Chapter 3: Learning Objectives

* Metals bind to small molecules, proteins, nucleic acids, and other compounds in biological systems, and hard-soft acid-base theory provides a conceptual framework for predicting the binding preferences.
* Many of these interactions involve protonation/deprotonation, and the charges on ions and residues have important effects.
* Proteins are chains of amino acids that are found in specific "folded" forms. The primary, secondary, and tertiary structures in proteins may be categorized for predictive ability. Their stable structures are most affected by the hydrophobic effect and hydrogen bonding. Folding is slow (ms to s), and is only metastable under ambient conditions.
* Only some amino acids have competent donors on their sidechains. Occasionally, amino acids are modified ("post-translational modification") by the organism, which leads to additional chemical diversity beyond the 20 amino acids.
* The preference for different metals (and different metal oxidation states) is typically dictated by the available binding sites in the protein. However, in some cases, there are "chaperone" proteins that overcome the thermodynamic preferences of a protein.
* The structure of a protein may hold a metal in an unusual geometry ("entatic state"), which can often be learned using techniques such as EPR and electronic absorption spectroscopy.
* On the other hand, the metal may be important in maintaining the folded structure of a protein. In these cases, it is important to think about the energetics carefully.
* The three-dimensional structure of a protein may be queried using techniques such as CD, FRET, and X-ray crystallography. Structures are viewed using increasingly convenient software (in this course, we use VMD).
* Functionally equivalent enzymes from different organisms often have many differences in amino acids, but the residues important for structure and catalysis are conserved. Therefore, alignment of primary structures is a useful tool for learning the mechanistic importance of amino acids.
* Single amino acids may be purposely changed through site-specific mutations to ask specific questions about the role of specific amino acids in function. This has become easy through advances in PCR and gene insertion into yeast and *E. coli*.