PHAS0103 – Molecular Biophysics (Term 1)

Prerequisites
It is recommended but not mandatory that students have taken PHAS0006 (Thermal Physics). PHAS0024 (Statistical Physics of Matter) would be useful but is not essential. The required concepts in statistical mechanics will be (re-)introduced during the course.

Aims of the Course

The course will provide the students with insights in the physical concepts of some of the most fascinating processes that have been discovered in the last decades: those underpinning the molecular machinery of the biological cell. These concepts will be introduced and illustrated by a wide range of phenomena and processes in the cell, including bio-molecular structure, DNA packing in the genome, mechanics of the cytoskeleton, molecular motors and neural signaling.
The aim of the course is therefore to provide students with:

- Knowledge and understanding of physical concepts which are relevant for understanding biology at the micro- to nano-scale.
- Knowledge and understanding of how these concepts are applied to describe various processes in the biological cell.

Learning Outcomes

After completing this half-unit course, students should be able to:

- Give a general description of the biological cell and its contents.
- Explain the concepts of free energy, entropy and Boltzmann distribution and discuss protein structure, ligand-receptor binding and ATP hydrolysis in terms of these concepts.
- Explain the statistical-mechanical two-state model, describe ligand-receptor binding and phosphorylation as two-state systems and give examples of “cooperative” binding.
- Describe how polymer structure can be viewed as the result of random walk, using the concept of persistence length, and discuss DNA and single-molecular mechanics in terms of this model.
- Explain the worm-like chain model and describe the energetics of DNA bending and Cytoskeletal deformation; explain how such models are relevant for understanding the rigidity of cells.
- Explain the low Reynolds-number limit of the Navier-Stoke's equation and discuss its consequences for motion in biological environment.
- Describe simple solutions of the diffusion equation in biological systems and their consequences for understanding diffusion and transport of molecules in cells.
- Explain the concept of rate equations for chemical reactions and apply it to step-wise molecular reactions, enzyme kinetics and polymerization of cytoskeletal filaments.
- Give an overview of the physical concepts involved in the dynamics of molecular motors and apply them to derive quantitative models of motor driven motion and force generation inside the cell.
- Describe neural signaling in terms of propagating action potentials and ion channel kinetics.
- Link the material in the course to at least one specific example of research in the recent scientific literature.

Methodology and Assessment

This is a half-unit course, with 30 hours of lectures. Basic problem-solving skills will be built by the setting of bi-weekly problem questions. The marks on these problem questions will account for 10% of the overall course assessment. The remaining 90% is determined via an unseen written examination.

Textbooks

The course will make extensive use of the following book, parts of which will be obligatory reading material:

- *Physical Biology of the Cell*, 1st Edition, R. Phillips, J. Kondev, and J. Theriot, Garland Science 2009

Other books which may be useful include the following. They cover more material than is in the syllabus.

- *Biological Physics*, 1st Edition, Philip Nelson, W.H. Freeman, 2004
- *Mechanics of Motor Proteins and the Cytoskeleton*, 1st Edition, J. Howard, Sinauer Associates, 2001
- *Protein Physics*, 1st Edition, A.V. Finkelstein and O.B. Ptitsyn, Academic Press, 2002
- *Molecular Driving Forces*, 1st Edition, K.A. Dill and S. Bromberg, Garland Science, 2003

The following books may be useful for biological reference.

- *Molecular Biology of the Cell*, 4th Edition, B. Alberts et al., Garland Science, 2002
- *Cell Biology*, 2nd Edition, T.D. Pollard, W.C. Earnshaw and J. Lippincott-Schwartz, Elsevier, 2007

Syllabus
(The approximate allocation of lectures to topics is given in brackets below)

Physical Biology of the Cell [3]
Introduction to the physical biology of the cell; The Central Dogma of Molecular Biology; Structure of DNA, RNA, and Proteins; Overview of functional processes in cells; Quantitative Modelling approaches; Biological Time Keeping.

Statistical Mechanics in the Cell [3]
Deterministic versus Thermal Forces; Equilibrium Models of cellular processes; Free-energy minimization and Entropy; Statistical Microstates and Boltzmann distribution; Partition Function; Applications: Ligand-receptor binding and Ion Channel Gating; Law of Mass Action; Cooperative ligand-receptor binding & Hill Equation.

Two-state Systems [3]
Macromolecules with multiple states; Applications: Ion channel gating, RNA hairpin folding; Gibbs distribution; Chemical Potential; Applications: Ligand-receptor binding, Phosphorylation; Cooperative binding in Hemoglobin and Dimoglobin.

Structure of Macromolecules [3]
Random walk models of polymers; Entropy, Elastic properties and Persistence length of polymers; Chromosome Organization; DNA looping; Single-molecule mechanics; Force-extension relation of random walk polymers.

Mechanics of Biological Filaments [3]
Elasticity theory of Beam deformation; Worm-like chain model; Beam theory applied to the mechanics of DNA and the Cytoskeletal Filaments; Buckling of biopolymers.

Fluid Dynamics in Biology [3]
Navier-Stokes Equation; Viscosity and Reynolds number in cells; Fluid Dynamics of Blood; Mechanics of Leukocyte rolling; Low Reynolds number world; Stokes Flow; Swimming of microorganisms; The Scallop Theorem.

Diffusion in Cells [3]
Active vs Passive Transport in Cells; Fick's Law for diffusive transport; Diffusion equation and its solutions; Application: Fluorescence Recovery after Photobleaching; Driven diffusion – Smoluchowski equation and the Einstein Relation; Diffusion limited capture.

Chemical Reactions in the Cell [3]
Actin-based cell motility; Rate equations for chemical reactions; Decay processes; Biomolecular reactions; Michaelis-Menten and Enzyme kinetics; Polymerization dynamics of cytoskeletal filaments; Dynamic Instability in Microtubules.

Molecular Motors [3]
Molecular motors in the cell; Mechanics of muscle contraction; Stepping dynamics of motors; Rectified Brownian motion; Driven diffusion equation for a molecular motor; Energy states and two-state model for molecular motors; Force generation by polymerization.

Action Potentials in Nerve Cells [3]
Charge state of the cell; Electrochemical equilibrium and Nernst Potential; Two-state model for ion channels; Cell membrane as an electrical circuit; Dynamics of membrane voltage; Cable equation for voltage propagation; Hodgkin-Huxley model for propagation of action potentials.