

Study Guide – Lehninger Principles 5th Edition

Chapter Two

By Frank Deis

Homework: 5-12. 2.1 There are four "weak" forces, or interactions, which are very important in biochemistry. These weak forces determine the folding of macromolecules like proteins and nucleic acids. They are what attracts a substrate to an enzyme's active site, or a transmitter to a receptor. What do we mean by "weak"? A carbon-carbon bond has a bond dissociation energy of 348 kJ/mol. A hydrogen bond can be broken with only 23 kJ/mol, less than 10% of a C-C bond (p. 44). The other weak forces are in this same ballpark. The list includes **hydrogen bonds**, **electrostatic** (or ionic) **interactions**, **hydrophobic interactions**, and **van der Waals** forces. Hydrogen bonds need a "donor" (usually OH or NH, never CH) and an "acceptor" with a free unshared electron pair, see Fig 2.3. Thus a water molecule can bond to four other water molecules and in ice all water molecules are connected this way (Fig 2.2). Hydrogen bonds are directional, and are strongest when the OH lines up with the acceptor orbital. Ionic forces are familiar, like charges repel and unlike charges attract. As substances dissolve in water there are both enthalpic effects (the energy of hydrogen bond formation) and entropic effects. When a crystal of Sodium Chloride dissolves, the ionic bonds in the crystal are disrupted (for an unfavorable, positive ΔH) but the dispersal of the ions in water gives a large favorable (positive) $T\Delta S$. Along the same lines – when a molecule has a hydrophobic portion, with which the water can't make H-bonds, the water is forced to form a sort of clathrate or cage structure around it. This lowers the entropy of the water and that is why we observe what looks like an attraction between hydrophobic groups (Fig 2.7). Finally van der Waals forces are the weakest of these weak interactions, and can involve essentially any structure, including methyl groups. This attraction at close range (actually an induced dipole) accounts for the "closing up" of gaps and holes in macromolecular folding. Osmotic forces can be best understood using the Gibbs Free Energy equation but that isn't done in the textbook.

2.2 The section of the chapter on pH should be a review for you of material you have had in General Chemistry and other courses. Study Fig 2.15, what sort of pKa values do you observe for carboxylic acids? For amine bases? Understand what is going on with the titrations and titration curves in Fig 2.16 and 2.17.

2.3 Learn and understand the **Henderson Hasselbalch Equation** (p.60). Work through the online handout and some old exams. See "worked examples" on 61-62. Remember that amides are not ionizable, and reacting an amino group with a carboxyl group means that you can forget both pKa values and ignore the peptide bond. Another "trick" to remember is that in calculating the isoelectric point for an amino acid with an ionizable side chain (see page 81 in Chapter 3) use the *higher* pKa's for a basic amino acid and the *lower* pKa's for an acidic amino acid. Amino acids and other ionizable molecules are good buffers near their pKa values, where there is a 50/50 mixture of two charge forms. Note that they are very bad buffers at the isoelectric point.

2.4 The section on water as a reactant touches various bases – the use of water in Hydrolase enzymes, where something is split by hydrolysis; the production of water as a product of metabolism; the very fast-acting enzyme Carbonic Anhydrase; and water as a source of hydrogen (and thus oxygen) in photosynthesis.

2.5 It is remarkable that the Earth has had liquid water on its surface for nearly 4 billion years. This has made it a friendly place for living things.