Chem 352 - Lecture 3
The Energetics of Life

Question of the Day: *"What makes Free Energy free?"*

Introduction

Introduction

In this lecture we will be looking quantitatively at how living systems obtain, store, and utilize energy .

- ***Bioenergetics*** is the study of energy transformations (thermodynamics) in biological systems.
- We will be using the following thermodynamic state functions,
  - Enthalpy, *H*
  - Entropy, *S*
  - Free Energy, *G*

These are all *state functions*, meaning their values will depend only on the initial and and final states of the system, *viz.*,

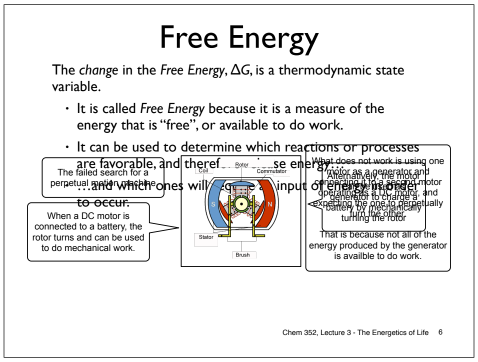
$$\Delta H = H_{final} - H_{initial}$$

Introduction

Topics covered will include,

- Free Energy
- Free Energy and the Second Law of Thermodynamics in an open system
- The relationships between Free Energy, the equilibrium state, and the reactant and product concentrations when not at equilibrium.
- Free Energy considerations in biological systems

Free Energy



Free Energy

The *change* in the *Free Energy*, ΔG, is a thermodynamic state variable.

- It is called *Free Energy* because it is a measure of the energy that is “free”, or available to do work.
- It can be used to determine which reactions or processes are favorable, and therefore release energy…
- …and which ones will require an input of energy in order to occur.

The failed search for a perpetual motion machine

When a DC motor is connected to a battery, the rotor turns and can be used to do mechanical work.

What does not work is using one motor as a generator and connecting it to a second motor operating as a DC motor, and expecting the one to perpetually turn the other.

That is because not all of the energy produced by the generator is availble to do work.

Alternatively, the motor can be used as a generator to charge a battery by mechanically turning the rotor

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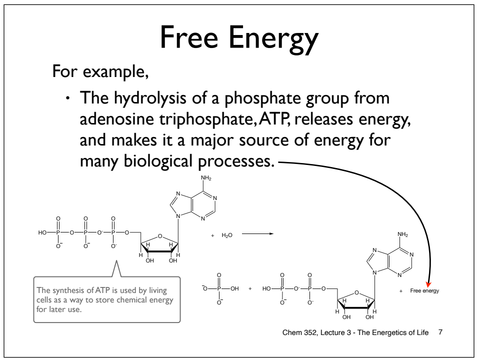

Free Energy

For example,

- The hydrolysis of a phosphate group from adenosine triphosphate, ATP, releases energy, and makes it a major source of energy for many biological processes.

The synthesis of ATP is used by living cells as a way to store chemical energy for later use.

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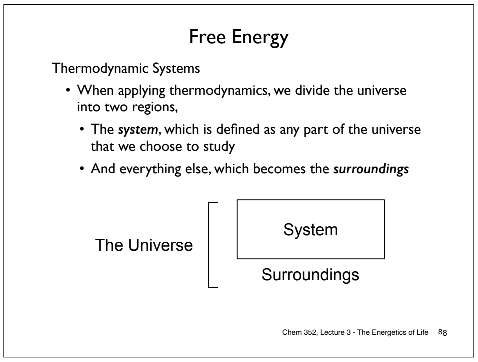

Free Energy

Thermodynamic Systems

- When applying thermodynamics, we divide the universe into two regions,
  - The ***system***, which is defined as any part of the universe that we choose to study
  - And everything else, which becomes the ***surroundings***

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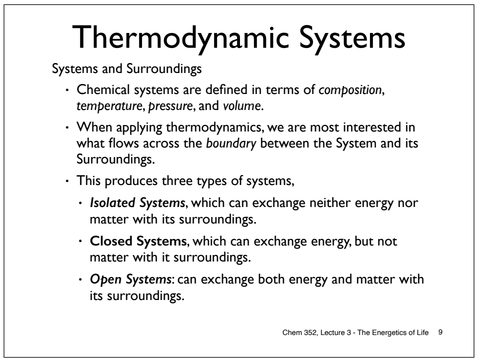

Thermodynamic Systems

Systems and Surroundings

- Chemical systems are defined in terms of *composition*, *temperature*, *pressure*, and *volume*.
- When applying thermodynamics, we are most interested in what flows across the *boundary* between the System and its Surroundings.
- This produces three types of systems,
  - ***Isolated Systems***, which can exchange neither energy nor matter with its surroundings.
  - **Closed Systems**, which can exchange energy, but not matter with it surroundings.
  - ***Open Systems***: can exchange both energy and matter with its surroundings.

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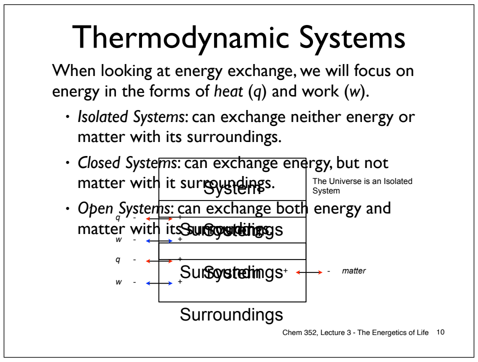

Thermodynamic Systems

When looking at energy exchange, we will focus on energy in the forms of *heat* (*q*) and work (*w*).

- *Isolated Systems*: can exchange neither energy or matter with its surroundings.
- *Closed Systems*: can exchange energy, but not matter with it surroundings.
- *Open Systems*: can exchange both energy and matter with its surroundings.

The Universe is an Isolated System

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Free Energy

The First Law of Thermodynamics and Enthalpy

- Thermodynamics is defined in terms of Laws
- The **First Law of Thermodynamics** states that *the total energy of an isolated system is a constant.*
- Since the universe is an isolated system, this means that energy can be converted form one form to another, but it ***can be neither created nor destroyed***.
  - This also means for closed system, the change in energy for the system (ΔU_{system}) is equal to the negative change in energy for the surroundings ($-\Delta U_{surroundings}$)

$$\Delta U_{system} = -\Delta U_{surroundings}$$

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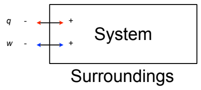
Free Energy

The First Law of Thermodynamics and Enthalpy

- There is another way to state this for a ***closed system***



$$\Delta U_{system} = q + w$$

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Free Energy

The First Law of Thermodynamics and Enthalpy

- If we limit ourselves to ***pressure-volume*** work, under conditions of constant pressure.

$$w = -P\Delta V$$

$$\Delta U_{system} = q_P - P\Delta V$$

- The state variable ***Enthalpy*** (***H***) is defined as the heat absorbed by a system under conditions of constant pressure

$$\Delta H_{system} = q_P$$

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Free Energy

The First Law of Thermodynamics and Enthalpy

- The energy content of the foods we eat can be correlated to the heat that is released when they undergo a combustion reaction.
- The reactions that living system use to extract energy from the foods we eat are primarily combustion-like oxidation reactions.
  - For example, the conversions of the fatty acid, Palmitic acid, to CO_2 and H_2O.

$$\mathrm{CH_3(CH_2)_{14}COOH\ (solid) + 23\,O_2(gas) \longrightarrow 16\,CO_2(gas) + 16\,H_2O\ (liquid)}$$

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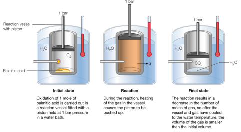
Free Energy

- These heats can be measured using a calorimeter.

Constant Pressure Calorimeter



Initial state
Oxidation of 1 mole of palmitic acid is carried out in a reaction vessel fitted with a piston held at 1 bar pressure in a water bath.

Reaction
During the reaction, heating of the gas in the vessel causes the piston to be pushed up.

Final state
The reaction results in a decrease in the number of moles of gas, so after the vessel and gas have cooled to the water temperature, the volume of the gas is smaller than the initial volume.

$$\Delta H = q_P$$

- The one shown here does this at constant pressure

$$\mathrm{CH_3(CH_2)_{14}COOH\ (solid) + 23\,O_2(gas) \longrightarrow 16\,CO_2(gas) + 16\,H_2O\ (liquid)}$$

$$\Delta H = q_P = -9977.6\ \frac{kJ}{mol}$$

These heats are listed as dietary Calories on food packaging.
1dietary Calorie = 1,000 thermodynamic calories
1 cal = heat needed to raise the temperature of 1 g of H_2O by 1°C

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Free Energy

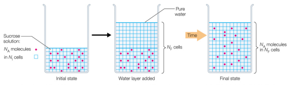
The Driving Force for a Process

- While Δ*H* can provide us with a measure of how much energy is absorbed or release in a process, it cannot tell us whether a process is favorable or not.
- **Concept**: *Reversible processes always occur near a state of equilibrium; irreversible processes* start some distance from equilibrium and *drive towards equilibrium.*
  - A process is ***favorable*** if it is irreversible and moving in the forward direction.
  - It is ***unfavorable*** if it is irreversible and moving in the backward direction
- Determining whether a process is favorable or not requires the ***Second Law of Thermodynamics***, along with considering another state variable, ***Entopy (S)***.

Free Energy

Entropy

- **Concept**: *Entropy is a measure of the disorder in a system.*



(a) High entropy. Initially, the sucrose solution is at equilibrium because its N_A molecules are distributed randomly throughout the N_I cells in the initial volume.

(b) Low entropy. When a layer of pure water is added without mixing, the system is no longer at equilibrium. It has become more ordered, with all the occupied cells located in one-half of the solution.

(c) Higher-entropy final state. As sucrose and water molecules continue to move randomly, their arrangement becomes more dispersed (i.e., less ordered) because every cell has an equal chance of being occupied. Eventually, the solution reaches a new equilibrium, with sucrose molecules randomly distributed throughout the larger number of cells (N_F) in the final volume.

Sucrose molecules are in a disordered state.

Sucrose molecules are now in a more ordered state.

favorable →

Sucrose molecules become more disordered again.

Free Energy

Entropy

- Entropy is a measure of order
  - The more disordered a system is, the greater its entropy.

$$S = k_B \ln(W)$$

  - where
    - k_B is Boltzman's constant = R/N_A
    - *W* is the number of substates of equal energy

TABLE 3.1 Examples of lower-entropy and higher-entropy states

Lower Entropy	Higher Entropy
Ice, at 0 °C	Water, at 0 °C
Water, at 10 °C	Water vapor, at 10 °C (e.g., fog)
An unblended mixture of yogurt, whole bananas, honey, and whole strawberries	A fruit smoothie (i.e., the same ingredients *after* blending)

Free Energy

The Second Law of Thermodynamics

- The entropy of an isolated system will tend to increase to a maximum value.
- **Concept**: *The fact that the entropy of an isolated system will tend to increase to a maximum value explains the thermodynamic driving force for a favorable process.*
- Since the universe is an isolated system, it means that for any favorable process, the entropy of the universe must increase.

$$\Delta S_{universe} > 0 \quad \text{(favorable)}$$
$$\Delta S_{universe} < 0 \quad \text{(unfavorable)}$$
$$\Delta S_{universe} = 0 \quad \text{(at equilibrium)}$$

Free Energy: The Second Law in Open Systems

Free Energy: The Second Law

Biological systems are open system systems because they exchange both energy and matter with their surroundings.

- **Concept**: *In an open system, such as a living cell, $\Delta S_{universe}$ must also increase for a process to be favorable.*
- Since

$$\Delta S_{universe} = \Delta S_{system} + \Delta S_{surroundings}$$

- This means that the entropy of a system can decrease, as long as there is an overcompensating increase in the entropy of the surroundings.

Free Energy: The Second Law

Free Energy Defined in Terms of Enthalpy and Entropy Changes in the System

- J. Willard Gibbs showed that if the pressure and temperature are held constant for a process, the value $-TS_{universe}$ is a state variable.
  - This new state variable is now called the *Gibb's Free Energy* (*G*).

$$\Delta G = -T\Delta S_{universe}$$

  - He also showed that $\Delta G_{universe}$ can be determined from ΔH_{system} and ΔS_{system}.

$$\Delta G = \Delta H_{system} - T\Delta S_{system}$$

Free Energy: The Second Law

Free Energy Defined in Terms of Enthalpy and Entropy Changes in the System

- **Concept**: *A thermodynamically favored process tends in the direction that minimizes free energy (results in a negative ΔG). This is one way of stating the second law of thermodynamics.*

TABLE 3.2 Free energy rules

If ΔG is . . .	Free energy is . . .	The process is . . .
Negative	Available to do work	Thermodynamically favorable (and the reverse process is unfavorable)
Zero	Zero	Reversible; the system is at equilibrium
Positive	Required to do work	Thermodynamically unfavorable (and the reverse process is favorable)

Free Energy: The Second Law

The Interplay of Enthalpy and Entropy: A summary

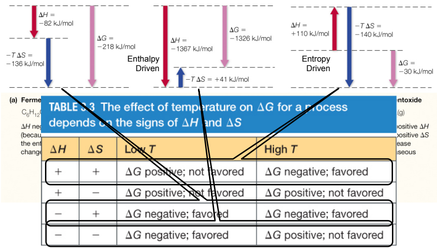


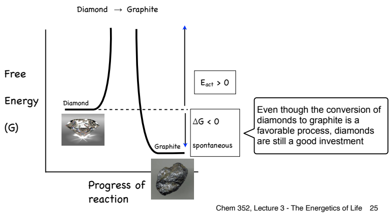
TABLE 3.3 The effect of temperature on ΔG for a process depends on the signs of ΔH and ΔS

ΔH	ΔS	Low T	High T
+	+	ΔG positive; not favored	ΔG negative; favored
+	−	ΔG positive; not favored	ΔG positive; not favored
−	+	ΔG negative; favored	ΔG negative; favored
−	−	ΔG negative; favored	ΔG positive; not favored

Free Energy: The Second Law

The Interplay of Enthalpy and Entropy: A summary

- **Concept**: *Just because a process is favorable it does not mean that it proceeds rapidly.*



Even though the conversion of diamonds to graphite is a favorable process, diamonds are still a good investment

Free Energy: The Second Law

The Interplay of Enthalpy and Entropy: A summary

- **Concept**: *Living systems create order from chaos and lead to a decrease in entropy. This is paid for by the expenditure of energy (ΔH_{system}<0), which increases the entropy of the surroundings ($\Delta S_{surroundings}$>0).*

$$\Delta S_{system} < 0$$

$$\Delta S_{surroundings} > 0$$

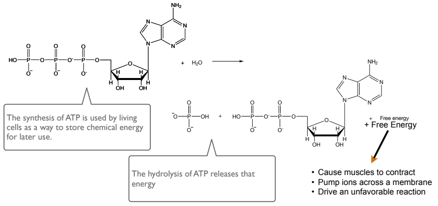
$$\Delta S_{surroundings} = -\frac{q_P}{T} = -\frac{\Delta H_{system}}{T}$$

$$\Delta H_{system} < 0 \text{ and } < T\Delta S_{system}$$

Free Energy: The Second Law

Free Energy and Useful Work

- **Concept**: *The free energy change, ΔG, is a measure of the maximum useful work obtainable from any reaction.*



The synthesis of ATP is used by living cells as a way to store chemical energy for later use.

The hydrolysis of ATP releases that energy

- Cause muscles to contract
- Pump ions across a membrane
- Drive an unfavorable reaction

Free Energy and Concentrations of Reactants and Products.

Free Energy and Concentrations

Equilibrium, Le Chatelier's Principle, and the Standard State

- **Concept**: *Le Chatelier's Principle state that for any system not at equilibrium, there is a thermodynamic driving force that favors the reestablishing of the equilibrium state.*
- Living systems exist far from an equilibrium state

Free Energy and Concentrations

Chemical reactions and the equilibrium state

- Consider the reaction A + B goes to form C + D
  - If we start with only the reactants A and B, there is only one direction for the reaction to go,

$$A + B \longrightarrow$$

  - Likewise, if we start with only the products C and D, there is only one direction for the reaction to go

$$\longleftarrow C + D$$

  - The ***Law of Mass Action*** tells us that as either of these reaction proceeds, their rates will slow as the concentrations of the reactants decrease.

Free Energy and Concentrations

Chemical reactions and the equilibrium state

- Consider the reaction A + B goes to form C + D
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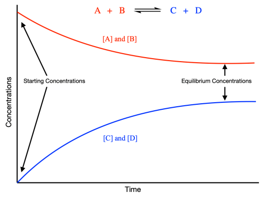

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Free Energy and Concentrations

Chemical reactions and the equilibrium state

- Consider the reaction A + B goes to form C + D
  - To balance this equation, we may also need to include coefficients for each to the reactants and products.

$$a\,\mathrm{A} + b\,\mathrm{B} \rightleftharpoons c\,\mathrm{C} + d\,\mathrm{D}$$

  - When the reaction reaches equilibrium, the concentrations of the reactants and products will stop changing.
  - The equilibrium concentrations can then be used to define an equilibrium constant that is characteristic of a given reaction

$$K = \left(\frac{[\mathrm{C}]^c\,[\mathrm{D}]^d}{[\mathrm{A}]^a\,[\mathrm{B}]^b}\right)_{\mathrm{eq}}$$

Free Energy and Concentrations

Change in Concentration and ΔG

- Without proof, the free energy of each component in a reaction is related to its concentration according to the following equation,

$$G_A = G_A^\circ + RT\ln[\mathrm{A}]$$

- Where G_A^o is the standard state free energy
- We do this because there is no reasonable way to determine the actual free energy of A, so it is determined relative to an arbitrarily defined state.
- The standard state we will be using is
  - P = 1 bar
  - T = 25°C (298.1 K)
  - [A]=[B]=[C]=[D]=1 M

Free Energy and Concentrations

Change in Concentration and Δ*G*

- To determine the Δ*G* for a reaction, we sum up all the free energies for the products, and subtract from that the sum of the free energies for the reactants.

$$\Delta G = (\Sigma G_{products} - \Sigma G_{reactants})$$

$$\Delta G = (cG_{\mathrm{C}} + dG_{\mathrm{D}}) - (aG_{\mathrm{A}} + bG_{\mathrm{B}})$$

- Substituting in the equations for the free energies of each reactant and product produces the following equation,

This is the equation you will want to memorize

$$\boxed{\Delta G = \Delta G^\circ + RT\ln\left(\frac{[\mathrm{C}]^{\mathrm{c}}\,[\mathrm{D}]^{\mathrm{d}}}{[\mathrm{A}]^{\mathrm{a}}\,[\mathrm{B}]^{\mathrm{b}}}\right)}$$

These are not the equilibrium concentrations. This ratio is sometimes represented by the letter *Q*

Free Energy and Concentrations

Change in Concentration and Δ*G*

- **Concept**: *The free energy change in a chemical reaction depends on the standard state free energy change (ΔG°) and on the concentrations of reactants and products (described by RT ln Q)*

$$\Delta G = \Delta G^\circ + RT\ln Q$$

$$\text{where } Q = \left(\frac{[\mathrm{C}]^{\mathrm{c}}\,[\mathrm{D}]^{\mathrm{d}}}{[\mathrm{A}]^{\mathrm{a}}\,[\mathrm{B}]^{\mathrm{b}}}\right)$$

- When a reaction reaches equilibrium *Q* = *K*

Free Energy and Concentrations

ΔG versus ΔG°, Q versus K, and Homeostasis *versus* Equilibrium

- **Concept**: *The equilibrium constant K can be calculated from the standard free energy change (ΔG°) and vice vera.*
  - *At equilibrium ΔG = 0, therefore,*

$$\Delta G = \Delta G^\circ + RT\ln\left(\frac{[\mathrm{C}]^\mathrm{c}\,[\mathrm{D}]^\mathrm{d}}{[\mathrm{A}]^\mathrm{a}\,[\mathrm{B}]^\mathrm{b}}\right)$$

$$0 = \Delta G^\circ + RT\ln\left(\frac{[\mathrm{C}]^\mathrm{c}\,[\mathrm{D}]^\mathrm{d}}{[\mathrm{A}]^\mathrm{a}\,[\mathrm{B}]^\mathrm{b}}\right)_\mathrm{eq}$$

$$\Delta G^\circ = -\ RT\ln\left(\frac{[\mathrm{C}]^\mathrm{c}\,[\mathrm{D}]^\mathrm{d}}{[\mathrm{A}]^\mathrm{a}\,[\mathrm{B}]^\mathrm{b}}\right)_\mathrm{eq}$$

$$\boxed{\Delta G^\circ = -\ RT\ln K_{eq} \quad \text{and} \quad K_{eq} = e^{\left(\frac{-\Delta G^o}{RT}\right)}}$$

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Free Energy and Concentrations

ΔG versus ΔG°, Q versus K, and Homeostasis *versus* Equilibrium

- **Concept**: *The homeostatic condition, which is far from equilibrium and a characteristic of living cells, must not be confused with true thermodynamic equilibrium.*
- The narrow range of conditions, such as *pH,* temperature, and concentrations of metabolites and ions is referred to as the ***homeostatic*** conditions or ***homeostasis***.
  - Many reactions and processes are not favorable (*ΔG > 0*) under homeostatic conditions, therefore, energy is required to maintain homeostasis

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Free Energy and Concentrations

ΔG versus ΔG°, Q versus K, and Homeostasis *versus* Equilibrium

- **Concept**: It *is ΔG, as determined by the actual concentrations of reactants and products in the cell, and not ΔG°, that determines whether or not a reaction is favorable in vivo.*

TABLE 3.4 Relationships between *K, Q,* and Δ*G* for a reaction

Value of Q	Value of ΔG	Favored Direction
$<K$	<0	Forward reaction (formation of products)
$=K$	$=0$	Neither (system at equilibrium)
$>K$	>0	Reverse reaction (formation of reactants)

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Free Energy and Concentrations

ΔG versus ΔG°, Q versus K, and Homeostasis *versus* Equilibrium

- **Concept**: Th*ermodynamically unfavorable reactions become favorable when Q < K and/or when coupled to a strongly favorable (i.e., highly exergonic, ΔG << 0) reaction.*

$$\text{Since } \Delta G = \Delta G^\circ + RT\ln Q$$

$$\Delta G = RT\ln\left(\frac{Q}{K_{eq}}\right)$$

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Free Energy and Concentrations

Water, H^+ in Buffered Solution, and the "Biochemical Standard State"

- **Concept**: *Biochemists use a slightly different definition for the Standard Free Energy Change (ΔG°')*
  - *Whenever water is a reactant or product in a reaction it activity is set equal to 1, instead of its concentration, ~55M.*
  - *The standard state for [H⁺] is* 1×10^{-7} *M instead of 1 M, so its activity at pH 7 becomes 1.*

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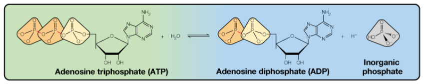
Free Energy and Concentrations

ΔG *versus* ΔG°, *Q versus K*, and Homeostasis *versus* Equilibrium

Problem:

The hydrolysis of the terminal phosphate group from adenosine triphosphate (ATP) to produce adenosine diphosphate (ADP) has a high negative ΔG and serves a major source of energy in living cells.

$$\text{ATP} + H_2O \longrightarrow \text{ADP} + HPO_4^- + H^+ \quad \Delta G^{\circ\prime} = -32.\text{kJ/mol}$$



Free Energy in Biological Systems

Free Energy in Biological Systems

Many reactions and process in biological systems are unfavorable.

- To make them favorable, they must be coupled to a reaction or process that is favorable.
- For example, the first reaction in the glycolytic pathway phosphorylates glucose to make glucose-1-phosphate.

$$\text{glucose} + P_i \longrightarrow \text{glucose-1-phosphate} + H_2O \quad \Delta G^{\circ\prime} = +20.9.\text{kJ/mol}$$

Unfavorable

$$\text{ATP} + H_2O \longrightarrow \text{ADP} + P_i \quad \Delta G^{\circ\prime} = -32.2\ .\text{kJ/mol}$$

Favorable

$$\text{glucose} + \text{ATP} \longrightarrow \text{glucose-1-phosphate} + \text{ADP} \quad \Delta G^{\circ\prime} = -11.3\ \text{kJ/mol}$$

Favorable

The unfavorable phosphorylation reaction is made favorable, by coupling the reaction to the hydrolysis of a phosphate from ATP, which is a favorable reaction

Since ΔG° is a state function, the overall ΔG° for the coupled reactions is just the sum of the ΔG°'s for the individual reactions

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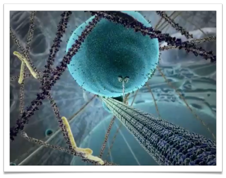
Free Energy in Biological Systems

Many reactions and process in biological systems are unfavorable.

- The hydrolysis of ATP also provide the energy required by the motor protein kinesis, to move vesicles around the cell.



Free Energy in Biological Systems

Organic Phosphate Compounds as Energy Transducers

- The hydrolysis of phosphoryl groups from organic phosphate compounds is a favorable reaction and displays a range of negative Standard Free Energy values.

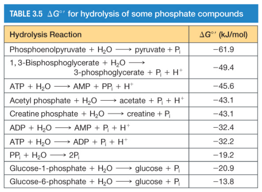


TABLE 3.5 $\Delta G^{\circ\prime}$ for hydrolysis of some phosphate compounds

Hydrolysis Reaction	$\Delta G^{\circ\prime}$ (kJ/mol)
Phosphoenolpyruvate + $H_2O \longrightarrow$ pyruvate + P_i	−61.9
1, 3-Bisphosphoglycerate + $H_2O \longrightarrow$ 3-phosphoglycerate + P_i + H^+	−49.4
ATP + $H_2O \longrightarrow$ AMP + PP_i + H^+	−45.6
Acetyl phosphate + $H_2O \longrightarrow$ acetate + P_i + H^+	−43.1
Creatine phosphate + $H_2O \longrightarrow$ creatine + P_i	−43.1
ADP + $H_2O \longrightarrow$ AMP + P_i + H^+	−32.4
ATP + $H_2O \longrightarrow$ ADP + P_i + H^+	−32.2
PP_i + $H_2O \longrightarrow 2P_i$	−19.2
Glucose-1-phosphate + $H_2O \longrightarrow$ glucose + P_i	−20.9
Glucose-6-phosphate + $H_2O \longrightarrow$ glucose + P_i	−13.8

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Free Energy in Biological Systems

Organic Phosphate Compounds as Energy Transducers

- **Concept**: *The phosphoric group transfer potential shows which compounds can phosphorylate others under standard conditions.*

TABLE 3.5 $\Delta G^{\circ\prime}$ for hydrolysis of some phosphate compounds

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Phosphoenolpyruvate + $H_2O \longrightarrow$ pyruvate + P_i	−61.9
1, 3-Bisphosphoglycerate + $H_2O \longrightarrow$ 3-phosphoglycerate + P_i + H^+	−49.4
ATP + $H_2O \longrightarrow$ ADP + P_i + H^+	−32.2
Glucose-1-phosphate + $H_2O \longrightarrow$ glucose + P_i	−20.9

Later, when we study the reactions in the glycolytic pathway, we will see a reaction where a phosphryl group is transferred from ATP to glucose to make glucose-1-phosphate. [illegible]

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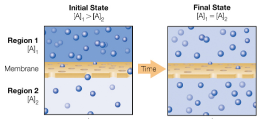
Free Energy in Biological Systems

Concentration gradients across membranes are a way that cells store energy



at equilibrium $[A]_1 = [A]_2$

$$K_{eq} = \frac{[A]_2}{[A]_1} = 1 \quad \text{and} \quad \Delta G^{\circ\prime} = -RT\ln(K_{eq}) = 0$$

when $[A]_1 \neq [A]_2$ $\quad \Delta G = RT\ln\left(\frac{[A]_2}{[A]_1}\right)$

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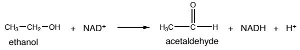
Free Energy in Biological Systems

Determining the $\Delta G^{\circ\prime}$ for oxidation/reduction reactions

- Many of the important reactions we will encounter are oxidation/reduction reactions.
  - For example, if you imbibe ethanol, the first step in breaking it down occurs in liver where it is oxidized by nicotinamide-adenine dinucleotide (NAD^+) to acetaldehyde.



$$\underset{\text{ethanol}}{CH_3{-}CH_2{-}OH} + NAD^+ \longrightarrow \underset{\text{acetaldehyde}}{H_3C{-}\overset{\overset{O}{\parallel}}{C}{-}H} + NADH + H^+$$

  - The $\Delta G^{\circ\prime}$ for oxidation/reduction can be determined from the standard reduction potentials, $E^{\circ\prime}$ for the electron donor and acceptor in the reaction.

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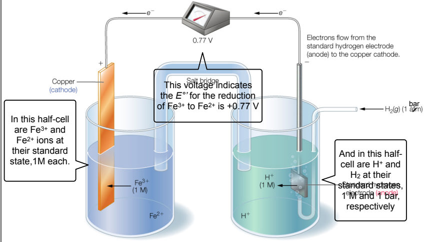
Free Energy in Biological Systems

This cell is set up to measure the reduction potential for reducing Fe^{3+} to Fe^{2+}

Determining the $\Delta G^{\circ\prime}$ for oxidation/reduction reactions



This voltage indicates the $E^{\circ\prime}$ for the reduction of Fe^{3+} to Fe^{2+} is +0.77 V

In this half-cell are Fe^{3+} and Fe^{2+} ions at their standard state,1M each.

And in this half-cell are H^+ and H_2 at their standard states, 1 M and 1 bar, respectively

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Free Energy in Biological Systems

Determining the $\Delta G^{\circ\prime}$ for oxidation/reduction reactions

- **Concept**: *The greater the standard reduction potential, the greater the tendency of the oxidized form of a redox couple to attract electrons.*

TABLE 3.6 A few standard reduction potentials ($E^{\circ\prime}$) of interest in biochemistry

Oxidant (e^- acceptor)		Reductant (e^- donor)	n	$E^{\circ\prime}$ (V)
$H^+ + e^-$	$\rightleftharpoons$	$\frac{1}{2}H_2$	1	−0.421
$NAD^+ + H^+ + 2e^-$	$\rightleftharpoons$	NADH	2	−0.315
1,3-Bisphosphoglycerate + $2H^+ + 2e^-$	$\rightleftharpoons$	Glyceraldehyde-3-phosphate + P_i	2	−0.290
FAD + $2H^+ + 2e^-$	$\rightleftharpoons$	$FADH_2$	2	−0.219
Acetaldehyde + $2H^+ + 2e^-$	$\rightleftharpoons$	Ethanol	2	−0.197
Pyruvate + $2H^+ + 2e^-$	$\rightleftharpoons$	Lactate	2	−0.185
$Fe^{3+} + e^-$	$\rightleftharpoons$	Fe^{2+}	1	+0.769
$\frac{1}{2}O_2 + 2H^+ + 2e^-$	$\rightleftharpoons$	H_2O	2	+0.815

Note: $E^{\circ\prime}$ is the standard reduction potential at pH 7 and 25 °C, n is the number of electrons transferred, and each potential is for the partial reaction written as follows:

$$\text{Oxidant} + ne^- \rightarrow \text{reductant}$$

The entry for the H^+/H_2 couple $E^{\circ\prime} = -0.421$ V is not zero because it is measured with $[H^+] = 1$ M in the reference cell (i.e., the standard hydrogen electrode) and $[H^+] = 10^{-7}$ M in the test cell.

Free Energy in Biological Systems

Determining the $\Delta G°'$ for oxidation/reduction reactions

- The standard reduction potentials for the proton acceptor and proton donor can then be used to determine $\Delta G°$ using the Nernst equation.

$$\Delta G°' = -n\mathscr{F}\Delta E°'$$

where $\mathscr{F}$ is Faraday's constant (=96.5 kJ mol^{-1} V^{-1})

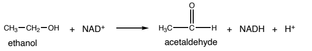
n is the number of electrons being transferred

$$\Delta E°' = E°'_{acceptor} - E°'_{donor}$$

Free Energy in Biological Systems

Determining the ΔG°' for oxidation/reduction reactions

- For the oxidation of ethanol to acetaldehyde by NAD+



$$\underset{\text{ethanol}}{CH_3-CH_2-OH} + NAD^+ \longrightarrow \underset{\text{acetaldehyde}}{H_3C-\overset{\overset{O}{\|}}{C}-H} + NADH + H^+$$

- The two have reactions are

Donor

$$\text{acetaldehyde} + 2\,H + 2e^- \longrightarrow \text{ethanol} \qquad E°' = -0.197\ V$$

$$NAD^+ + 2\,H + 2e^- \longrightarrow NADH + H^+ \qquad E°' = -0.315\ V$$

Acceptor

$$\Delta G°' = -n\mathscr{F}\Delta E°' = -2(96.2\,\frac{kJ}{mol\,V})(-0.315\,V - (-0.197\,V))$$

$$\Delta G°' = +22.8\,\frac{kJ}{mol}$$

Free Energy in Biological Systems

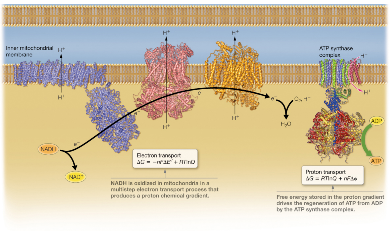
Determining the ΔG for oxidation/reduction reactions

- For conditions other than standard state condition, ΔG is determined as before

$$\Delta G = \Delta G°' + RT\,\ln(Q)$$

Free Energy in Biological Systems

A Brief Overview of Free Energy Changes in Cells



Electron transport
$\Delta G = -nF\Delta E°' + RT\ln Q$

NADH is oxidized in mitochondria in a multistep electron transport process that produces a proton chemical gradient.

Proton transport
$\Delta G = RT\ln Q + nF\Delta\psi$

Free energy stored in the proton gradient drives the regeneration of ATP from ADP by the ATP synthase complex.

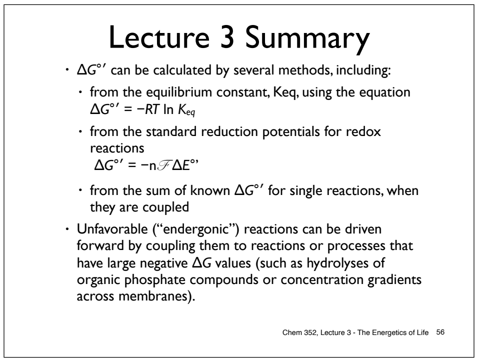
Lecture 3 Summary

- The principles of thermodynamics explain how cell-based living systems extract energy from their environment and use it to drive cellular processes

- Each of these processes must be favorable to occur spontaneously, that is, the free energy change, $\Delta G = \Delta H - T\Delta S$, must be negative ("exergonic") rather than positive ("endergonic")

- Thus, $\Delta G = \Delta G°' + RT\ln Q$, where $\Delta G°'$ represents the free energy change under standard biochemical conditions

- Living systems operate far from equilibrium, therefore they require a constant source of external energy to maintain this state.



Lecture 3 Summary

- $\Delta G°'$ can be calculated by several methods, including:
  - from the equilibrium constant, Keq, using the equation $\Delta G°' = -RT \ln K_{eq}$
  - from the standard reduction potentials for redox reactions $\Delta G°' = -n\mathscr{F}\Delta E°'$
  - from the sum of known $\Delta G°'$ for single reactions, when they are coupled
- Unfavorable ("endergonic") reactions can be driven forward by coupling them to reactions or processes that have large negative ΔG values (such as hydrolyses of organic phosphate compounds or concentration gradients across membranes).