

Chapter 13 Principles of Bioenergetics

Problems

2-6, 8, 10, 13,14, 20-22

Read Intro to part II on your own

13.1 Bioenergetics and Thermodynamics

A. Biological Transformations obey Laws of thermodynamics

1st law, - in any physical or chemical change total amount of E in universe is constant
(E not created or destroyed)

2nd law entropy of universe (S) is always increasing

Background - what is entropy

use 3 quantities to describe the energy of chemical processes

Enthalpy (ΔH j/mol) heat content of the system, is negative if heat released

Entropy (ΔS J/mol·K) randomness of the system, is positive if gets more random

Free Energy (ΔG j/mol) energy available for doing work is - for spontaneous reactions

Review of Gen Chem terms

Internal Energy -E -Sum of kinetic and potential energy of all particles in a system

Enthalpy -H- heat content of a reaction

Entropy -S- a measurement of randomness in a system

Gibbs Free Energy -G- Amount of energy available to do work

In biological systems, P, T constant

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

Since ΔH is a measure of heat released to surrounding you can think of as randomness of surroundings

ΔS is randomness of system itself

So ΔG is a measure of overall randomness of universe and as long as that is negative, the randomness of universe has increased and the reaction can be spontaneous

B. Cells Require Sources of Free Energy

Most cells are in isothermal and isobaric environment
(Constant T and P)

Since constant T, cannot use heat flow as energy source

So Gibbs Free energy is only form of energy available

C. Free energy related to K_{eq}
 $aA + bB \rightarrow cC + dD$

$$K_{eq} = \frac{[C]^c [D]^d}{[A]^a [B]^b}$$

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

If not at equilibrium will try to move in that direction

ΔG° is a measure of how far from equilibrium you are when everything is

$$[] = 1M$$

$$T = 298$$

$$P = 1atm$$

$$[gas] = 1 atm$$

Not a great def for biochemists

$$1M H^+ = pH 0$$

$$[H_2O] = 55.5M \text{ and essentially a constant}$$

ΔG° used in Biochem for $pH=7$, $[H_2O]=55.5M$ and essentially a constant

$$\Delta G^\circ = -RT \ln K'_{eq}$$

Note 1: $-\Delta G^\circ$, $K_{eq} > 1$, reaction go toward products

$+\Delta G^\circ$, $K_{eq} < 1$, reaction go toward reactants

can use to convert from ΔG to K_{eq}

Note 2: This book state that $[Mg^{2+}]$ is also treated as a constant. I have not seen that before

Problem 2(b) from end of chapter

Calculate ΔG° for the reaction:

Dihydroxyacetone phosphate \rightleftharpoons glyceraldehyde 3-phosphate

Given that the K'_{eq} for the reaction is 0.0475

$$\begin{aligned} \Delta G^\circ &= -RT \ln K'_{eq} \\ &= 8.3145 \text{ J/K}\cdot\text{mol} \times 298\text{K} \times \ln(0.0475) \\ &= +7550 \text{ J/mol} \\ &= 7.55 \text{ kJ/mol} \end{aligned}$$

D. Actual free-energy changes depend on reactant and product concentrations

ΔG° the energy change when $[]$ start at 1M

ΔG the energy change that occurs for a reaction under a particular set of conditions

Note these are different.

Lots of tables around that tabulate ΔG° for various biochemical reactions

And this is often used to determine if a reaction will be spontaneous in a cell
 however [] are never 1M, so may not apply

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

Example 2. Continue on with previous example of Dihydroxyacetone phosphate \rightleftharpoons glyceraldehyde 3-phosphate $\Delta G^{\circ} = 7.55$ kJ/mol pretty highly unfavorable. Say we had other processes in the cell that kept the concentration of the reactant high, say 1M, but kept the concentration of the product low, say .01M. What does this do to our ΔG ?

$$\begin{aligned} \Delta G &= \Delta G^{\circ} + RT \ln Q \\ &= 7,500 + 8.3145(298) \ln([\text{products}]/[\text{reactants}]) \\ &= 7,500 + 8.3145(298) \ln(.01/1) \\ &= 7,500 + 8.3145(298) \ln(.01) \\ &= 7,500 - 11,400 \text{ J} \\ &= -3900 \text{ J} \\ &= -3.9 \text{ kJ} \end{aligned}$$

In this case our cellular conditions have made a reaction that we thought was unfavorable with a + ΔG into one that is favorable with a - ΔG .

Thus always have to put in cellular concentrations to find out if really spontaneous in cell

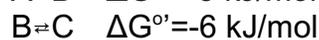
Other points

ΔG° and ΔG are measures of the *maximum* amount of free energy that an reaction can *theoretically* deliver under *ideal* conditions... actual results may be less and usually are.

Remember, just because $\Delta G^{\circ} < 0$ does not mean will occur. Just that it can occur. Kinetics and high activation energy may prevent reaction from occurring without a catalyst

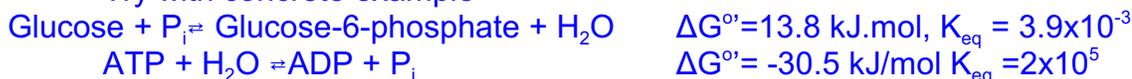
When you use a catalyst, only changes the rate does not change the energy

E. Free energy changes are additive



$$K_{eq} = K_{eq1} \times K_{eq2}$$

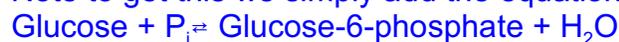
Try with concrete example



What is ΔG° and K_{eq} for



Note to get this we simply add the equations together



And the P_i and H_2O fall out of both sides of the equation to give us the equation we want

if you add the equations you add the ΔG° s

$$\text{So } \Delta G^{\circ} = 13.8 + (-30.5) = -16.7 \text{ kJ/mol}$$

if you add the equations you multiply the K_{eq}

$$3.9 \times 10^{-3} \times 2 \times 10^5 = 7.8 \times 10^2$$

If you had to subtract the second equation what would you have done?

(Subtract the ΔG° , divide the K_{eq})

13.2 Chemical logic and common Biochemical reactions

Cells can't do all the different chemical reaction yu learned in organic class

So this section emphasizes the types of chemistry seen in cells

5 main categories

Make or break C-C bonds

internal rearrangements

Isomerizations

Eliminations

Free-radical reactions

Group transfers

oxidation/reduction

Two other principles

When breaking a covalent chemical bond, where do the electrons go?

Figure 13-1

Homolytic cleave - each atom in bond get an electron so each is a radical

Heterolytic Cleavage (more common) 1 atom retains both electrons, other atom goes without

Many biochemical (and organic reactions) involve interactions between:
 Electrophiles = electron seeking = electron deficient = electron acceptor = Lewis Acid
 Nucleophiles = + charge seeking = electron rich = electron donor = Lewis Base

Figure 13-2

Reactions that make or break C bonds

Heterolytic cleavage of a C-C bond yields carbocation and carbanion.

Reverse is

Formation of a C-C bond usually involves a nucleophilic carbanion (L.B.)

And an electrophilic carbocation (L.A.)

Carbanions and carbocations are so unstable that do not occur in Biochemistry, so neither reaction can take place biochemically when only C is involved.

Can only occur if adjacent functional groups contain electronegative atoms like N or O so electronic structure of adjacent to C atom helps stabilize ion in a Biochemical Reaction

Figure 13-3

Look for reaction that occur adjacent to Carbonyls (Figure 13-4)

Rearrangements, isomerizations and eliminations

redistribution of electrons around a molecule

Can be simple as water elimination (right column page 498)

Or complicated internal oxidation/reduction Figure 13-6

Free Radical Reactions

Once thought to be rare (free radicals are very reactive and dangerous to cells)

Now has been observed in many reactions

See Figure 13-7

Group Transfers

the transfer of acyl, glycosyl and phosphoryl groups from one nucleophile to another is common

left column page 499

Good old S_N1 or S_N2 type reactions

Will see a lot with PO_4 group (next section)

Oxidation/Reduction

C can be in 5 oxidation states (Figure 13-9)

Reaction where compound loses 2 electrons and 2 protons - dehydrogenations

When C become bound to an oxygen - oxidases

Unless O comes directly from O₂ then - oxygenase

Oxidation requires a reduction
 Oxidations release energy
 Involved in release of E for cell energy

Most of above reaction require cofactors

Biochemical and Chemical Equations are not equivalent
 Biochemical reactions are usually simplifications
 For instance $\text{ATP} + \text{H}_2\text{O} \rightarrow \text{ADP} + \text{P}_i$
 Different forms of ATP, ADP and P⁻ depending on pH
 Also Mg²⁺ is part of reaction
 So a whole lot of things are swept under the table
 PH7, 1mM Mg²⁺ are part of ΔG°

13.3 Phosphoryl Group Transfers and ATP

You already know that ATP is the major energy currency in cell will use this E for virtually every thing from active transport to synthesis of a new protein

let's examine the energy of this process in more detail

A. Free E change for ATP hydrolysis is large and negative

Figure 13-11 on board

Lots of E released -30.5 kJ/mol

Why is this energetically favored process?

1. ATP had a -4 charge
 Releasing Pi allows some of the charges to separate thus lowering E of system
2. Pi itself, resonance stabilized so likes to be in that form
3. As shown ADP-H^{2-} will ionize to ADP^{3-} releasing another H⁺
 To low [H⁺] of solution (10⁻⁷ H⁺)
4. Go from 2 molecules to 3 molecules... entropy increases

Also remember earlier note ΔG° is at 1M conc. What about real conc in cell

(See worked example 13-2 for full analysis)

ATP and ADP usually associated with Mg²⁺

see table 13-5 for example concentrations

[ATP]= 2,25x10⁻³

[ADP] = 2.5x10⁻⁴

[Pi]=1.65x10⁻³

Final answer -51.8 kJ/mol!!!

(That also means it takes that much E to make ATP)

Say phosphorylation potential is -50 to -65 kJ/mol

B. Other Phosphorylated compounds and Thioesters

There are several phosphorylated compounds that have a higher dephosphorylation energy than ATP, and these compounds can be used to make ATP

1,3-Bisphosphoglycerate (figure 13-14)

Phosphoenolpyruvate, PEP Figure 13-13

Phosphocreatine Figure 13-15

In all cases can see that the product has some resonance stabilization that help to drive the reaction toward the product

Will see 1,3 Bisphosphoglycerate and PEP as intermediates in glycolysis (breakdown of sugar to make E without oxygen)

Phosphocreatine is used to store E in muscles

So far have looked at phopho- anhydrides ...Thioesters are another set of high e compounds

Thioesters have a higher E than plain old esters because regular esters have some degree of resonance stabilization relative to thioesters, so have a lower starting E (see figure 13-17)

Thioesters aren't used so much for energy, but as a high energy intermediate that helps to donate acetate groups to other compounds

One of the biggies is Acetyl-CoA. Will see a lot of this guy in oxidative phosphorylation and in fatty acid synthesis because loves to donate the acetate group. (No structure at this point)

C. ATP provides E by group transfer, not simple hydrolysis

Figure 13-18

often you will see ATP driving reaction written as 1 step reactions

This implies that ATP is simply hydrolyzed for the reaction to occur

This is oversimplification.

If ATP simply hydrolyzed, then E is released as heat, and not useful

Usually is a 2 step process

P_i or PP_i or AMP is covalently attached either to substrate or to enzyme

This forms a High E intermediate

This group then comes off in a second step where the product is formed

Thus ATP is usually part of covalent catalysis

I said usually above because there are some process where ATP (or GTP) is bound, and its hydrolysis is used to toggle protein conformations

Used in mechanical motion

Used in transport?

Phosphate compound usually divided arbitrarily into

High E (>-25 kJ/mole)

Low E (<-25 kJ.mole)

ATP an the likes are high E

Glu-6-P low

Watch out for tem “High Energy Phosphate bond”

Its not that the bond has lots of E, but, as seen above, its that the products have a much lower E than the combined compound.

Often due to resonance forms that occur in the products that weren't there in the parent.

One final point about why ATP is a good E storage compound

1. Releases large amount of E

2. Actually is kinetically very stable

Requires large activation energy (200-400kJ/mole)

Thus does not spontaneously hydrolyze

D. ATP Donate more than just P_i

ATP reaction usually SN_2 Nucleophilic reactions (figure 13-20)

As such 3 different places to attack (α , β , γ)

And each place can collapse in different directions, so 6 different possible products

Actually see three in biological systems

hydrolysis of $\beta\gamma$ linkage releases 31 kJ

hydrolysis of $\alpha\beta$ linkage releases 46 kJ so more E

Further push is PP_i to $2P_i$ give additional 19 kJ

use this linkage when need more E

E. Assembly of Information molecules requires E - nothing special use ATP or NTP or dNTP

F. ATP Energy for active transport and muscle contraction

Saw some transports go through phosphorylated intermediate

Other didn't

Won't study muscle contraction here, but think that conformational toggling

Between ATP and ADP + Pi forms so no direct phosphorylated intermediate

So simple hydrolysis

G. Transphosphorylations between nucleotides occur in all cell types

Focused on ATP

But GTP, UTP CTP, dATP, dGTP, dTTP and dCTP are all energetically equivalent

all cells have nucleoside diphosphate kinases

$ATP + NDP \rightleftharpoons NTP + ADP$

In presence of Mg^{2+}

Delta G about 0, so K about 1

But big excess of ATP drives forward

Let's skip Adenylate kinase, creatine kinase

H. Skip Inorganic Phosphate

13.3 Biological Redox Reactions

transfer of phosphate groups is one way to move E in metabolism, but there is a second way

transfer of electrons in redox reactions

The math to understanding this is linked to redox reaction and redox potentials.

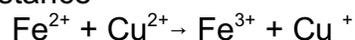
Some of you had redox potentials in Analytical some of you haven't so let's explore this for a bit

Note: Not taking book method

A. A reminder of Oxidation math & concepts

In any redox reaction there is always one species undergoing oxidation, and one undergoing reduction. That is why we call it a re-dox reaction

For instance



Has the two half reactions

$\text{Fe}^{2+} \rightarrow \text{Fe}^{3+} + \text{e}^-$ Electrons on right - oxidation or
positive charge increased -oxidation

$\text{Cu}^{2+} + \text{e}^- \rightarrow \text{Cu}^+$ Electron on left reduction, or
Positive charge reduced - reduction

You might want to brush up on how to balance redox reactions, I won't go into it here

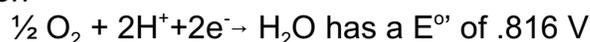
If you never saw this reaction before. How would you know that the reaction goes as written, and not in the reverse direction??

B. Reduction potentials

This is tied to a quantity called the **reduction potential**

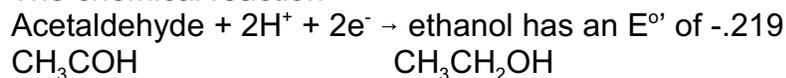
Reduction potential is a number that is used to tell the tendency of a reaction to occur as a reduction reaction. When you combine two reaction the reaction with the large reduction potential will occur as a reduction, while the $\frac{1}{2}$ reaction with the smaller reduction potential will go in the opposite direction and become an oxidation.

For instance on page 511 you have a table 13-7 that says that the reaction

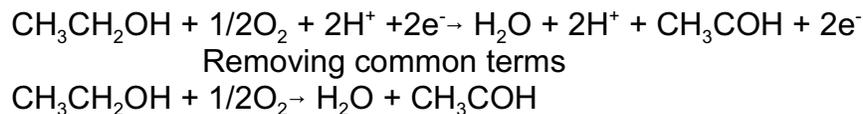


E° the potential when everything is at 1M concentration, pH 7, the usual biological assumptions

The chemical reaction



Based on these two E° you would predict that the 1st reaction should go as written, as reduction that requires electrons, and that it can reverse reaction 2 do it will go as an oxidation to supply the electrons thus the reaction will be



Thus you have predicted that ethanol can be oxidized to acetaldehyde

Reduction potentials are established by measuring each $1/2$ reaction against the reaction $\text{H}^+ + \text{e}^- \rightarrow 1/2 \text{H}_2$ as shown in figure 13-14

This reaction has been chosen as our 0 point and is given the potential 0.00 V

(That explains why some potential listed in table are + and some are -)

C. Reduction potentials and ΔG

Just like the ΔG and ΔG° we out table is established using 1M concentrations (ΔG°), but you can find the E of any given reaction by using an equation that adjusts for concentration terms.

This equation is:

$$E = E^\circ + RT/nF \ln [\text{product}]/[\text{reactants}]$$

Where product and reactant refer to the reduction reaction equation

If T is 25° C, RT/N is a constant, so you will see the equation

$$E = E^\circ + .026\text{V}/n \ln[\text{product}]/[\text{reactants}]$$

Where n is the number of electrons in the reaction

There is a direct te between ΔG and E°

$$\Delta G = -nFE$$

Or, at standard state

$$\Delta G^\circ = -nFE^\circ$$

Where F is Faraday's constant = 96.5 kJ/V·mol

If you had Analytical you know there is a lot more calculation than we can do here. But for Biochem we will stop here.

Remember that you can convert between E° and ΔG

And that the reaction with the more positive E° goes forward, while the one with the less positive E° gets reversed.

D. Biological oxidations

Note figure 13-13 in text oxidation state of C compounds. Get much different numbers than the methods taught in General Chem may want to point this out

When C is in the CH_4 for it is the most reduced, that is

Assign H = +1

Then C = -4

CH_3OH methanol

H=+1, O= -2 C= -2

CH_2O formaldehyde

H=+1, O= -2, C=0

HCOOH Formic acid

H = +1, O= -2, C = +2

When C is in CO_2 it is in its most oxidized form

Assign O = -2

Then C = +4

As C is attached to more O it gets more and more oxidized

Since our biochemistry is based on getting E from oxidizing things, the more reduced and saturated a C is the more energy it can give you. This is why fats, $-\text{CH}_2-$ store more energy than sugars $-\text{CHOH}-$ because the alcoholic C are already partially oxidized

Thus one way to oxidized C is to simply add more O

C are also more oxidized when they have multiple bonds to other C

CH_3-CH_3

H=+1, C = -3

CH_2-CH_2

H=+1, C = -2

HCCH

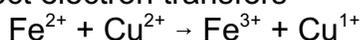
H=+1, C= -1

Thus a second way to oxidize C is to remove H from it in a dehydrogenation reaction (done by a dehydrogenase enzyme)

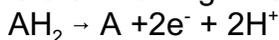
Not all biological redox reaction involve C, thus let's generalize just a bit more

All redox reactions involve the transfer of electrons. Based on how these electrons are transferred we group biological redox reactions into 4 different forms

1. Direct electron transfers



2. Transfers involving H^+ or H atoms

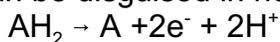


2 notes here

This is NOT an acid reaction

We did not end up with A^{2-} but $\text{A} + 2\text{e}^-$

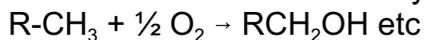
this can be disguised in net reactions



3. Transfers involving the hydride ion (H^-) ($:\text{H}^-$)

Will see more of this in a bit

4. Direct combinations of C with Oxygen



All 4 happen in cells

Will talk about reducing equivalents, or the number of electrons transferred in a reaction, and may ignore the details of what other atoms were moved or transformed

E. Oxidation of glucose to CO_2 will involve the release of lots of energy. Only a few of the steps will involve direct phosphorylation intermediates, and direct synthesis of ATP. There are many other steps where oxidation and reduction are performed and two major carriers of electrons in these reactions are $\text{NAD}^+/\text{NADP}^+$ and FAD or FMN

The book spends some time talking about these, but I think I will skip until we are further along. We will come back to these important cofactors when we have them in actual reactions.