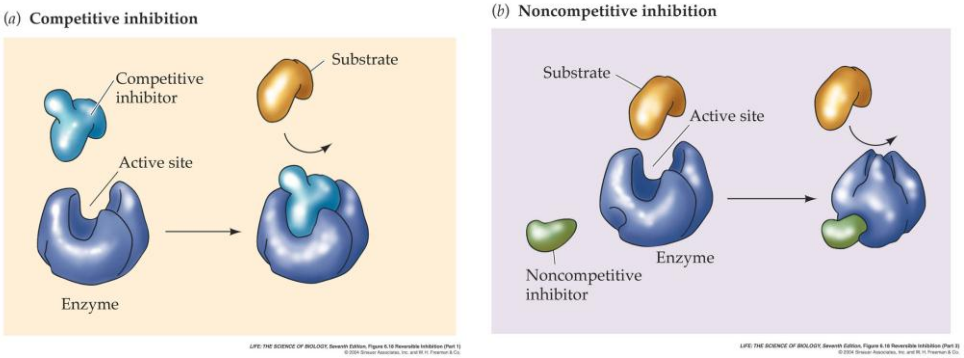
Multiple feedback control allows cells to adjust the ratio of different compounds (e.g. amino acids)

Enzyme Regulation

- Enzyme activity can be inhibited by natural and artificial binders
- Naturally occurring inhibitors regulate metabolism
- Irreversible inhibition occurs when the inhibitor destroys the enzyme's ability to interact with its normal substrate

DIPF, a nerve gas, irreversibly inhibits acetylcholinesterase

- When an inhibitor binds reversibly to an enzyme's active site, it competes with the substrate for the binding site and is called a **competitive inhibitor**
- When an inhibitor binds reversibly to a site distinct from the active site, it is called a **noncompetitive inhibitor or negative allosteric regulator**; they act by changing the shape of the enzyme in such a way that the active site can no longer bind to the substrate
- Allosteric regulators can stabilize the inactive for as described above, **but they can also stabilize the active form (positive allosteric regulator)** → Allosteric regulation is much more efficient than competitive inhibition



- **Cooperative** allosteric transition – occurs with two or more subunits
  - When one binding site is occupied, it changes the other(s) so that they bind additional substrate molecules more readily
  - When a multi-subunit enzyme is allosterically regulated, enzyme activation or inhibition occurs very quickly, like in a switch. The enzyme becomes very sensitive to regulator concentration

  The first step in a metabolic pathway is nearly always a multi-subunit enzyme negatively regulated by cooperative allostery