**PHAS0078 – Physical Models of Life (Term 2)**

**Prerequisites**
It is recommended but not mandatory that students have taken PHAS0006 (Thermal Physics). PHAS0024 (Statistical Physics of Matter), and PHAS0103 (Molecular Biophysics). The required concepts in physics will be (re-)introduced during the course.

**Aims of the Course**

The students will be given background in Physical theories developed specifically for understanding Biological Systems. As these systems function out of equilibrium, very different and novel physical properties emerge that are not covered by classical physics.

The syllabus will be subdivided as follows:
-**Computational modelling of biological processes**. Computer simulations act as a bridge between molecular scales and the macroscopic world, and can serve as a mediator between analytical theory and experiment. These lectures will focus on advanced computational techniques developed to treat a large ensemble of explicit biological objects, such as macromolecules or cells. Emphasis will be placed on understanding how their complex interactions and stochastic nature lead to emergent collective behaviour. Taking inter-cellular trafficking, and protein aggregation in cells, as our case studies, we will discuss obtaining quantitative physical measurements in computer simulations that can be directly compared with experiments, and associated challenges.
-**Physics of biological flows**. This section of the course covers the physical theories that describes deformation of living matter at the scale of cells and tissues. We will start by introducing the hydrodynamics of simple fluids and the physics of biological swimmers. We will then present hydrodynamic theories of active complex fluids, which describe large scale flows of matter driven out of equilibrium by chemical energy, such as ATP consumption by myosins in the cytoskeleton. We will discuss physical models of morphogenesis of tissues at the end of the course.
-**Noise, fluctuations and robustness in Biological systems**: This section of the course will start by introducing students to advanced concepts in statistical mechanics. It will then examine noise that arises from sources intrinsic and extrinsic to a given biological system. It will investigate how gene expression is regulated in the presence of noise, how concentration of substances are sensed by living organisms, and how cell size and divisions are controlled.

**Objectives**

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

- Give a general description of the biological cell and multicellular tissues.
- Have knowledge and understanding of physical concepts which are relevant for understanding biology across scales.
- Have knowledge and understanding of how these concepts are applied to describe various processes in Biology.
- Understand how theoretical physical concepts can be applied to biology.
- Understand basic concepts of physics out-of-equilibrium.
- Be familiar with the original properties of active matter and its relation to biology.
- Be familiar with the unique properties of soft matter and nanoscale materials of biological relevance.
- Understand processes on small scales undergoing stochastic behaviour.
- Grasp fundamental physical behaviours of biological systems at the scale of proteins, cells and tissues.

- Know strategies for development of minimal theoretical models of complex biological problems.
- Be familiar with concepts necessary for bridging scales in biology: from molecules to organisms.
- 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 problem questions. Three written assignments will each account for 10% of the overall course assessment. The remaining 70% is determined via an unseen written examination.

**References and textbooks**

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

- Phillips, Rob, Jane Kondev, Julie Theriot, and Hernan Garcia. *Physical biology of the cell*. Garland Science, 2012.

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

- W. Bialek, Biophysics: Searching for Principles, (2012).
- J. Howard, Mechanics of Motor Proteins and the Cytoskeleton, (2001)
- M. Rubinstein and R. H. Colby, Polymer Physics, (2003)
- D. Frenkel and B. Smit, Understanding Molecular Simulations, (2001)
- U. Alon, An Introduction to Systems Biology: Design Principles of Biological Circuits, (2006)
- J. N. Israelachvili, Intermolecular and Surface Forces, Third Edition: Revised Third Edition, (2011)
- S. Safran, Statistical Thermodynamics of Surfaces, Interfaces, And Membranes (Frontiers in Physics), (2003)

The following books may be useful for biological reference.

- *Molecular Biology of the Cell*, 4$^{th}$ Edition, B. Alberts et al., Garland Science, 2002
- *Cell Biology*, 2$^{nd}$ 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)

**1. Interactions on nanoscale [3]**

- What is soft matter, Nanoparticles and colloids as models: statistical mechanics recapitulation
- Hard core repulsion, dispersion forces, depletion interaction, charged interactions
- Entropy-driven ordering & phase transitions, Hydrophobic interaction

**2. Computer Modelling [3]**

- Monte Carlo, Molecular Dynamics
- Application to polymers: Scaling of Ideal, Self-avoiding, and Real chains
- Steric and fluctuation forces

- Phase separation and membrane-less organelles

**3. Biological self-organisation and phase behaviour [3]**
- Amphiphilic molecules and geometric packing: micelles, bilayers, vesicles
- Formation of biofilaments: thermodynamics and kinetics

**4. Biological membranes [3]**
- elastic properties, fluidity, role of curvature
- membrane-mediated interactions, membrane remodelling, and cellular trafficking

**5. Biological swimmers [3]**
- Low Reynolds number hydrodynamics
- Scallop theorem
- Simple swimmer

**6. Physics of Active Matter I: Theory and Concepts [3]**
- Liquid crystals, isotropic-nematic phase transition
- Non-equilibrium physics close to equilibrium
- Entropy production
- Onsager relations

**7. Physics of Active Matter II: Applications [3]**
- Dynamics of defects
- Instability of a thin film
- Flows driven by chemical activity

**8. Tissue morphogenesis and mechanics [3]**
- Turing patterning mechanism
- Establishment of morphogen gradients
- Physical description of tissue mechanics
- Tissue sorting

**9. Noise in Biology [3]**
- Intrinsic and Extrinsic noise
- Gene expression
- Fluctuations and chemical reactions
- Proofreading

**10. Growth and form [3]**
- Cell growth, size and division control
- Ribosome synthesis and constitutive gene expression
- Coordination of cell growth and metabolism