Catalogue description

BSCI404 Cell Biology from a Biophysical Perspective; (3 credits)

Cell Biology from a Biophysical Perspective. Credits: 3. Grading Method: Regular, Pass-Fail, Audit

Prerequisite: BSCI230 or BSCI330. Recommended: PHYS121 and PHYS122. Also offered as: BIOL704, BIPH704. Credit only granted for: BSCI338O, BSCI404, BIOL704, BIOL708O, or BIPH704. Formerly: BSCI338O. An approach to cell biology by focusing on mechanisms and unifying physical paradigms. It will not assume a great deal of factual biological knowledge, but will expect a background that prepares students to think mechanistically and quantitatively.

0101 Sergei Sukharev Seats (Total: 15, Open: 2, Waitlist: 0) TuTh 3:30pm - 4:45pm PLS 1113

Syllabus

BSCI404/BIOL704/BIPH704- Fall 2013

Cell Biology from a Biophysical Perspective (PLS 1113; Tue, Thu 3:30-4:45)

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Main Texts: Molecular Cell Biology by Lodish et al., 6th edition.

Physical Biology of the Cell by Phillips et al.

Additional biophysical and quantitative aspects will be provided by the instructor.

Rationale. This course will approach Cell Biology focusing on mechanisms and unifying paradigms. It will not assume a great deal of factual biological knowledge on the part of the incoming student but rather will expect a background that prepares the student to think mechanistically and quantitatively. Thus it is ideal for students in Engineering, Chemistry and Physics with a strong background in basic science but lacking a substantial biological foundation. It is also attractive to students in Biology who prefer to think about and understand biological processes rather than memorizing constellations of facts. It is hoped that interaction between students from the various disciplines will produce a rich learning environment with students eager to challenge each other's conceptual frameworks.

The course will be taught to students at the senior level and at the graduate level. The graduate students will generally be incoming students that lack upper-level cell biology and thus will not be at a significant advantage over their undergraduate counterparts.

Learning outcomes. The course will include both descriptive and quantitative treatments; links to the physico-chemical properties of the cellular components and their interactions; a consideration of the energetic, spatial and time scales of the processes in cells. Students will perform relevant quantitative estimates and learn strategies and key experimental approaches used in studies. The course will help students identify interesting mechanistic biological problems that they can pursue in new ways utilizing their unique background.

Exams: One take-home mid-term (~30% of total), one in-class final (~30% of total). Four problem sets (~10% each). Graduate students will be required to present research papers on selected topics.

Final exam is on Saturday, December 21, 10:30am-12:30pm, PLS 1113

Policy on academic dishonesty: Please read the policy in the Schedule of Classes.

Approximate lecture schedule/topics

Lecture 1. Introduction. Goals of the course and today's Biological research. The cell and the length and time scales for biological processes. Physics uses simplified representations of essential biological processes. Examples of classical problems in cell biology and biophysics. Unifying principles of cellular function and reproduction: genome, proteome and functional phenotypes. The tree of life and model organisms. Life evolves while Physics holds everywhere.

Lecture 2. Forces and energies. Barometer and Boltzmann. The notion of free energy. Internal energy, enthalpy, entropy and differences of microscopic systems from macroscopic. Polymeric chains. Energy scales for intermolecular interactions.

Lecture 3. Building blocks: amino acids. Peptide bonds and chain architecture. Protein structure and hierarchy. Graphical representations of protein structure. Examples of binding: small molecules, interacting protein domains, ligand-receptor interactions, antibody-antigen recognition. Energetic and entropic contributions into binding.

Lecture 4. Coulombic interactions in dielectric environment. Born energy. Coulombic interactions and screening by ions. Debye length. Dipole-dipole interactions and their scaling. Van der Waals and dispersion forces. Examples of electrostatic interactions. Building blocks continued: water, hydrogen bonds.

Lecture 5. Water. Structure of liquids. Effects of H-bonding on radial distribution functions. Hydrophilic solvation. The hydrophobic effect.

Lecture 6. More about entropy: classical and statistical definitions. Entropies of different distributions. Changes of entropy with temperature and volume (heating, dilution, mixing). The standard form of chemical potential.

Lecture 7. Simple binding. Competitive binding. Cooperative binding (hemoglobin), Langmuir and Hill isotherms. Binding energy put to work: a brief account of enzyme mechanisms and kinetics.

Lecture 8. A toolbox for mechanistic biologists: principles and methods for cell component separation and cell manipulation.

Lecture 9. Why genetics? Forward and reverse approaches. The predictive power of genetic screens. Basic molecular genetics tools for mechanistic biologists (cloning, expression, tissue-specific experiments).

Lecture 10. Structure of the chromatin, accessibility and transcriptional control. Histone modifications. Electrostatics versus bending. Rigidity and persistence length of polymers. Simple transcriptional control in bacteria: Lac operon.

Lecture 11. DNA replication. Transcription mechanism. RNA polymerase as molecular motor.

Lecture 12. Genome: the abundance of non-transcribed DNA. Crossing-over, repeats, gene duplication, domain swapping and protein evolution. Transposons and genome inflation.

Lecture 13. Intron-exon structure of genes, RNA processing and splicing.

Lecture 14. Genetic code, base pairing and protein synthesis.

Lecture 15. Cell compartmentalization. Membrane structure and lipids. Model systems: monolayers, planar bilayers and liposomes. Observations of phase transitions. Membrane interfaces: electrostatics and its role in signaling.

Lecture 16. Membrane anisotropy and lateral pressure profile. Membrane electrostatics and its microscopic representation, role of water. Effects of environment on membrane proteins.

Lecture 17. Diffusion as means for transport. Lateral diffusion of membrane components. Diffusion across the membrane: partitioning and permeation. Diffusion through channels: Ussing's coupling of fluxes. Active transport and co-transport.

Lecture 18. Active and passive transport in excitable cells. Pumps and ion channels. Introduction to Electrophysiology, Nernst and Goldman equations, components responsible for resting potential and spike generation.

Lecture 19. Binding again: ionic selectivity. Ion channel mechanisms: voltage gating and inactivation. Cable properties of axons and the speed of spike propagation.

Lecture 20. Synaptic transmission, membrane fusion and fission. Allosteric mechanisms of channel gating by ligand, structures of AChBP and nicotinic AChR.

Lecture 21. Introduction to mechanobiology. Forces acting on cells. Osmoregulation. Types of mechanosensors. Channel gating by tension. (Projects in the Sukharev Lab). Eukaryotic mechanosensors and the cytoskeleton.

Lecture 22. Signaling at the surface, diversity of receptors: G proteins and GPCRs, visual cascade.

Lecture 23. The cytoskeleton and molecular motors. Dynamics of actin filaments: treadmilling. Myosins and their functional cycle.

Lecture 24. Tubulins and microtubule dynamics. Kinesins and dyneins.

Lecture 25. Bioenergetics: macroergic phosphodiester compounds, electronegativity and oxidation. Proton gradient across a closed membrane as a coupling intermediate. Proton gradient coupled processes: mechanical work, co-transport.

Lecture 26. Mitochondrial processes: Redox reactions, production of NADH, electron and proton transport.

Lecture 27. FoF1 ATPase mechanism. Thermodynamics of ATP synthesis coupled to H+ transport.

Lecture 28. Evolvability: housekeeping mechanisms versus signaling pathways.