## Introduction to Bioenergetics

## Reference: Lehninger, Nelson & Cox (Edition 5): Chapter: 13

1. Living cells constantly perform work. They require energy for maintaining their highly organized structures, synthesizing cellular components, generating electric currents, and many other processes.

2. Bioenergetics is the quantitative study of energy relationships and energy conversions in biological systems. Biological energy transformations obey the laws of thermodynamics.

3. All chemical reactions are influenced by two forces: the tendency to achieve the most stable bonding state (for which enthalpy, H is a useful expression) and the tendency to achieve the highest degree of randomness expressed as entropy, S. The net driving force in a reaction is ΔG, the free-energy change, which represents the net effect of these two factors: G = H – TΔS

4. The standard transformed free-energy change, ΔG'o, is a physical constant that is characteristic for a given reaction and can be calculated from the equilibrium Constant for the reaction: Δ G'o: -RT lnK’eq The actual free-energy change, ΔG, is a variable that depends on Δ G'o and on the concentrations of reactants and products:

Δ G = ,Δ G'o + RTln ([products]/[reactants]).

When Δ G is large and negative, the reaction tends to go in the forward direction; when ΔG is large and positive, the reaction ends to go in the reverse direction; and when Δ G : 0, the system is at equilibrium. The free-energy change for a reaction is independent of the pathway by which the reaction occurs.Free-energy changes are additive; the net chemical reaction that results from successive reactions sharing a common intermediate has an overall free-energy change that is the sum of the ΔG values for the individual reactions.

**1. State functions:**

- ✓ In thermodynamics, a state function or function of state or point function is a function defined for a system relating several state variables or state quantities that depends only on the current equilibrium state of the system, for example a gas, a liquid, a solid, crystal, or emulsion.
- ✓ State functions do not depend on the path by which the system arrived at its present state. A state function describes the equilibrium state of a system and thus also describes the type of system. For example, a state function could describe an atom or molecule in a gaseous, liquid, or solid form; a heterogeneous or homogeneous mixture; and the amounts of energy required to create such systems or change them into a different equilibrium state.
- ✓ For example, internal energy, enthalpy, and entropy are state quantities because they describe quantitatively an equilibrium state of a thermodynamic system, irrespective of how the system arrived in that state. In contrast, mechanical work and heat are process quantities or path functions, because their values depend on the specific transition (or path) between two equilibrium states. Heat in certain discrete amounts can describe a certain state function, such as enthalpy, but in general, does not truly describe the system unless it is defined as the state function of a certain system, and thus enthalpy is described by an amount of heat. This can also apply to entropy when heat is compared to temperature.

2. **Equilibrium constant** of a chemical reaction is the value of its reaction quotient at chemical equilibrium, a state approached by a dynamic chemical system after sufficient time has elapsed at which its composition has no measurable tendency towards further change. For a given set of reaction

conditions, the equilibrium constant is independent of the initial analytical concentrations of the reactant and product species in the mixture. Thus, given the initial composition of a system, known equilibrium constant values can be used to determine the composition of the system at equilibrium. However, reaction parameters like temperature, solvent, and ionic strength may all influence the value of the equilibrium constant.

## 3. Coupled Reactions

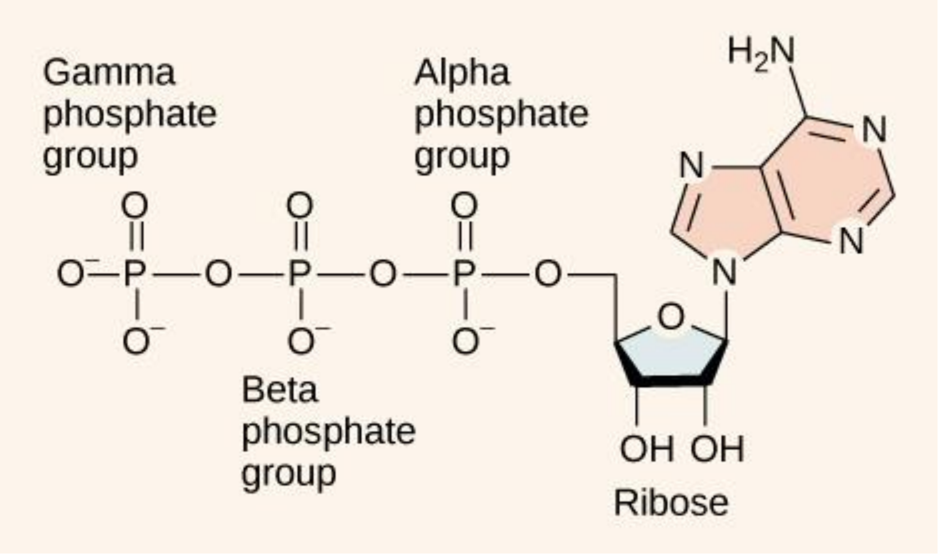
Two or more reactions in a cell sometimes can be coupled so that thermodynamically unfavourable reactions and favorable reactions are combined to drive the overall process in the favourable direction. In this circumstance the overall free energy is the sum of individual free energies of each reaction.

## 4. ATP cycle and coupled reactions

A cell can be thought of as a small, bustling town. Carrier proteins move substances into and out of the cell, motor proteins carry cargoes along microtubule tracks, and metabolic enzymes busily break down and build up macromolecules. Even if they would not be energetically favorable (energy-releasing, or exergonic) in isolation, these processes will continue merrily along if there is energy available to power them (much as business will continue to be done in a town as long as there is money flowing in). However, if the energy runs out, the reactions will grind to a halt, and the cell will begin to die. Energetically unfavorable reactions are “paid for” by linked, energetically favorable reactions that release energy. Often, the "payment" reaction involves one particular small molecule: adenosine triphosphate, or ATP.

### ATP structure and hydrolysis

Adenosine triphosphate, or ATP, is a small, relatively simple molecule. It can be thought of as the main energy currency of cells, much as money is the main economic currency of human societies. The energy released by hydrolysis (breakdown) of ATP is used to power many energy-requiring cellular reactions. Structurally, ATP is an RNA nucleotide that bears a chain of three phosphates. At the center of the molecule lies a five-carbon sugar, ribose, which is attached to the nitrogenous base adenine and to the chain of three phosphates. The three phosphate groups, in order of closest to furthest from the ribose sugar, are labeled alpha, beta, and gamma. ATP is made unstable by the three adjacent negative charges in its phosphate tail, which "want" very badly to get further away from each other. The bonds between the phosphate groups are called phosphoanhydride bonds, and you may hear them referred to as “high-energy” bonds.

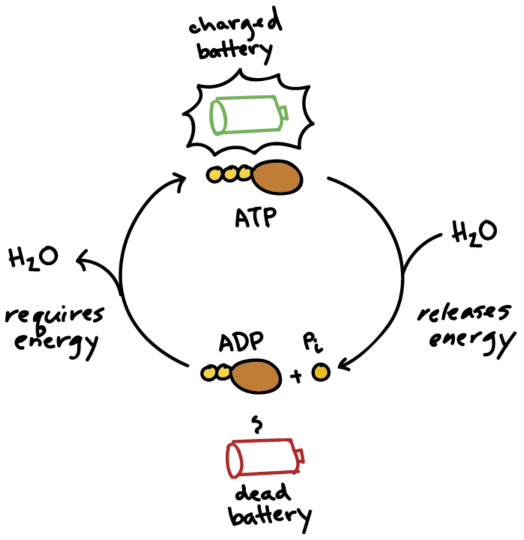


All this really means is that an appreciable amount of energy is released when one of these bonds is broken in a hydrolysis (water-mediated breakdown) reaction. ATP is hydrolyzed to ADP in the following reaction:

**Hydrolysis of ATP**

ATP + H2O = ADP + Pi + Energy

Like most chemical reactions, the hydrolysis of ATP to ADP is reversible. The reverse reaction, which regenerates ATP from ADP +Pi, requires energy. Regeneration of ATP is important because cells tend to use up (hydrolyze) ATP molecules very quickly and rely on replacement ATP which is being constantly produced.



You can think of ATP and ADP as being sort of like the charged and uncharged forms of a rechargeable battery (as shown above). ATP, the charged battery, has energy that can be used to power cellular reactions. Once the energy has been used up, the uncharged battery (ADP) must be recharged before it can again be used as a power source. The ATP regeneration reaction is just the reverse of the hydrolysis reaction:

Energy + ADP + Pi = ATP + H2O

a bunch of free energy is released during ATP hydrolysis. ΔG for the hydrolysis of one mole of ATP into ADP and \text Pi is −7.3 kcal/mol under standard conditions (1M concentration, $25^0$C, pH=7) while ΔG for the hydrolysis of one mole of ATP in a living cell is almost double the value at standard conditions, around -14Kcal/mol (-57KJ/mol).

**Reaction coupling**

How is the energy released by ATP hydrolysis used to power other reactions in a cell?

In most cases, cells use a strategy called reaction coupling, in which an energetically favorable reaction (like ATP hydrolysis) is directly linked with an energetically unfavorable (endergonic) reaction. The linking often happens through a shared intermediate, meaning that a product of one reaction is “picked up” and used as a reactant in the second reaction.

When two reactions are coupled, they can be added together to give an overall reaction, and the ΔG of this reaction will be the sum of the ΔG values of the individual reactions. As long as the overall ΔG is negative, both reactions can take place. Even a very endergonic reaction can occur if it is paired with a very exergonic one (such as hydrolysis of ATP). For instance, we can add up a pair of generic reactions coupled by a shared intermediate, B, as follows:

$A \longrightarrow B$ $\Delta G = X$

$\underline{+B \longrightarrow C + D}$ $\Delta G = Y$

$A \longrightarrow C + D$ $\Delta G = X + Y$

Intermediate, B, doesn't appear in the overall coupled reaction. This is because it appears as a both a product and a reactant, so two Bs cancel each other out when the reactions are added.

### ATP in reaction coupling

When reaction coupling involves ATP, the shared intermediate is often a phosphorylated molecule (a molecule to which one of the phosphate groups of ATP has been attached).

**Eg.1**

Glucose + Fructose $\longrightarrow$ Sucrose $\Delta G = +27 kJ/mol$

ATP + H2O = ADP + Pi + Energy $\Delta G = -30 kJ/mol$

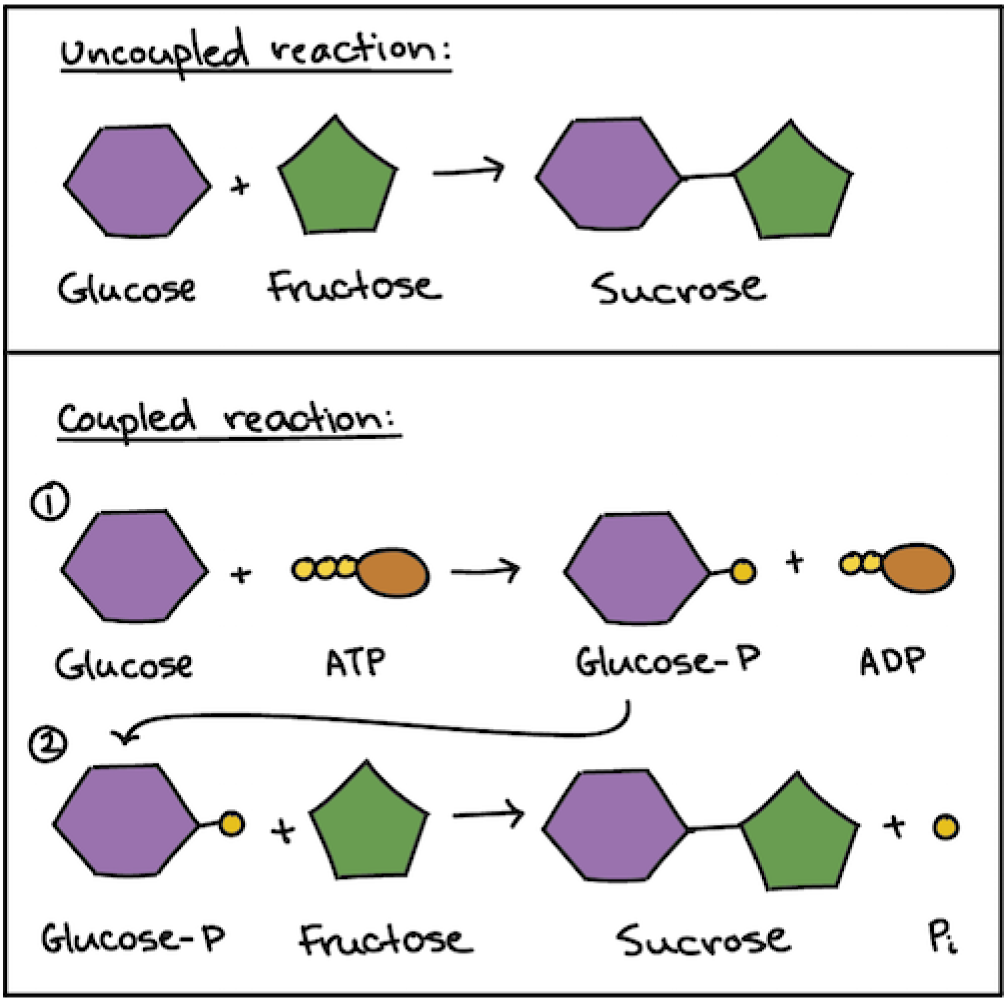
Glucose + Fructose + ATP + H2O = Sucrose + ADP + Pi + Energy $\Delta G = -3 kJ/mol$

### How is the energy released in ATP hydrolysis channelled into the production of a sucrose molecule?

As it turns out, there are actually two reactions that take place, not just one big reaction, and the product of the first reaction acts as a reactant for the second.

In the first reaction, a phosphate group is transferred from ATP to glucose, forming a phosphorylated glucose intermediate (glucose-P). This is an energetically favourable (energy-releasing) reaction because ATP is so unstable, i.e., really "wants" to lose its phosphate group.

In the second reaction, the glucose-P intermediate reacts with fructose to form sucrose. Because glucose-P is relatively unstable (thanks to its attached phosphate group), this reaction also releases energy and is spontaneous.



This example shows how reaction coupling involving ATP can work through phosphorylation, breaking a reaction down into two energetically favoured steps connected by a phosphorylated (phosphate-bearing) intermediate. This strategy is used in many metabolic pathways in the cell, providing a way for the energy released by converting ATP to ADP to drive other reactions forward.

## **Phosphoryl Group Transfer and ATP**

ATP is the chemical link between catabolism and anabolism. It is the energy currency of the living cell. The exergonic conversion of ATP to ADP and Pi, or to AMP and PPi, is coupled to many endergonic reactions and processes. Direct hydrolysis of ATP is the source of energy in some processes driven by conformational changes, but in general it is not ATP hydrolysis but the transfer of a phosphoryl, pyrophosphoryl, or adenylyl group from ATP to a substrate or enzyrne that couples the energy ofATP breakdown to endergonic transformations of substrates. Through these group transfer reactions, ATP provides the energy for anabolic reactions, including the synthesis of information macromolecules, and for the transport of molecules and ions across membranes against concentration gradients and electrical potential gradients. To maintain its high group transfer potential, ATP concentration must be held far above the equilibrium concentration by energy-yielding reactions of catabolism. Cells contain other metabolites with large, negative, free energies of hydrolysis, including phosphoenolpyruvate1, ,3-bisphosphoglycerataen, d-phosphocreatine. These high-energy compounds, Iike ATP have a high phosphoryI group transfer potential. Thioesters also have high free energies of Hydrolysis. Inorganic polyphosphate present in all cells, may serve as a reservoir of phosphoryl groups with high group transfer potential.

## Redox Reactions

In many organisms, a central energy-conserving process is the stepwise oxidation of glucose to CO2, in which some of the energy of oxidation is conserved in ATP as electrons are passed to O2. Biological oxidation-reduction reactions can be described in terms of two half-reactions, each with a characteristic standard reduction potential, E'o. When two electrochemical half-cells, each containing the components of a half-reaction, are connected, electrons tend to flow to the half-cell with the higher reduction potential. The strength of this tendency is proportional to the difference between the two reduction potentials (AE) and is a function of the concentrations of oxidized and reduced species. The standard free-energy change for an oxidation-reduction reaction is directly proportional to the difference in standard reduction potentials of the two half-cells: $\Delta G'0 = -nJ\Delta E'0$. Many biological oxidation reactions are dehydrogenations in which one or two hydrogen atoms: (H+ e-) are transferred from a substrate to a hydrogen acceptor. Oxidation-reduction reactions in living cells involve specialized electron carriers. NAD and NADP are the freely diffusible coenzymes of many dehydrogenases. Both NAD+ and NADP+ accept two electrons and one proton. FAD and FMN, the flavin nucleotides, serve as tightly bound prosthetic groups of flavoproteins. They can accept either one or two electrons and one or two protons. Flavoproteins also as light receptors in cryptochromes and photolyases.