The course provides an introduction to the molecular building blocks and the structure of three major components of the living cells: the nucleic acids, the phospho-lipids membrane, and the proteins. The nucleic acids, DNA and RNA, linear information storing structure as well as their three-dimensional structure will be covered in relationship to their function. We will focus on the physical-chemical basis of protein structure and function, including signal transduction, enzymatic catalysis, and gene regulation. The problems and current approaches to predicting protein structure including those using homology, energy minimization and modeling will be introduced. The future implications of our expanding biomolecular knowledge and of rational drug design will also be discussed.

A standard bioscience or engineering background is assumed. This should include two undergraduate semesters of basic biology (or one semester of biochemistry), introductory chemistry and/or physics along with the associated mathematics courses. The level of understanding that to be achieved should allow the student to read most of the current protein research literature and extract the key ideas and new developments. We will extensively use a variety of public software for sequence analysis, molecular simulations, and visualization.

Grades will be based on three written exams (25% of grade each), and weekly homework assignments (25%). You can get additional 5% improvement (if needed) by presenting a paper at the end of the course. Suggestions for potential papers will be provided, but you can also suggest a paper to present.

Textbook:


Slides & Handouts on Blackboard, [https://learn.bu.edu/](https://learn.bu.edu/)

Web-based tutorials

1. **Introduction: Biological macromolecules.** (Slides 1, ch. 1, 6)

2. **Amino acids and water** (Slides 2, ch. 1-5)
   - Chemical structure and properties of amino acids. pH and pKa. Hydrogen
bonding. The structure of water. Hydration. (Sept. 8)

3. **Protein structure** (Slides 3 and 3A, ch. 1-5)
   The polypeptide chain, degrees of freedom (external and internal coordinates), observed 1-2-3-D structure hierarchies, Ramachandran plot, α–helix, β–strands, type I and type II turns, the major "forces" folding peptide chains, hydrogen bonding and hydrophobicity patterns, most frequent all-α, all-β, and αβ proteins. (Sept 10, Sept 15, Sept. 17, Sept. 22)

4. **Free energy of protein folding and binding** (handouts)
   Thermodynamic basis of free energy.
   Energetic contribution to folding of peptide chains, hydrogen bonding and hydrophobicity patterns. Elementary interactions in proteins. Protein folding in vitro and in vivo. Chaperons. (Sept. 24)

5. **Proteins in solution and in membranes** (ch. 13)
   Globular proteins, stability of folded conformations; mechanism and kinetics of protein folding.
   Membrane structure, membrane proteins and their role in signal transduction; (Sept. 29)

6. **Molecular Mechanics** (handouts)
   Comparison of quantum and molecular mechanics, potential functions, energy terms (bond stretching, angle bending, nonbonded, torsional, electrostatic); dipole moment and polarizability; components of the van der Waals interactions (Keesom, Debye, and London effects). The role and origin of solvation, calculation of solvation terms by atomic solvation parameter (ASP) and continuum electrostatic (CE) methods; side chain entropy loss and its calculation. (Oct. 1 & Oct. 6)

7. **Protein modeling and design I** (handouts, ch 16.)
   Continuous conformational space and energy minimization; Monte Carlo and simulated annealing methods; Applications: homology modeling, side chain search and loop structure determination. (Oct. 8)

**EXAM 1: October 15**

8. **Molecular recognition in the immune system** (ch. 12).
   Molecular interactions. Location of binding sites. The nature of binding sites.
   The origin and calculation of binding free energy. Proteins in the immune system: immunoglobulins and the Major Histocompatibility Complex. Immunoglobulins: genetics and structure. Antibody-antigen interactions. Peptide binding to major histocompatibility complex (MHC) proteins. (Oct. 20)

   Equilibrium expressions for single and multiple binding sites. The Adair equation.

10. **Enzymes.** (ch. 15)
Catalysis. Active site geometry. Stabilization of transition states. The catalytic mechanism of proteases. Enzyme engineering. (Oct. 29)

11. **The role of molecular structure in genetic regulation.** (ch. 7)
Molecular biology into systems biology. The molecular switch in the lambda phage: explanation in terms of molecular structure, binding, and cooperativity. Protein-DNA interactions (ch.6-8) (Nov. 3)

EXAM II (November 5)

12. **The role of molecular structure in metabolism and metabolic regulation.** (handouts)

13. **Signal transduction.** (handouts)
Classification and examples of signal transduction pathways. Specificity, amplification, and signal integration. (Nov. 12)

14. **Methods for determining structures** (ch. 17)
X-ray crystallography (basic concepts only); NMR analyses (basic concepts only)
Computational methods in structure determination. Refinement tools. Review. (Nov 17)

15. **Docking and drug design.** (handout) (Nov 19 & 24)

EXAM III: December 1

16. **Student presentations** (Dec. 3, 8, 10)