Lecture 2  
Tuesday, January 08, 2008

1. Foundations

- Non-covalent interactions in biomolecules
- Water and the hydrophobic effect
- Biochemical Thermodynamics
- pH and the Henderson - Hasselbalch Equation
- Biochemical buffers

2. Protein Composition and Structure

- Amino acids and peptides
- Titration
- Secondary structures

Recommended Problems

- Chapter 1: all.
- For Problem 1.4, identify the patterns that give $\Delta G < 0$ and think about how temperature would affect this.
- The pH calculation problems are not well explained in the text (there aren’t any examples). You may have to refer back to your Freshman Chemistry notes (if you still have them) or see the TAs during office hours. The first hyperlink below might be helpful here.

Helpful Web Sites

- Henderson-Hasselbalch Equation
- Biochemical buffering of blood pH.
B. Why does DNA form double-strand helices?
   - Why base pair like they do?

To address these questions by looking at structures & chemistry involved:

1. Covalent bonds of nucleotides
   
   \[
   \begin{align*}
   &C-C \quad C=O \\
   &C-N \quad N-H \\
   &C-O
   \end{align*}
   \]

   Arise from orbital overlap & sharing of e-

2. Non-covalent "bonds" or interaction
   4 major categories

   a. Electrostatic interactions
      - Charge-charge interactions
      - Dipole-dipole interactions
      - Strength depends on distance & environment

      \[ E \propto \frac{q_1 q_2}{r^2} \]
1. Charge or partial charge.

2. Dielectric constant. ($D$ in book)

3. Separation or distance between 2 atoms.

\[ E \propto \frac{q_1 \cdot q_2}{E^0 \cdot r^2} \]

- if $r$ very small
- if $E$ is large
- if $r$ large, $E$ small

As $E \uparrow$, $E \downarrow$

$E$ large in H$_2$O

As $E \downarrow$, $E \uparrow$

$E$ small in membrane.

b. Hydrogen bonds.

- O-H and N-H bonds are polar
- H has partial pos charge
- C=O & has partial negative charge.

H-bonds involve H on N-H or O-H interacting with N or O
H-bonding explains why DNA base pairs.

\[
\begin{align*}
\text{Sugar} & \quad - \quad - \quad H - H \cdots O
\end{align*}
\]

A : T

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\begin{align*}
\text{Sugar} & \quad - \quad - \quad H - N \cdots H
\end{align*}
\]

G : C

C. van der Waals. \\
Very weak, with strong distance dependence makes it very strong at small \( r \).

\[
E \propto \frac{g(r)}{r^6}
\]
arise from fluctuations in $e^-$ in $\pi$-orbitals.

- VdW interactions only significant when there is contact.

- understand base-stacking in helical DNA.

- hydrophobic interaction. 
  how non-polar molecules interact with polar molecules.

- polar molecule is generally $H_2O$

- water dominates as solvent
  water is $H_2O$
in solution, H$_2$O molecules interact

clusters of water molecules

- in solution, [H$_2$O]$^+_n$ H$^+$ n = 5-7
no H$_2$O in water!

- forms clusters thru H-bonding
  - each H$_2$O molecule prefers 4 H bonds.

- polar molecule, glucose $\cap$ ethanol $\supset$ interact like H$_2$O

- non-polar molecule, H H - C - H or fat $\supset$ these can't H-bond with H$_2$O
Non-polar molecules disrupt H-bond network.

- Orient H₂O molecules on surface of fat.

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- Under these conditions, non-polar molecules cluster together

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Hydrophobic effect describes the tendency of non-polar molecules to cluster together to form max. # of H₂O that can form max. H-bonds with other water.

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c. how "stable" is ds DNA

ds = double-stranded
ss = single-stranded

2 complementary strands of DNA in H2O form ds DNA at 799%.

If understand why form, how much energy is in ds DNA, then we understand energy required to open ds DNA in translation.

Use thermodynamics to discuss this.

In thermodynamics: system + energy = surroundings.

System - what you're interested in, everything else in universe.
First Law of Thermodynamics:
energy of a system and its surroundings is constant.

2 forms of energy:
work energy: energy xfer between syst. & surroundings that is "useful"

heat energy: dissipative, unuseful type of energy xfer

Second Law of Thermodynamics:
total entropy of system and surroundings increases in spontaneous process.

entropy is a measure of randomness.
-very useful concept.
-explains why diaphobia effect.
-gain entropy by releasing the molecules from surface of fats.
combine 1st & 2nd laws in Gibbs free energy equation:

\[ \Delta G = \Delta H - T \Delta S \]

- \( \Delta G \) = free energy
- \( \Delta H \) = enthalpy
- \( -T \Delta S \) = work content
- \( \Delta S \) = entropy

- which direction is spontaneous change.

if \( \Delta G < 0 \); spontaneous rxn

if \( \Delta G > 0 \); non-spontaneous rxn; rxn goes in other direction.

if \( \Delta G = 0 \); at equilibrium; no change.

see how these applied to understand ds DNA formation.

\[
\begin{align*}
\text{RNA} & \quad + \quad \text{DNA} \\
\text{H} & \quad \rightarrow \quad \text{ds DNA} \\
\rightarrow & \quad \text{AG} \\
\end{align*}
\]

\( \Delta G < 0 \)
Start with 2 single strands \( \rightarrow \) high entropy
- very flexible state
- high randomness.

- form ds DNA, reduce randomness
  entropy decreases; \( \Delta S < 0 \)

\[ \Delta G = \Delta H - T \Delta S \]

\( \Delta G > 0 \) unless \( T < 0 \) \( \rightarrow \) can't be.
  or \( \Delta H < 0 \)

- \( \Delta H \) must be large and negative.
- \( \Delta H < 0 \) due to H-bonds.
  vDW

  overcomes large negative \( \Delta S \)

D. pH and buffer.
DNA can be denatured by bases
by low pH.
When deprotonated, can't H-bond, ds DNA falls apart.

Example general acid dissociation reaction

\[ HA \rightleftharpoons A^- + H^+ \]

Equilibrium const. \( \frac{[H^+][A^-]}{[HA]} = K_a \)

\( K_a = \text{acid dissociation equilibrium constant} \)

\[ pK_a = -\log (K_a) \]

\( \text{low } pK_a \text{ means stronger acid.} \)

\[ \text{higher } pK_a \text{ means weaker acid.} \]

Sugar $\rightleftharpoons$ Sugar.
- Ionization reactions are central to understanding biochemistry.