Thermodynamics of Biological Systems
Thermodynamics: A collection of laws and principles describing the flow and interchange of heat, energy and matter in a system of interest.

Thermodynamics allows us to determine whether a chemical process or reaction will occur spontaneously (in the direction written).

Thermodynamics does not tell us about rates (that’s kinetics!).
First Law of Thermodynamics:

The total amount of energy in an isolated system is conserved, though the form of the energy may change.

Second Law of Thermodynamics:

In all natural processes, the entropy of the universe increases.
Thermodynamic Concepts: The system is the portion of the universe we are concerned with; everything else is the surroundings. The system + surroundings = universe

Closed system: No exchange of energy or matter
Isolated system: Energy exchange occurs

Open system: Energy or matter exchange occurs

Never at equilibrium!!
3 Thermodynamic quantities describe energy changes in living systems:

1. **Gibbs Free Energy** ($G$):

The amount of energy capable of doing work during a reaction at constant temperature and pressure.

When the system changes to possess less energy (free energy is released) then the free energy change ($\Delta G$) is negative and the reaction is exergonic (**SPONTANEOUS!**).
2. **ENTHALPY:** The heat content of a system \((H)\). When a chemical reaction releases heat, it is exothermic and has a negative \(\Delta H\).

3. **ENTROPY:** Randomness or disorder of a system \((S)\). When the products of a reaction are less complex and more disordered than the reactants, the reaction proceeds with a gain in entropy (positive \(\Delta S\)).
Entropy, enthalpy, and the Gibbs free energy are all **state functions**: they depend only on the nature of the reactants and products and are independent of the pathway by which the reaction occurs.
Gibbs Free Energy, Enthalpy and Entropy are related by:

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

- $T$ is in absolute temperature
- By convention, $\Delta S$ has a positive sign when entropy increases and $\Delta H$ has a negative sign when heat is released. Either of these conditions, typical of a spontaneous process, will make $\Delta G$ negative; so for a spontaneous process $\Delta G$ is negative!!!!
The standard free energy change is related to the Keq of a reaction:

• At equilibrium the rates of forward and reverse reactions are equal and no further change in the system occurs. When a system is not at equilibrium, the tendency to move toward equilibrium represents a driving force, the magnitude of which is ΔG.

• $\Delta G^o = \text{Free energy change under standard conditions: } 298K; \text{ reactants and products present at } 1M.$
Biochemical reactions occur at pH = 7 so we define $\Delta G^\circ$.

Relationship between $\Delta G^\circ$ and $K_{eq}$:

$$\Delta G^\circ = -2.303RT \log K_{eq}$$

$T=$ temperature in K;
$R=$ gas constant (8.314 J/mol x K)
$\Delta G^\circ' = -2.303RT \log Keq$

- If $Keq = 1.0$ (reaction at equilibrium) then $\Delta G$ is $= 0$!

- If $Keq$ is greater than 0, $\Delta G$ is negative (process is spontaneous)

- If $Keq$ is less than 0, $\Delta G$ is positive (process is NOT spontaneous and will proceed in the reverse direction)
Standard Free Energy Changes Are Additive!

\[ \Delta G^o' \]

Glucose + Pi $\rightarrow$ Glucose-6-phosphate + $H_2O$: 13.8 kJ/mol

ATP + $H_2O$ $\rightarrow$ ADP + Pi $\rightarrow$ −30.5 kJ/mol

ATP + Glucose $\rightarrow$ ADP + glucose-6-phosphate $\rightarrow$ −16.7 kJ/mol

Energy stored in the bonds of ATP is used to drive the synthesis of glucose-6-phosphate!
Other high energy phosphate compounds are hydrolyzed with a large $\Delta G$. These include:

1) acyl phosphates

$$\text{CH}_3\text{-C-OPO}_3^{-2} \quad \Delta G^{0'} = -43.3$$

2) enol phosphates

$$\text{CH}_2\text{=}\text{C-CH}_2\text{COO-} \quad \text{(PEP)} \quad \Delta G^{0'} = -62.2$$

3) phosphoguanidines

$$\text{H}_2\text{N=}\text{C-NH-OPO}_3^{-2} \quad \text{R-N-X}$$

$$\begin{cases} 
R = \text{CH}_2\text{COO-} \\
X = \text{CH}_3
\end{cases} \quad \text{phosphocreatine} \quad \Delta G^{0'} = -43.3$$
4) Thioesters such as acetyl CoA: \( \Delta G^{0'} = -31.5 \) kJ/mol

All of these compounds have a high phosphate group transfer potential.

They can transfer their phosphate group directly to ADP to form ATP. This is substrate level phosphorylation.
Another way of generating ATP is through the formation and discharge of a proton gradient across a membrane that is coupled to synthesis of ATP from ADP and Pi (oxidative phosphorylation and photophosphorylation).

A third way to generate ATP is through the action of adenylate kinase:

\[
\text{AMP} + \text{ATP} \rightarrow 2 \text{ADP}
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