Equilibrium (ΔG=0) and Standard State

$$\Delta G = \Delta G^\circ + RT \ln \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

At equilibrium $\quad \Delta G = 0 \quad$ & $\quad \ln \frac{[C]^c [D]^d}{[A]^a [B]^b} = \ln K_{eq}$

$$\therefore \Delta G^\circ = - RT \ln K_{eq}$$

- Rewrite $K_{eq} = e^{(-\Delta G^\circ / RT)}$
- R is 8.314×10^{-3} KJ/K.mol
- T is temperature in Kelvins

$$\Delta G^\circ = -RT \ln(K_{eq}) = -RT\, 2.303 \log(K_{eq})$$

ΔG under Nonstandard Conditions

- **ΔG and $\Delta G°$ are different**
- $\Delta G = \Delta G°$ only when the reactants and products are in their <u>standard states</u>
- ΔG tells you about spontaneity of process under given set of conditions

    = equal to maximum work that can be done by process/reaction

    $\Delta G < 0$ ➜ energy available for work

    = the more negative ΔG is, the more work that can be done

    $\Delta G = 0$ ➜ equilibrium – no work

- $\Delta G°$ tells you about magnitude of equilibrium constant (K)

    = $\Delta G° < 0$ ➜ large K value (equilibrium lies on products side)

    = $\Delta G° > 0$ ➜ small K value (equilibrium lies on reactants side)

$$\Delta G° = -RT \ln(K_{eq}) = -RT\ 2.303\ \log(K_{eq})$$

Table 3-3 Variation of K_{eq} with $\Delta G°$ at 25°C

K_{eq}	$\Delta G°$ (kJ · mol^{-1})
10^6	-34.3
10^4	-22.8
10^2	-11.4
10^1	-5.7
10^0	0.0
10^{-1}	5.7
10^{-2}	11.4
10^{-4}	22.8
10^{-6}	34.3

A *small change* in $\Delta G°$ causes a *large change* in K, due to their logarithmic relationship.

As $\Delta G°$ becomes *more positive*, K becomes *smaller*.

As $\Delta G°$ becomes *more negative*, K becomes *larger*.

At 298 K, a 10-fold change in K_{eq} is 5.7 kJ/mol change in $\Delta G°$
This is less than half the energy of a weak H-bond!

Cheat Sheet

For any process at constant *P* and *T*:
$$\Delta G = \Delta H - T\Delta S$$
$\Delta G < 0$ favorable   (exergonic)
$\Delta G > 0$ unfavorable (endergonic)

$$\Delta G = \Delta G^\circ + RT \ln \frac{[C]^c[D]^d}{[A]^a[B]^b}$$

At equilibrium $\quad \Delta G = 0 \quad \& \quad \ln \frac{[C]^c[D]^d}{[A]^a[B]^b} = \ln K_{eq}$

$$\therefore \Delta G^\circ = - RT \ln K_{eq}$$

R is 8.314×10^{-3} KJ/K.mol
T is temperature in Kelvins

Join the Dots

For any process at constant *P* and *T*:

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

Determination of ΔH° and ΔS°

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

$$-RT\ln K_{eq} = \Delta H^\circ - T\Delta S^\circ$$

$$\ln K_{eq} = -\frac{\Delta H^\circ}{R}\frac{1}{T} + \frac{\Delta S^\circ}{R}$$

$$y = mx + b$$

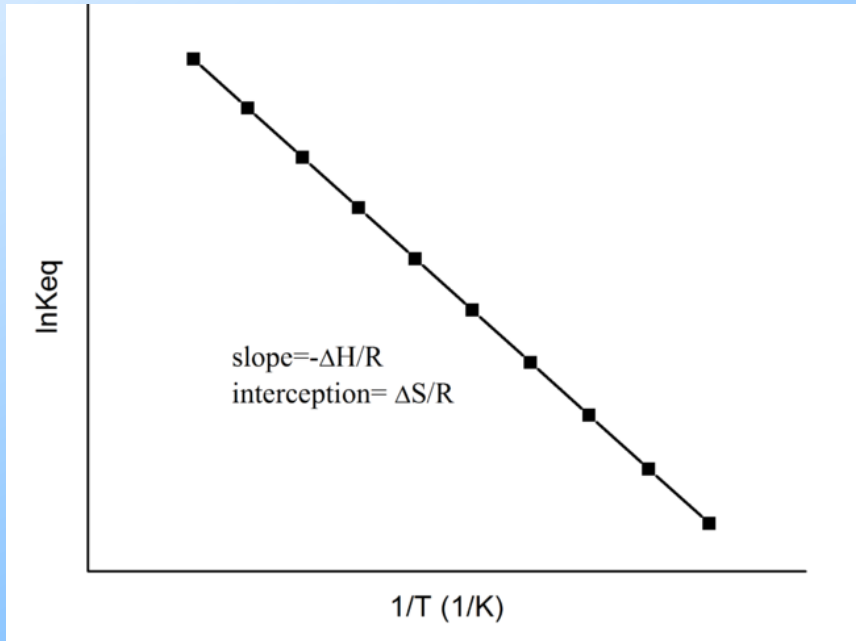Assuming that enthalpy and entropy are invariant with temperature, you can plot $\ln K_{eq}$ vs. $1/T$.

$$\text{Slope} = -\frac{\Delta H^\circ}{R}$$

$$\text{y-intercept} = \frac{\Delta S^\circ}{R}$$

Van't Hoff Plot

Allows ΔH^o and ΔS^o to be determined from measurement of K_{eq} at two or more different temperatures
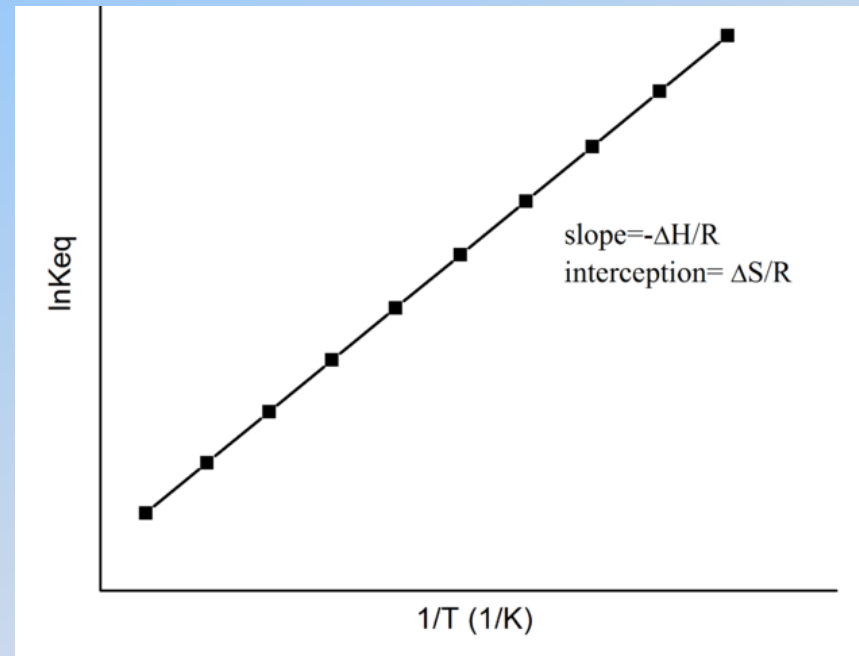
Van't Hoff Plots

Gradient is negative
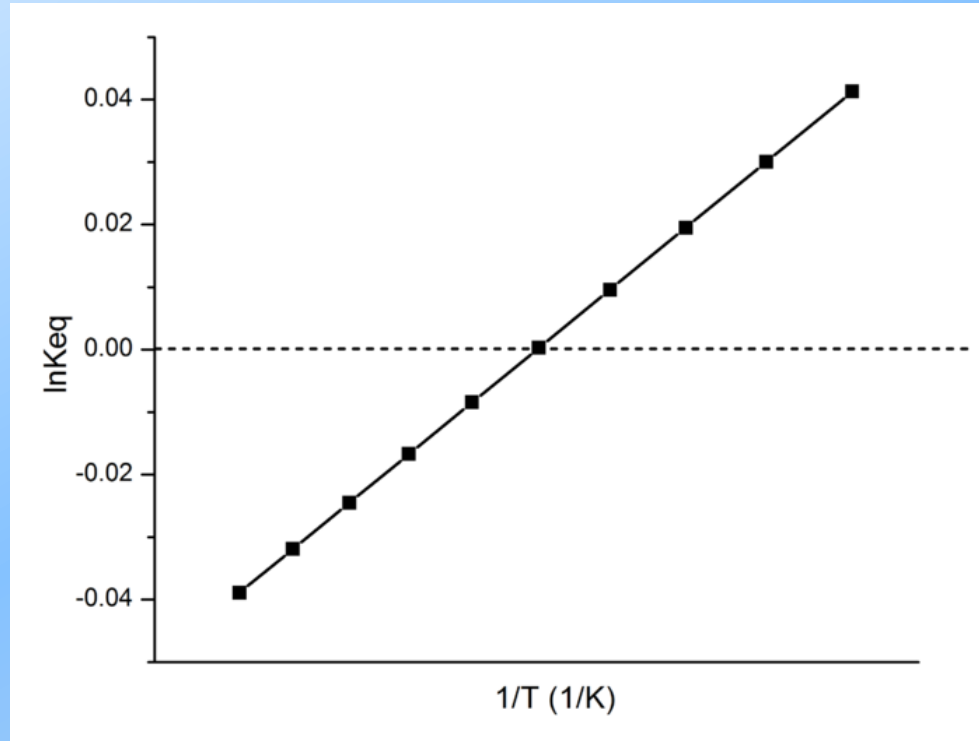
Gradient is $-\Delta H/R$

ΔH is positive

Endothermic

Gradient is positive

Gradient is $-\Delta H/R$

ΔH is negative

Exothermic

Van't Hoff Plot

$\Delta G^o = -RT \ln K_{eq}$

$\ln K_{eq}$ is positive so
ΔG^o is negative

$\ln K_{eq}$ is negative so
ΔG^o is positive

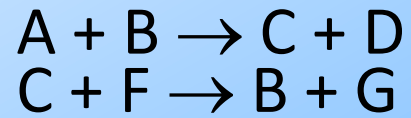Assumption is that ΔH^o and ΔS^o do
NOT change with temperature

$$\Delta G^o = -RT \ln(K_{eq}) = -RT \, 2.303 \log(K_{eq})$$

If the forward reaction has "ΔG^o"
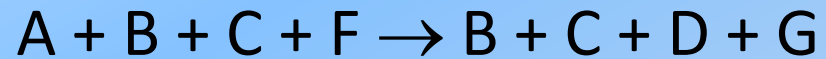then the reverse reaction has "$-\Delta G^o$"

A + B → C + D $\Delta G^{o'} = 33$ kJ/mol

D + C → B + A $\Delta G^{o'} = -33$ kJ/mol

Coupled Reactions

- Suppose we couple two equations:

$A + B \rightarrow C + D$ $\qquad\qquad$ $\Delta G^{o\prime} = x$
$C + F \rightarrow B + G$ $\qquad\qquad$ $\Delta G^{o\prime} = y$

- The result is:
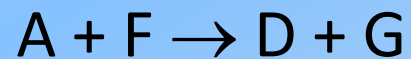
$A + B + C + F \rightarrow B + C + D + G$
or
$A + F \rightarrow D + G$ $\qquad\qquad$ $\Delta G^{o\prime} = x + y$

... since B and C appear on both sides

Couple Reactions

- Endergonic reactions (positive ΔG) can occur through coupling with exergonic reactions (negative ΔG)

- Coupling is essential in metabolic pathways

- The overall ΔG for a coupled reaction is the sum of the two ΔG values for the individual reactions

Reactions involved in Coupling

- Endergonic processes that maintain life are driven by exergonic reactions of nutrient oxidation

- Hydrolysis of high-energy (~)* phosphate compounds

      PEP – phosphoenolpyruvate

      CP – creatine phosphate

      ATP – adenosine triphosphate

- Reduction of coenzymes

      NADH

      $FADH_2$

high-energy normally means more negative than -25 kJ/mol

ATP is Adenosine-5'-triphosphate
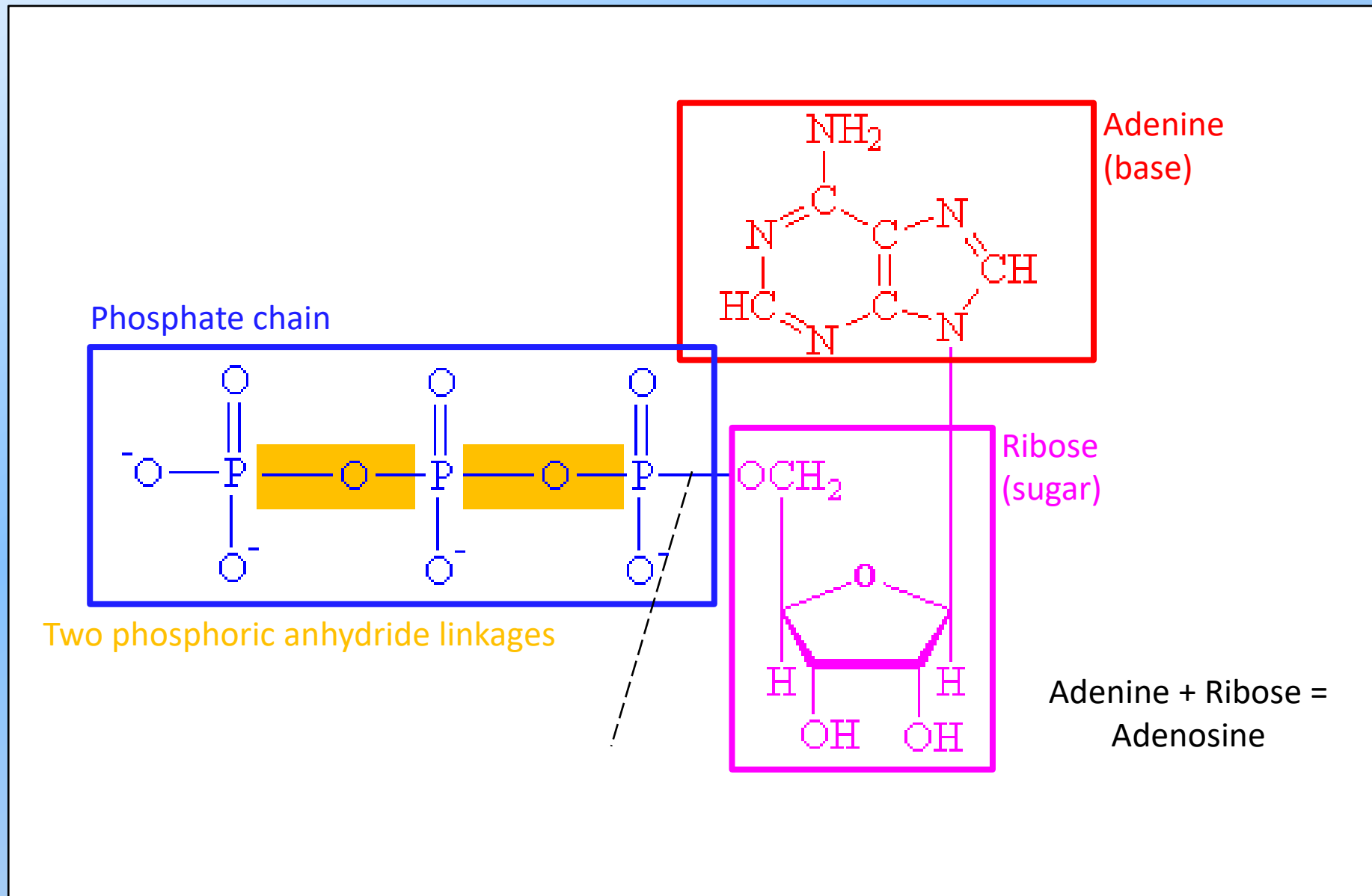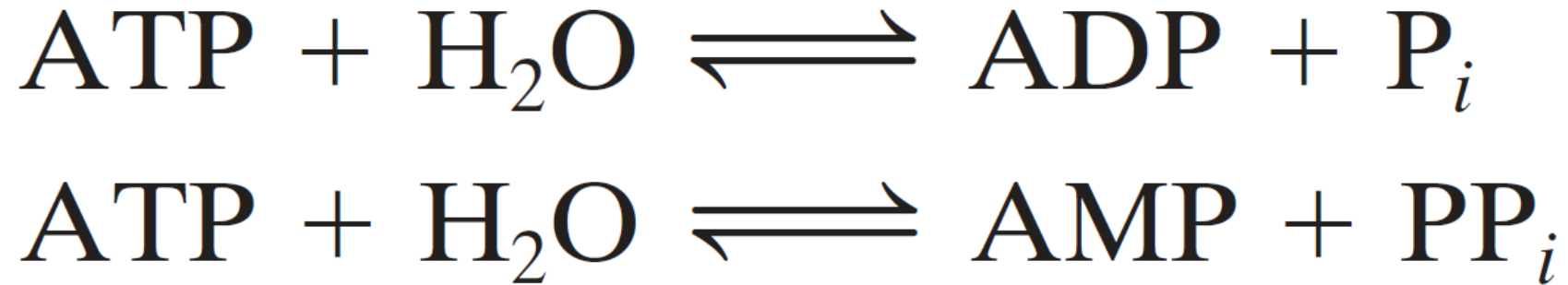
ATP Contains Two Pyrophosphate Linkages
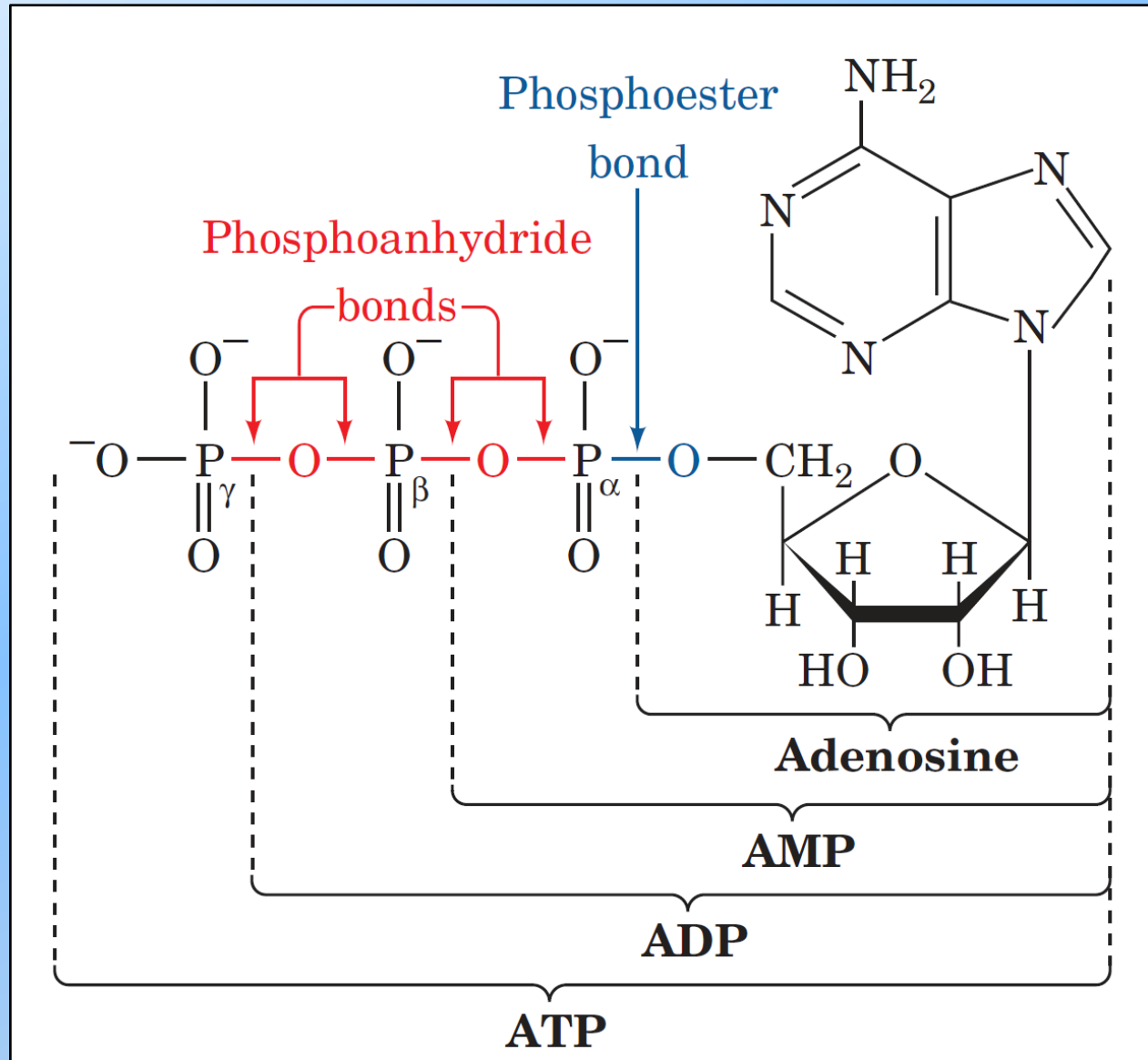
Adenosine monophosphate

Adenosine diphosphate

Adenosine triphosphate

Phosphoryl-Transfer Reactions

$$ATP + H_2O \rightleftharpoons ADP + P_i$$

$$ATP + H_2O \rightleftharpoons AMP + PP_i$$

Pi is orthophosphate (PO_4^{-3})

PPi is pyrophosphate ($P_2O_7^{-4}$)

Reactants and products	$\Delta G^{o\prime}_{hydrolysis}$ (kJ mol^{-1})
$ATP + H_2O \rightarrow ADP + P_i + H^{\oplus}$	-32
$ATP + H_2O \rightarrow AMP + PP_i + H^{\oplus}$	-45
$AMP + H_2O \rightarrow Adenosine + P_i + H^{\oplus}$	-13
$PP_i + H_2O \rightarrow 2P_i$	-29
$ADP + H_2O \rightarrow AMP + P_i$	-31

** Phosphoester bond

E.g. Coupled Reactions

$$\text{Glucose} + P_i \longrightarrow \text{glucose 6-phosphate} + H_2O$$
$$\Delta G'^\circ = 13.8 \text{ kJ/mol}$$

$$\text{ATP} + H_2O \longrightarrow \text{ADP} + P_i \qquad \Delta G'^\circ = -30.5 \text{ kJ/mol}$$

(1) $\quad \text{Glucose} + P_i \longrightarrow \text{glucose 6-phosphate} + H_2O$

(2) $\quad \text{ATP} + H_2O \longrightarrow \text{ADP} + P_i$

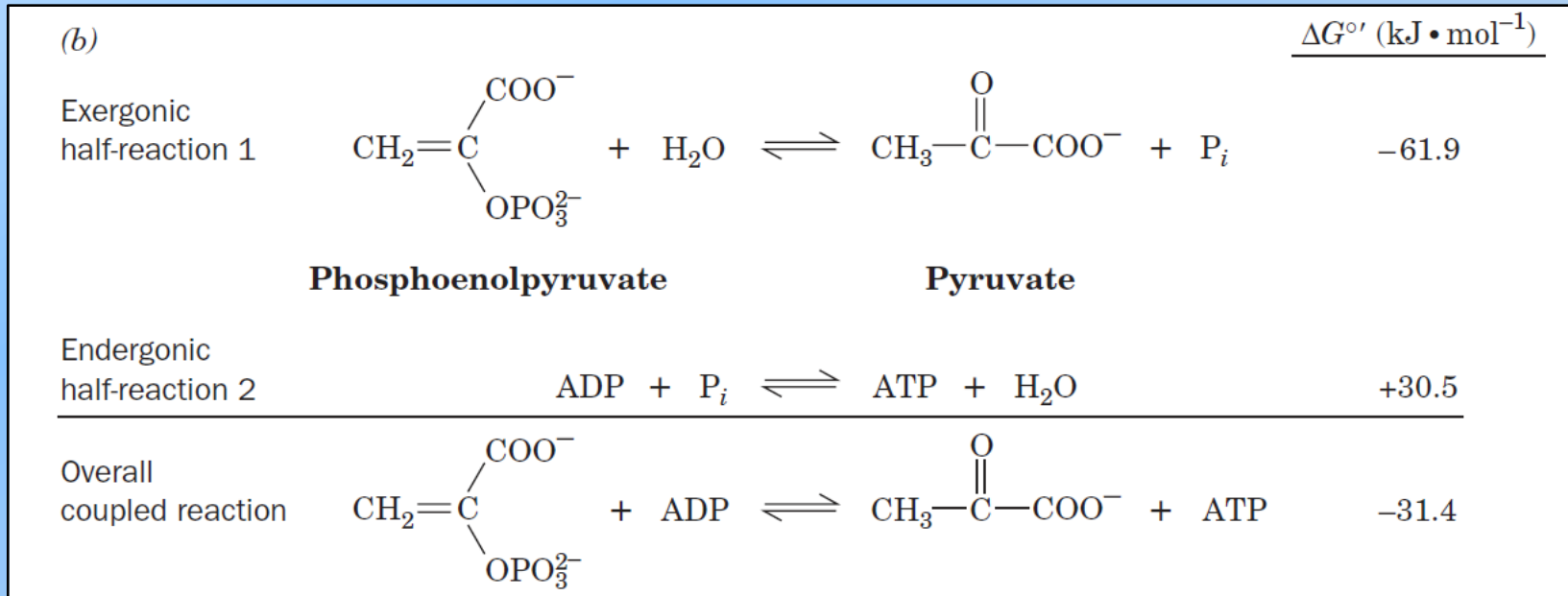_Sum:_ $\quad \text{ATP} + \text{glucose} \longrightarrow \text{ADP} + \text{glucose 6-phosphate}$
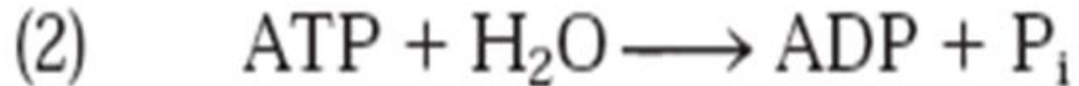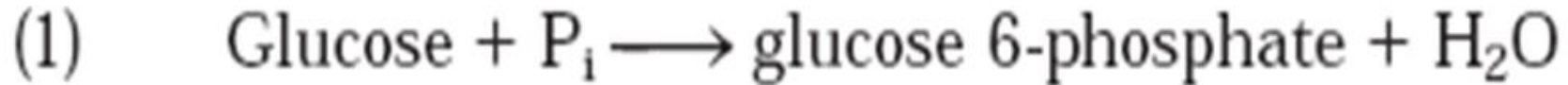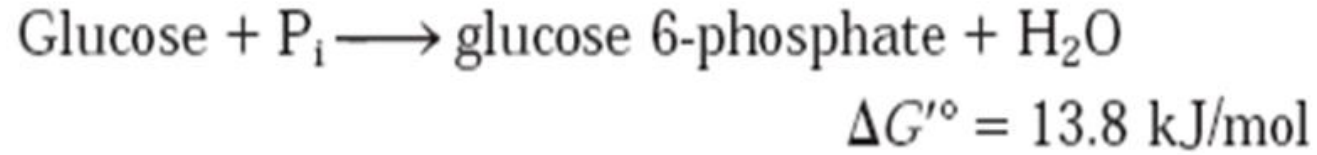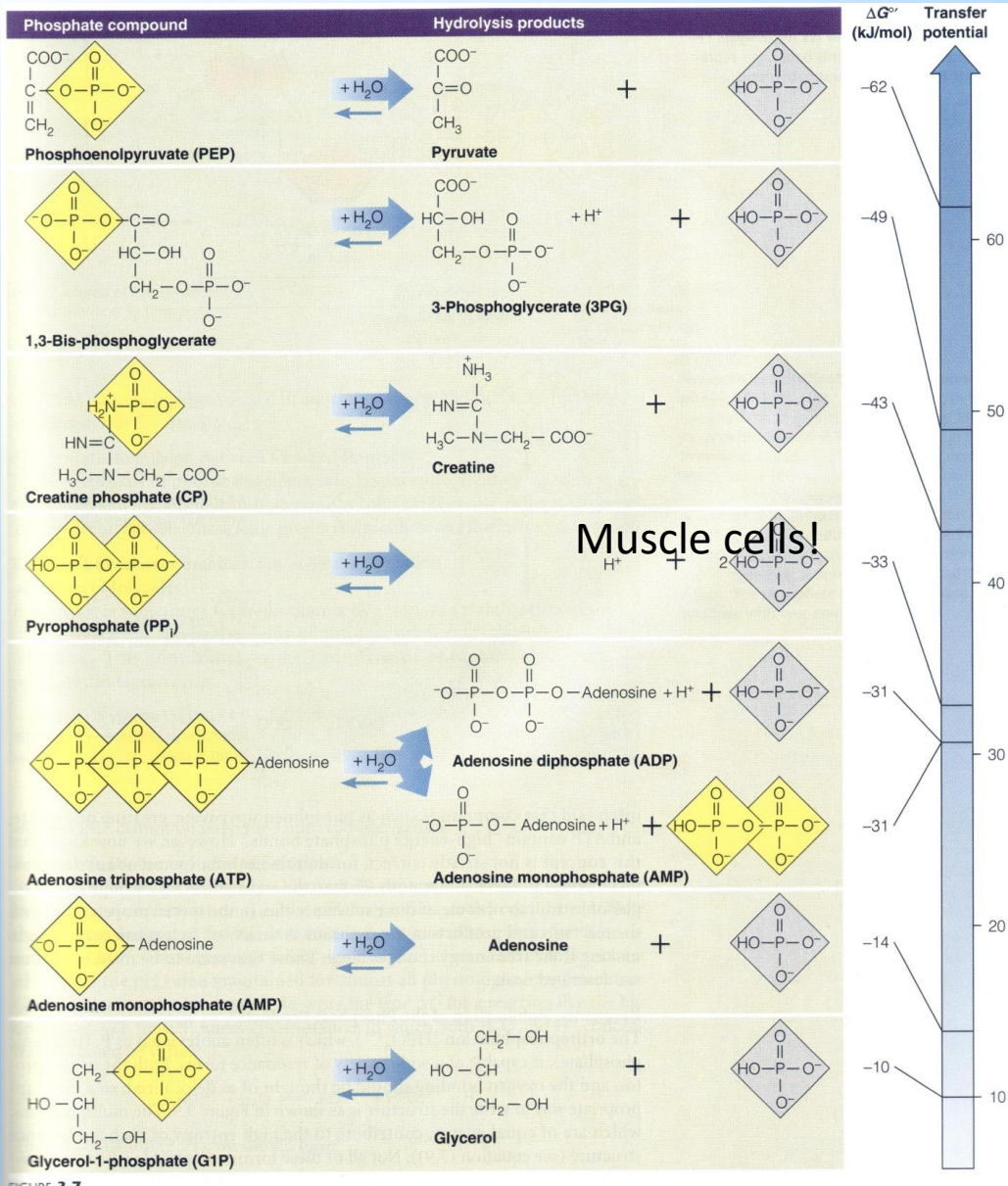
$$\Delta G'^\circ = 13.8 \text{ kJ/mol} + (-30.5 \text{ kJ/mol}) = -16.7 \text{ kJ/mol}$$

E.g. Coupled Reactions

ATP synthesis comes from more exergonic hydrolysis of phosphoenolpyruvate (*plus other pathways*)

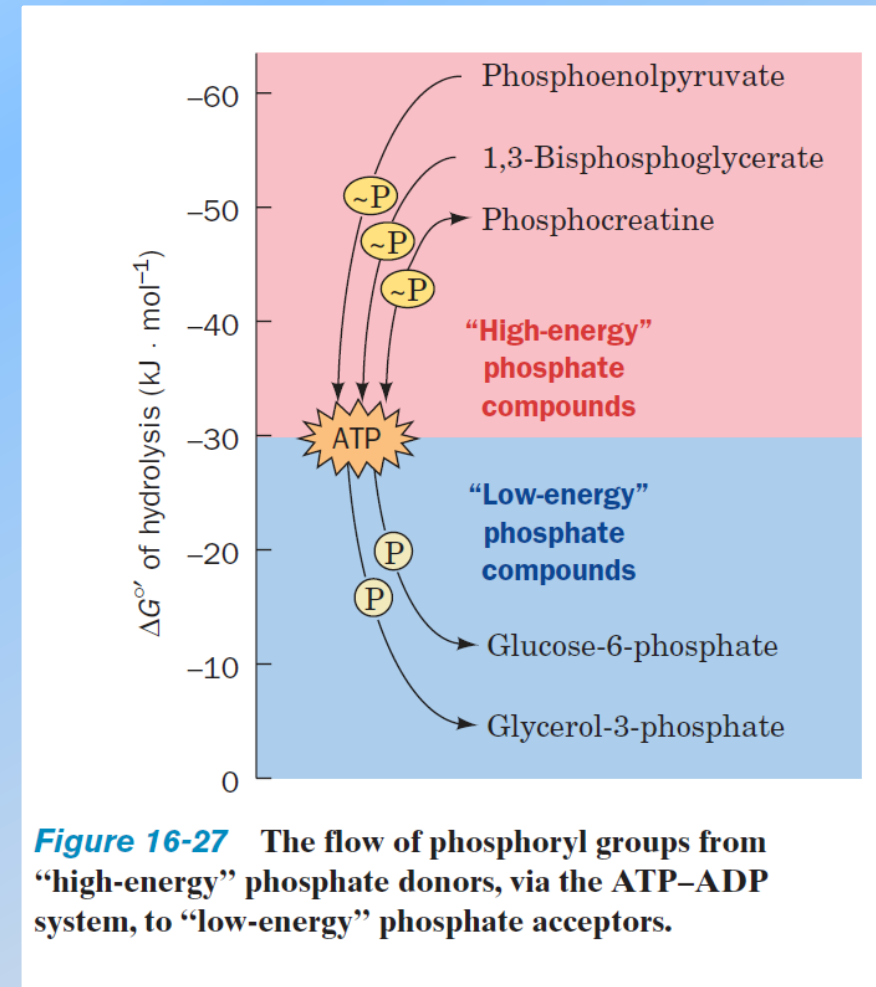Tendency of phosphoryl group to be transferred to water

Phosphates transferred 'downwards'

ATP has an intermediate phosphate group-transfer potential

Compound	$\Delta G^{\circ\prime}$ (kJ $\cdot$ mol^{-1})
Phosphoenolpyruvate	-61.9
1,3-Bisphosphoglycerate	-49.4
ATP ($\rightarrow$ AMP + PP$_i$)	**-45.6**
Acetyl phosphate	-43.1
Phosphocreatine	-43.1
ATP ($\rightarrow$ ADP + P$_i$)	**-30.5**
Glucose-1-phosphate	-20.9
PP$_i$	-19.2
Fructose-6-phosphate	-13.8
Glucose-6-phosphate	-13.8
Glycerol-3-phosphate	-9.2

Muscle cells!

ATP is an Energy Shuttle (*not a reservoir*)

- PEP and 1,3-BPG are created in the course of glucose breakdown; their energy is transferred to ADP to make ATP

- But ATP is only a transient energy carrier… it quickly passes its energy to a host of energy-requiring processes

- Often involves enzymes called **kinases**

Figure 16-27 The flow of phosphoryl groups from "high-energy" phosphate donors, via the ATP–ADP system, to "low-energy" phosphate acceptors.

Influences on the ΔG of ATP Hydrolysis

- Concentration of reactant and products (Of course!)
    - Intracellular [ATP], [ADP],and [Pi] are mM
    - Makes actual ΔG ~ -50 kJ/mol

- pH
    - Small effect

$$\Delta G = \Delta G^\circ_{RX} + RT \ln \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

- Divalent metal ion concentration
    - Small effect
    - Have high phosphate-binding affinities

Concentration Effects

The free energy of hydrolysis of ATP as a function of concentration at 38° C, pH 7.0.

[ATP], [ADP], & [Pi] in a typical bacterial cell at 25° C are maintained at roughly 8 mM, 8 mM, & 1 mM.

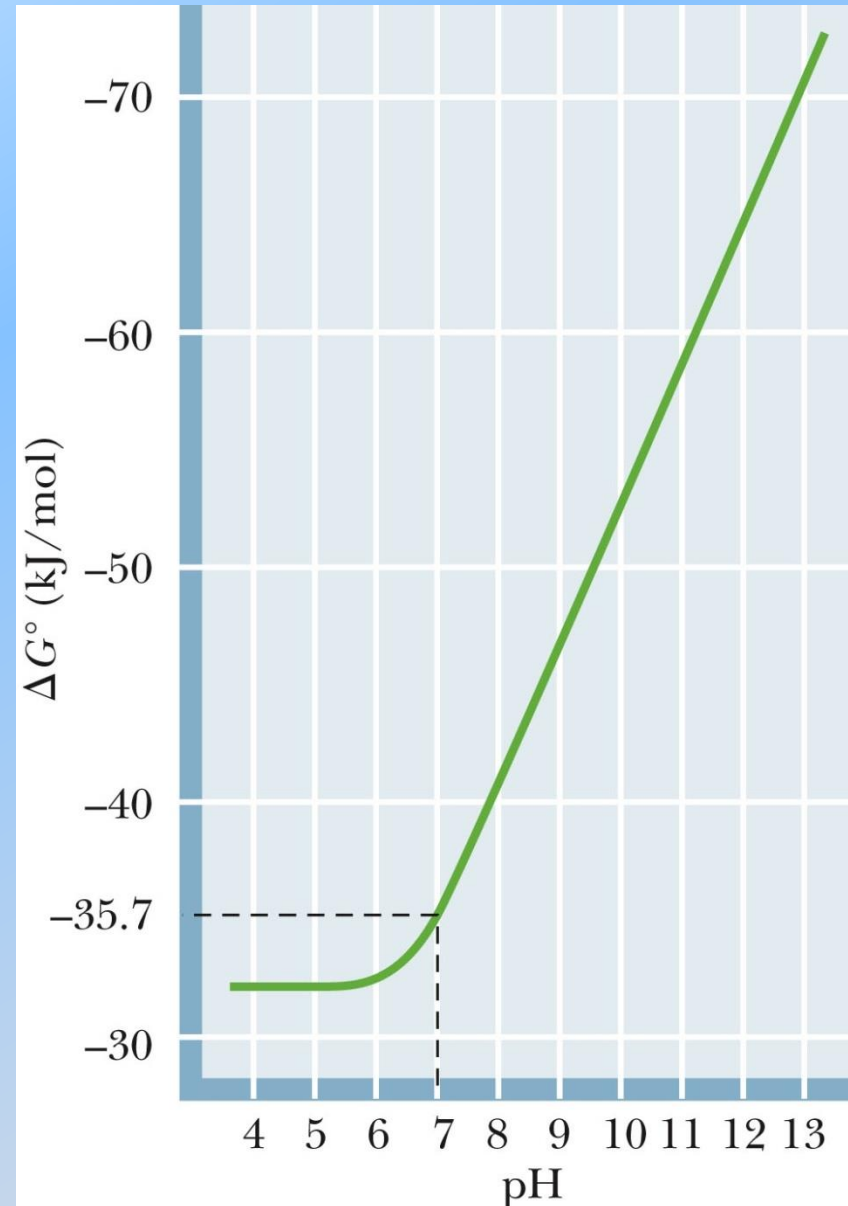Under these conditions, ΔG for ATP hydrolysis is approximately -47.6 kJ/mol.

Where C = concentration of
ATP, ADP, and P$_i$

$$\Delta G = \Delta G^{\circ}_{RX} + RT \ln \frac{[C]^c [D]^d}{[A]^a [B]^b}$$
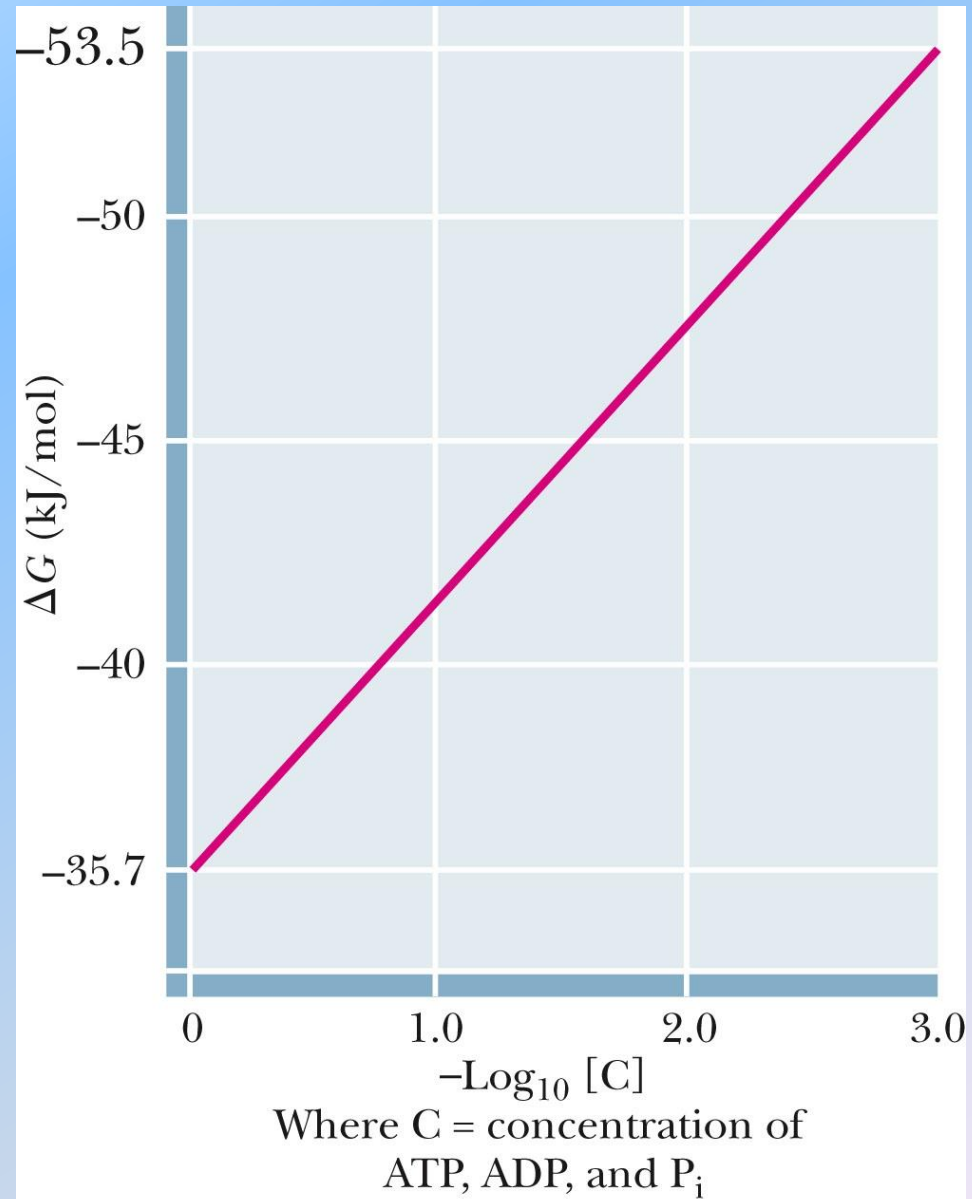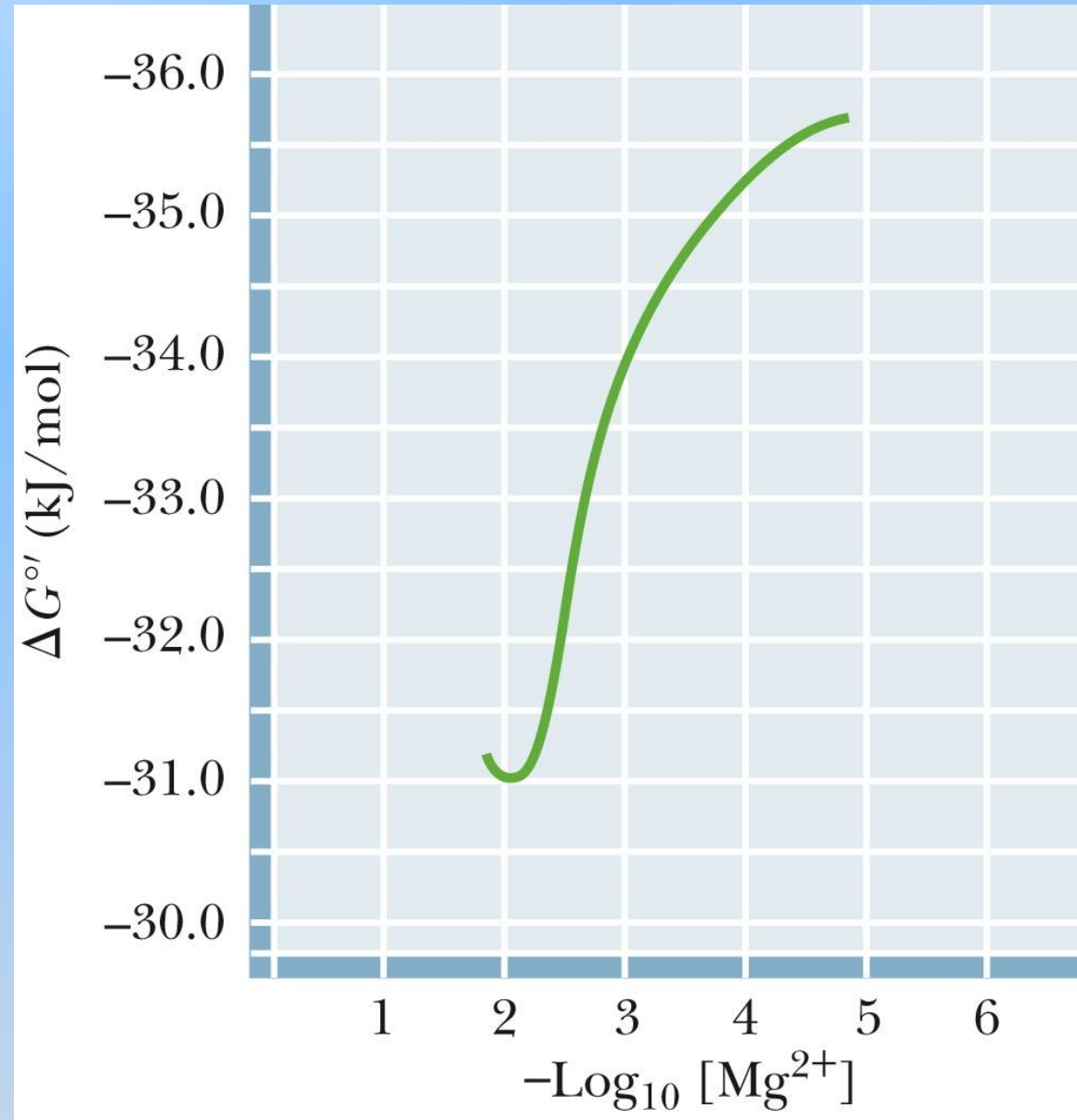
pH Effects

The pH dependence of the free energy of hydrolysis of ATP. Because pH varies only slightly in biological environments, its effect on ΔG is usually small.
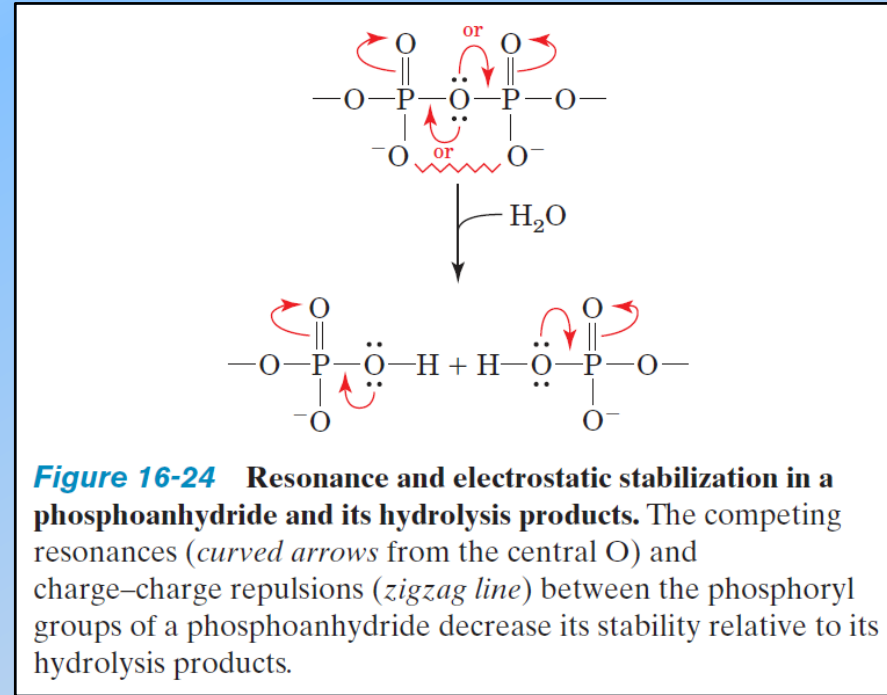
Metal Ions Effects

The free energy of hydrolysis of ATP as a function of total Mg^{2+} ion concentration at 38° C and pH 7.0.

What makes ATP hydrolysis so exergonic?

- Resonance destabilization of the phosphoanhydride bond in ATP (arrows)

- Charge-charge repulsions brought together in ATP (zig zag)

- Resonant forms of Pi restricted in ATP

- Resonant forms of non-Pi product also restricted

Figure 16-24 **Resonance and electrostatic stabilization in a phosphoanhydride and its hydrolysis products.** The competing resonances (*curved arrows* from the central O) and charge–charge repulsions (*zigzag line*) between the phosphoryl groups of a phosphoanhydride decrease its stability relative to its hydrolysis products.
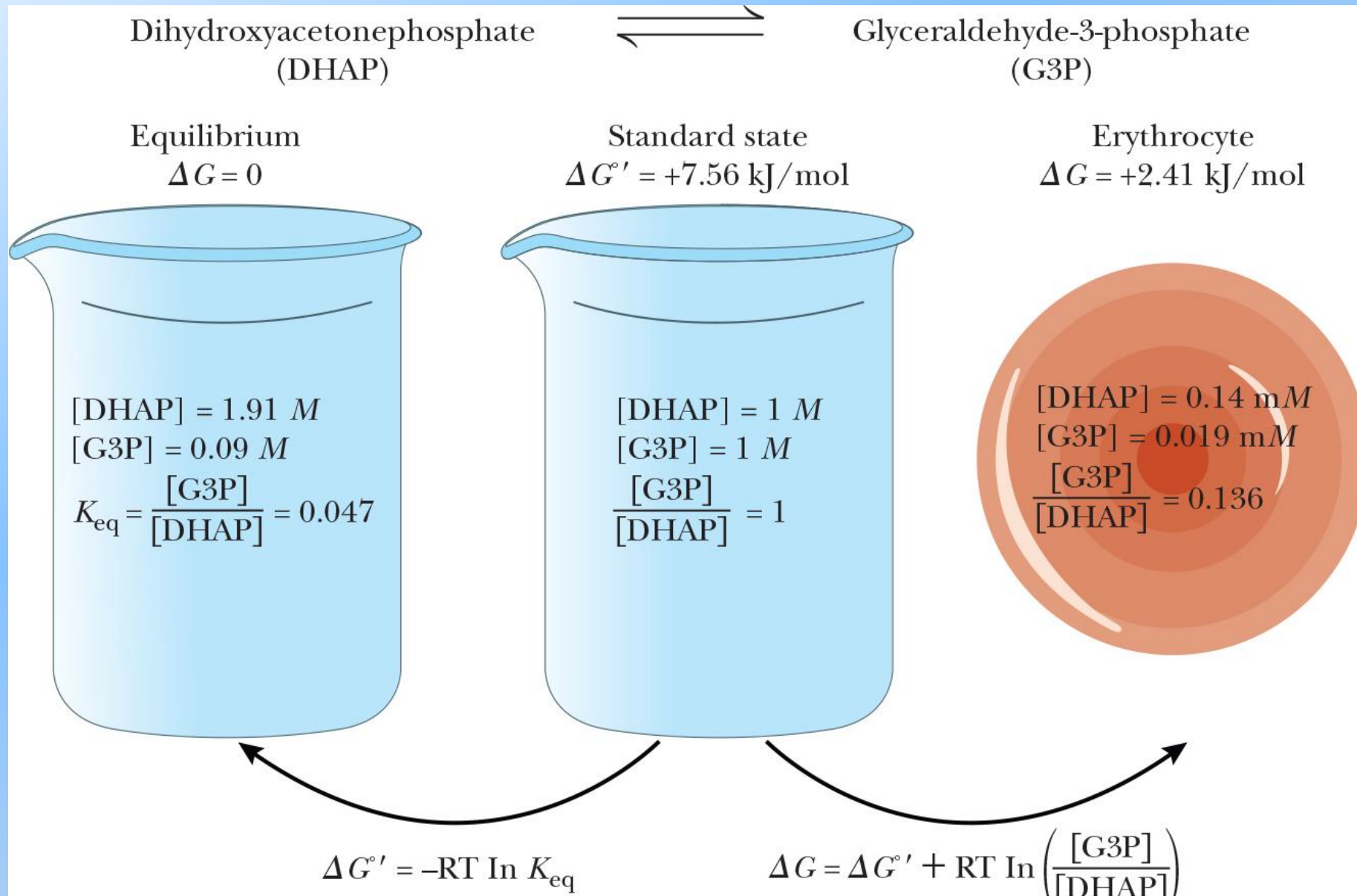
Cellular Conditions

- Cells are NOT at equilibrium or standard state

- Difficult to obtain equilibrium as system is open

- For a reaction, the magnitude of the cellular ΔG is a measure of how far cellular conditions are from standard state

$$A + B \rightleftharpoons C + D$$

$$\Delta G = \Delta G° + RT \ln\left(\frac{[C][D]}{[A][B]}\right)$$

I.e. Conc. other than 1 M will change ΔG

Cellular Conditions

Dihydroxyacetonephosphate (DHAP) $\rightleftharpoons$ Glyceraldehyde-3-phosphate (G3P)

Equilibrium
$\Delta G = 0$

$[DHAP] = 1.91\ M$
$[G3P] = 0.09\ M$
$K_{eq} = \dfrac{[G3P]}{[DHAP]} = 0.047$

Standard state
$\Delta G^{\circ\prime} = +7.56\ \text{kJ/mol}$

$[DHAP] = 1\ M$
$[G3P] = 1\ M$
$\dfrac{[G3P]}{[DHAP]} = 1$

Erythrocyte
$\Delta G = +2.41\ \text{kJ/mol}$

$[DHAP] = 0.14\ mM$
$[G3P] = 0.019\ mM$
$\dfrac{[G3P]}{[DHAP]} = 0.136$

$\Delta G^{\circ\prime} = -RT\ \ln K_{eq}$

$\Delta G = \Delta G^{\circ\prime} + RT\ \ln\left(\dfrac{[G3P]}{[DHAP]}\right)$

Quick Quiz

In cells, biochemical reactions are typically:

a. at equilibrium

b. occurring at standard state concentrations of reactants and products

c. at pH 5.5

d. none of the above

Quick Quiz

What will be the final pH of a solution made by mixing 20 ml of 12.5 mM Carbonic acid with 5 ml of 60 mM NaOH?

For H_2CO_3, pKa_1 = 3.77, pKa_2 = 10.24.

a. 10.24 + log (2/8)
b. 10.24 + log (8/2)
c. 3.77 + log (2/8)
d. 3.77 + log (8/2)

Quick Quiz

Formic acid has a K_a of 1.78×10^{-4} M. Ammonium has a K_a of 5.62×10^{-10} M. At pH 7.0:

a. Formic acid will be protonated, but Ammonium will be deprotonated
b. Formic acid will be deprotonated, but Ammonium will be protonated
c. Both Formic acid and Ammonium will be protonated
d. Both Formic acid and Ammonium will be deprotonated

Quick Quiz

Which of the following solvents will most effectively interfere with an ionic interaction?

a. Formamide (Dielectric Constant = 109)
b. Acetic acid (Dielectric Constant = 6.2)
c. Water (Dielectric Constant = 78.5)
d. Solvent does not interfere with ionic interactions

# Quick Quiz

If ΔH is 110 kJ/mol and $-T\Delta S$ is -140 kJ/mol, the reaction is:

a. spontaneous and driven by entropy
b. spontaneous and driven by enthalpy
c. non-spontaneous because of an entropic penalty
d. non-spontaneous because of an enthalpic penalty

E.g. Charging tRNAs

3. In protein synthesis, $tRNA^{Gly}$ is charged with glycine by the following reaction:

$$tRNA^{Gly} + glycine + ATP \leftrightarrows glycyl\text{-}tRNA + AMP + 2P_i$$
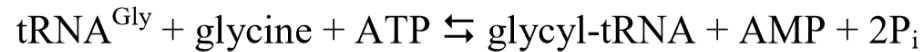
The $\Delta G°´$ for hydrolysis of glycyl-tRNA is -33 kJ/mol. For other $\Delta G°´$ values, use those given in Fig. 3.7 of the Mathews et al. Chapter 3 posted on the class eLearning site. Assume all values are for the standard temperature of 25°C.

a. Calculate $\Delta G°´$ for this charging reaction?
   This reaction is a coupled reaction, which is the sum of the following reactions:

$ATP \leftrightarrows AMP + PP_i$	$\Delta G^{o´} = -31$ kJ/mol (from Table 4.7, Chap. 3)
$PP_i \leftrightarrows 2P_i$	$\Delta G^{o´} = -33$ kJ/mol (from Table 4.7, Chap. 3)
$tRNA^{Gly} + glycine \leftrightarrows glycyl\text{-}tRNA$	$\Delta G^{o´} = +33$ kJ/mol (given in problem)

   Summing the $\Delta G^{o´}$ values = $\Delta G^{o´}$ for the overall charging reaction = -31 kJ/mol

   H_2O and H^+ are not included in the chemical equation since they are constant and subsumed in the $\Delta G^{o´}$ values.

b. What is the $Keq´$ for this charging reaction?
   $\Delta G^{o´} = -2.303RTlogKeq´$

   $Keq = 10exp\text{-}\Delta G^{o´}/5.71kJ/mol = 10exp\text{-}(-31$ kJ $mol^{-1}/5.71$ kJ $mol^{-1})$

   $= 10^{5.43} = 2.69 \times 10^5$ M

Daily Human Requirement for ATP

- The average adult human consumes approximately 11,700 *kJ* of food energy per day

- Assuming thermodynamic efficiency of 50%, about 5860 *kJ* of this energy ends up in form of ATP

- Assuming 50 *kJ* of energy required to synthesize one mole of ATP, the body must cycle through 5860/50 or 117 moles of ATP per day

- This is equivalent to 65 kg of ATP per day

- The typical adult human body contains 50 g of ATP/ADP

- Thus each ATP molecule must be recycled nearly 1300 times per day

- ATP supply in a cell provides free energy for only 1-2 minutes!

Weak Forces

- Energies of weak forces range from -0.4 to -40 kJ/mol

- Weak forces include:
  1. **Ionic interactions (-20 kJ/mol)**
  2. **Van der Waals interactions (-0.4 to -4 kJ/mol)**
  3. **Hydrogen bonds (-12 to -30 kJ/mol)**
  4. **Hydrophobic interactions (>-40 kJ/mol)**

By convention, an attractive interaction has a negative energy!

| Bond	Energy (kJ/mol)
H-H	436
C-H	414
C-C	343
C-O	351

Water Organization

- Hydrophobic molecules are non-polar and organize water into a clatharate-like structure

- The water becomes more ordered
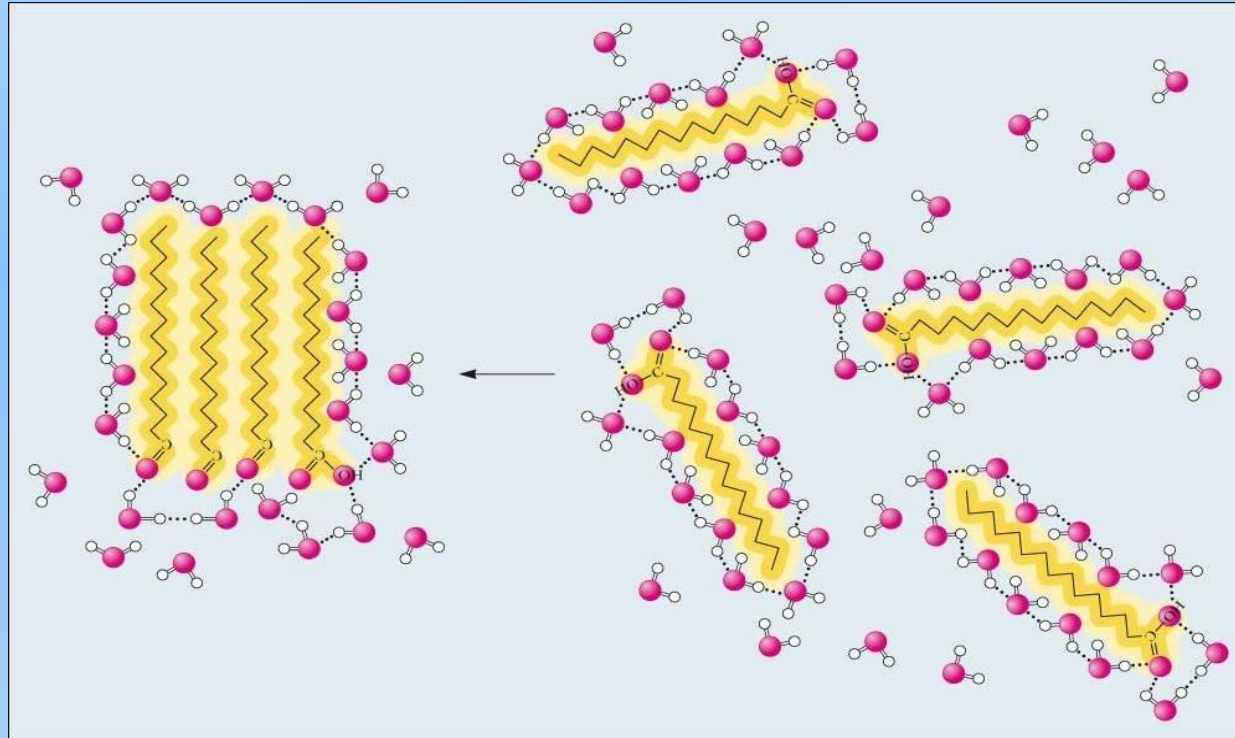
- *Unfavorable decrease in entropy?*
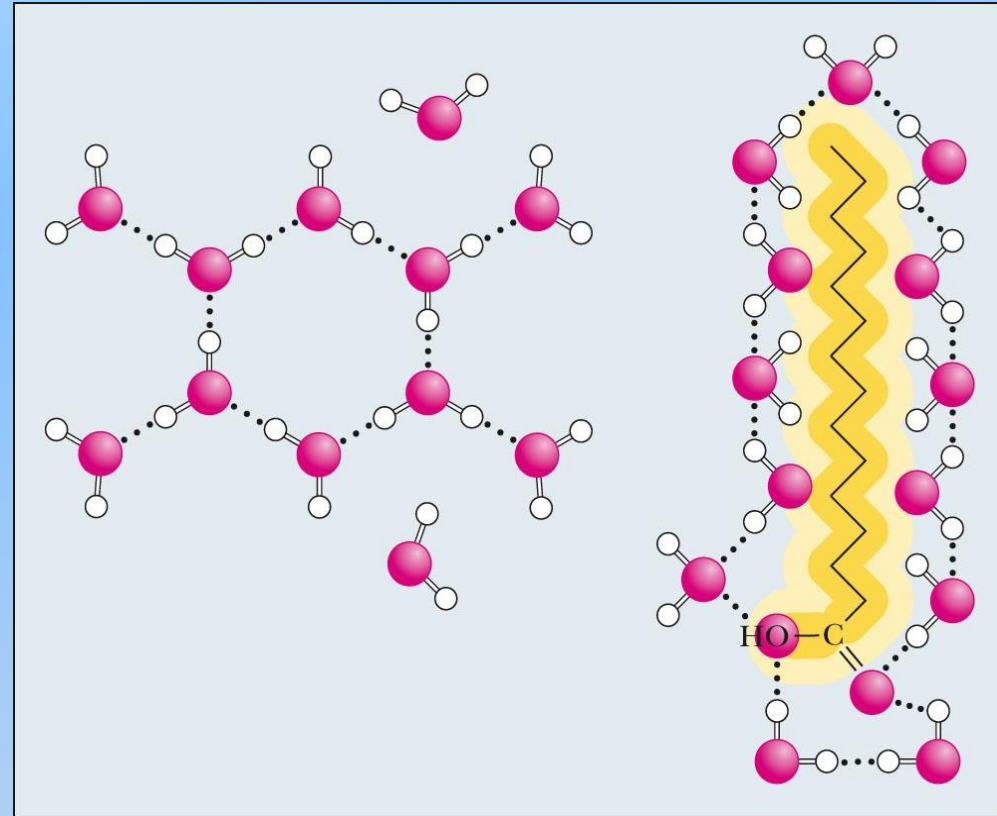
Entropy

- Non-polar molecules associate with each other… **ultimately organizing LESS water molecules**

- Minimum decrease in entropy by releasing water from the clathrate structures
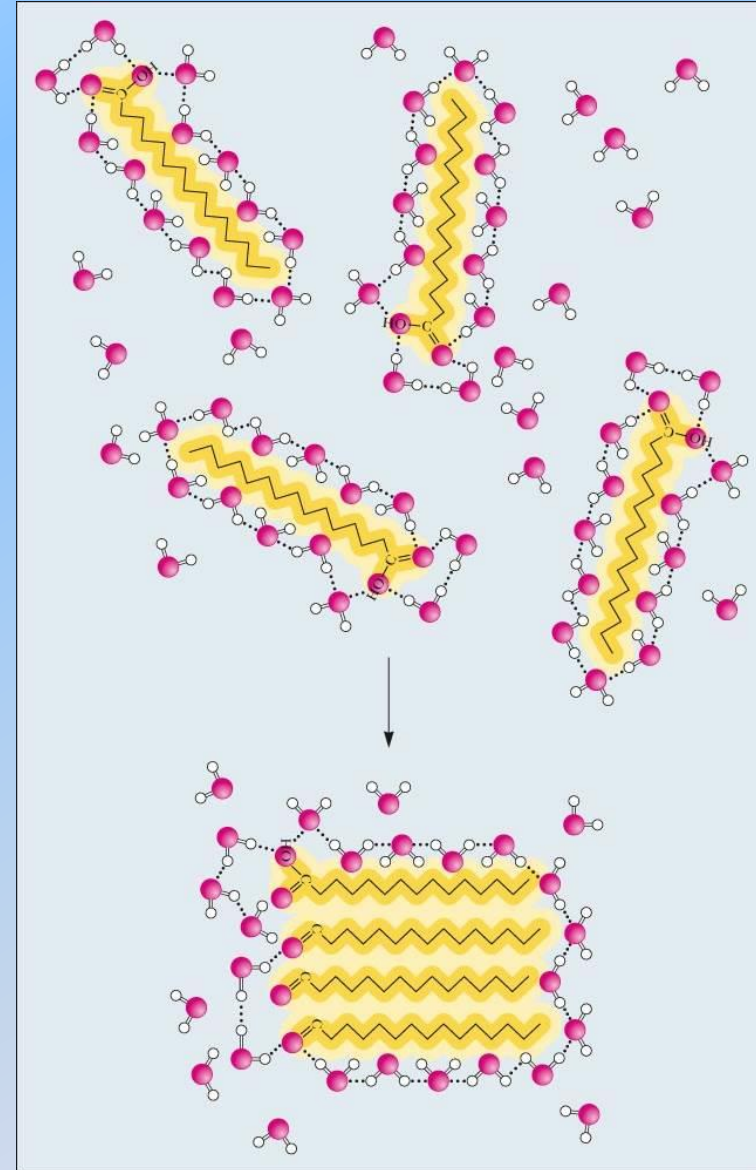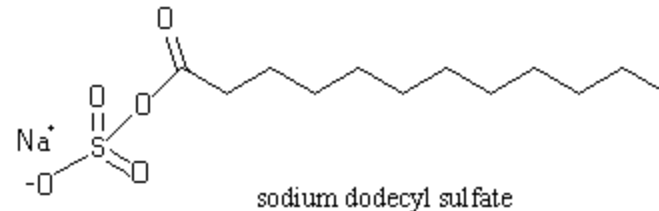
Hydrophobic Interactions

- Occur in water as hydrophobic molecules tend to interact with each other and exclude polar molecules
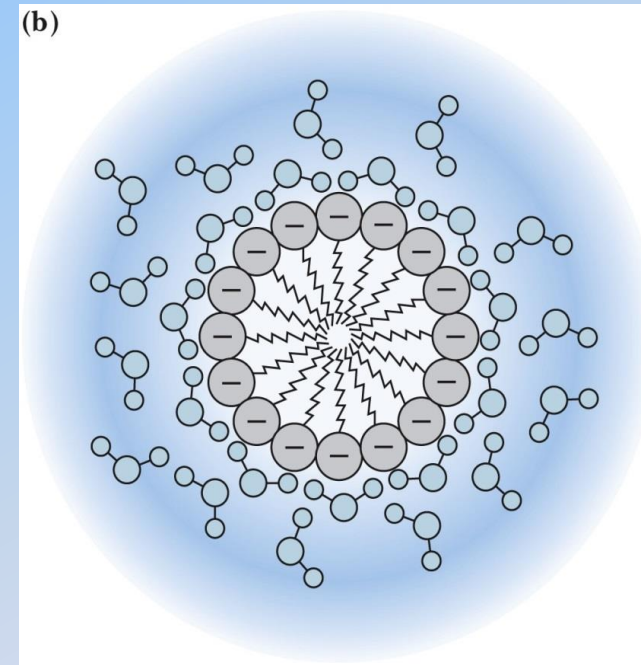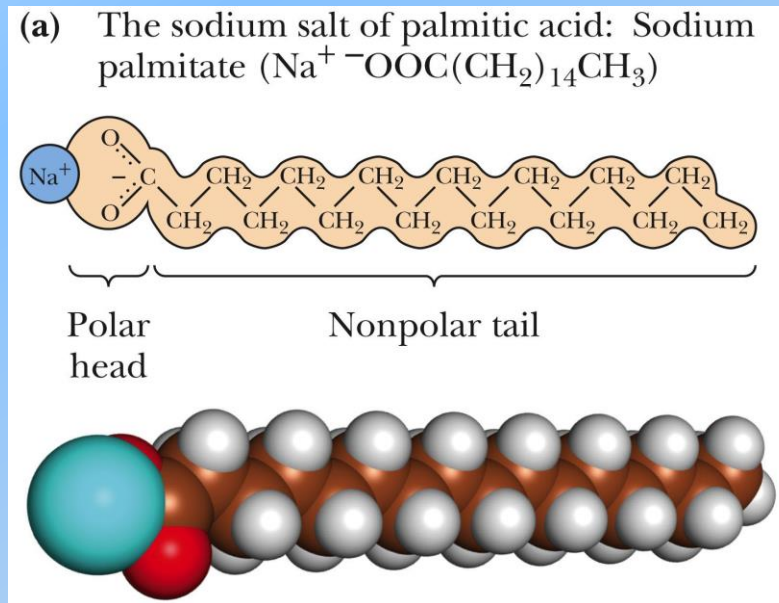
Amphiphilic Molecules

Also called "amphipathic"

- Refers to molecules that contain both polar and nonpolar groups

- These molecules are attracted to both polar and nonpolar environments

- E.g. fatty acids, detergents(SDS), and most amino acids

sodium dodecyl sulfate

Hydrophobic Interactions drive Micelle Formation by Amphipathic Lipids

- Negatively charged head groups orient to the micelle surface and interact with the polar H_2O molecules via H bonding.

- The nonpolar hydrocarbon tails cluster in the interior of the spherical micelle, driven by hydrophobic interactions

(a) The sodium salt of palmitic acid: Sodium palmitate $(Na^+ {}^-OOC(CH_2)_{14}CH_3)$

Polar head   Nonpolar tail

(b)

Quick Quiz

Hydrophobic interactions are entropically _____, as _____ water molecules are ordered when they form.

a. favorable, less
b. favorable, more
c. unfavorable, more
d. unfavorable, less

Study Guide

- ✓ 1st and 2nd laws of thermodynamics
- ✓ Meaning of state functions vs. path functions
- ✓ Definitions of endothermic, exothermic, exergonic, endergonic, amphipathic/amphiphilic, micelle
- ✓ Thermodynamic formulae and their use in problems
- ✓ Meaning of $\Delta G°$ and $\Delta G°'$
- ✓ Van't Hoff plots and using them to determine $\Delta H°$ and $\Delta S°$
- ✓ Coupled reactions and phosphoric acid anhydrides such as ATP
- ✓ Hydrophobic interactions