BY 502 Biophysics and Protein Engineering

Credit: 3-0-0-3 Approval: Approved in 8th Senate

Prerequisites: - IC 136 - Understanding basic Biotechnology & its Applications or Consent of Faculty member

Students intended for: UG/PG

Elective or Compulsory: Elective **Semester:** Odd/Even

Course Preamble: This course is a blend of modern discoveries and applications in protein sciences along with conventional protein science concepts, general biophysics and methods. Recent discoveries that some proteins without having structure in physiological buffer conditions are abundant in nature, constituting up to 40% of human proteome in part or full, lead to a new branch of Intrinsically Disordered Proteins (IDPs). IDPs are involved in cell signaling and responsible for a wide range of diseases. IDPs are also present in other domain of life and are responsible for many cellular functions. A combination of ordered and disordered protein knowledge will make a complete package for protein science understanding for students. By the end of this course, the students are expected to know how to apply Physics, Chemistry and Biology principles in order to understand the structure and the dynamics of biological systems, and which experimental approaches are best suited to extract the quantitative information.

Course Outline:

Module 1 [6 Lectures]

Course Introduction, what is biophysics? What will you learn? – A general outline of the course. Outlook: what is the use of what you will learn here?

The hierarchy and order of protein structure: amino acids and peptide bonds; the secondary structure: α-helices, β-sheets, turns and loops; super secondary structure – domains and motifs the tertiary and the quaternary structure. Hemoglobin and myoglobin as paradigm proteins, protein characteristics and structure-function relationships. Software and online/freeware tools for analyzing proteins e.g. Rasmol and PyMol. Homology modeling as exercise for structural elucidation of biological macromolecules.

Module 2 [6 Lectures]

Intrinsically Disordered Proteins: Sequence composition of IDPs, distribution of IDPs in nature and their physiological roles, intrinsically disordered regions, fuzzy complexes, designed linkers, folding and binding mechanisms of IDPs. Protein disorder in signaling and disease in human and plants.

Applications of IDPs or linkers in fusion proteins of clinical importance:. Chimeric Antigen Receptors as an example of multidomain fusion protein involving folded and unfolded polypeptide chains.

Module 3 [8 Lectures]

Thermodynamics: a brief introduction and thermodynamic principles. Gibbs free energy, thermochemistry and calorimetry. Protein folding theories and structural transitions in polypeptides.

Module 4 [15 Lectures]

Biophysical Methods: Absorption spectroscopy, UV/VIS spectroscopic analysis of biopolymers. Linear dichroism: transition dipole moments and the orientation of biomolecules. Circular Dichroism: the molecular origins of the rotational strength of molecules. Applications of polarized light interactions with chromophores in protein and DNA with case studies from literature.

Florescence spectroscopy: basic principles and instrumentation. Florescence of protein and DNA, florescence resonance energy transfer (FRET). Working principle and major application of other spectroscopic methods (FTIR, NMR, mass spectrometry and Ultrafast etc) for proteins.

Module 5 [16 Lectures]

Protein Engineering – Basic Principles and Rationale: Identification of putative enzymes in sequence databases, bioinformatic analysis. Enzymes, enzyme catalysis and kinetics, factors influencing the speed of enzymatic reaction. Enzyme applications, targets of protein engineering, protein engineering approaches, advantages and limitations. Rational design, comparative design, random methods; prediction of the structure of enzyme variant, evaluation of the effect of mutations on enzyme structure and function. Successful stories of application of protein engineering to improve enzyme catalytic efficiency, enzyme stability and folding. Therapeutic potentials of proteins with specific examples including insulin, anticoagulants, blood substitutes and vaccines. Sequence composition and heteromorphic pairs of proteins.

Text & Reference Books:

A nascent textbook mentioned below will be used as appropriate and several recent papers from peer reviewed journals like Nature, Science, Molecular Therapy, PNAS, Biochemistry, JBC etc.

Reference Books:

1. Donald Voet, Charlotte W. Pratt, Judith G. Voet. Principles of Biochemistry, 4/e, Wiley, 2012.
2. David L Nelson, Michael M Cox, Albert L Lehninger. Lehninger Principles of Biochemistry, 6/e New York: W.H. Freeman, 2013.
3. Irwin H. Segel. Biochemical calculations: how to solve mathematical problems in general biochemistry, 2/e Wiley, 1976.
4. T Palmer, P L Bonner. Enzymes, 2nd Edition Biochemistry, Biotechnology, Clinical Chemistry. 2/e Woodhead Publishing, 2007.
5. Peter Tompa, Alan Fersht. Structure and Function of Intrinsically Disordered Proteins. CRC Press, 2009.
6. David Sheehan. Physical Biochemistry: Principles and Applications, 2/e Wiley, 2009.