Coverage: Lectures 1-11.

Study Hints:

1. Understand the solution to problem sets 1-3, in-class examples, and recitation sessions.
2. Read the lecture notes first, then the relevant sections of OLI if necessary.

Topics:

A. Fundamentals of Molecular Interactions:

- electrostatics, van der Waals, enthalpy, entropy.

B. Water Structure

- Hydrogen bonds, you should be able to identify donors and acceptors in any compound
- Functional groups and solubility properties.

C. Acids and Bases

- Acid/base theory - meaning of pK_a, alteration of pK_a by environment.
- Titration curves, obtaining pK_a from inflection point.
- Buffer calculations, how to make a very simple buffer, either monoprotoic or polyprotic.
- How to adjust the pH of solutions, given the starting and ending pH.

D. Amino Acids

- Full names and structures.
- Properties of sidechains.
  1. Chemical properties: e.g. H-bonding (e.g. Thr), acid-base behavior & approximate pK_a values (e.g. Glu), nonpolar (e.g. Phe).
  2. Beer's Law: ($A=\varepsilon[C]l$) & UV absorbing groups, calculation of ε based on composition, concentration determination from absorbance.

E. Peptides

- Peptide bond formation, be able to identify the peptide bond, draw the structure of a peptide.
- *cis/trans* forms of peptide bond, why the *trans* form is generally preferred.
- Sequence nomenclature (NH_2-aa_1-aa_2-....-aa_n-COOH)
- Calculation of protonation state and net charge at given pH.

F. Proteins

- 1^o structure - sequence determination by mass spec and Edman, types of cleavage reactions (CNBr, Chymotrypsin, Trypsin)
- 2^o structure - properties of α-helix, β-sheet (geometry).
- Ramachandran plot – origin of energy contours for glycine, C_β amino acids, and proline.
- Super 2^o structure (ie. β-barrel and β-α-β) & forces that 'hold it together'
- 3^o structure - What are the common features of all globular proteins?
- Know the size and source of the dominant forces in protein folding. How do these forces result in the final folded form of the protein? Which are enthalphic? Which are entropic?
  - i) Conformational entropy, S=RlnW
  - ii) Hydrophobic effect (solvent entropy)
  - iii) Hydrogen bonding
  - iv) Van der Waals (packing of core)
  - v) Electrostatics (usually a minor role)

G. Thermodynamics: Be able to use the following equations: $\Delta G^0 = - RT\ln[U]_{eq}/[N]_{eq} = \Delta H^0 - T\Delta S^0$

- You should be able to calculate fraction unfolded given ΔG^o (or ΔH^o & ΔS^o) or ΔG^o given fraction folded.
- Remember the ΔH^o is obtained from the temperature dependence of K_{eq} (Plot ln K versus 1/T)
- What does the sign of ΔG^o tell you about the extent of a reaction?
- What do the signs of ΔH^o or ΔS^o tell you about a reaction?
- Come prepared to interpret thermodynamic parameters in the context of protein structure (e.g. mutant proteins)

H. Immunoglobulins

- Molecular structure:
  i) 4^o structure (2L+2H chains),
  ii) Variable region
  iii) Hypervariable loops.
  iv) Disulfide bonds & protein stability
- F_{ab} & F_V fragments
- Definition of Antigen/Hapten/Epitope
- Application of antibodies, e.g. drug detoxification, cancer treatment (F_V).

I. Introduction to Ligand Binding

1. Definition of M, L, and (ML)
2. k_{ON} same for all ligands, k_{OFF} small for tight binding. k_{OFF} is small when there are many interactions (H-bonds, van der Waals, hydrophobic effect, electrostatics)
3. K_D is the ligand concentration that give ½ saturation, [ML]=[M]. Lower K_D indicates better binding.
4. How to measure Y with eq. dialysis and UV absorption techniques.