BIO 466 / NS 566 Biophysics: Molecules and Systems - Spring 2011

(April 1, 2011)

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Lectures: Wed 12:40-13:30 FENS L067
Thr 11:40-13:30 FENS L067

Course Description: The course is organized around one main question: How do "intelligent" molecular-level biological processes emerge from nonintelligent driving forces? To pose the question in its proper setting, we first get familiar with the world in which biological molecules live, where everything—from stability of structures to operation principles of devices—looks very different than its counterpart in our everyday world. We then resort to the concepts of statistical and thermal physics, which provide us with a quantitative toolbox for making sense of the changes caused by driving forces at the molecular level. The introduced statistical mechanical thinking is used to rationalize the coupling between mechanosensitive ion channels and the lipid membrane. In addition, it also sheds light on the molecular processes responsible for the propagation of electrical signals in excitable cells like the neurons in our brain. With knowledge about biomolecular structure and understanding of entropy and free energy in place, we turn to the treatment of basic molecular processes like binding of small molecules (e.g., a hormone) by big molecules (e.g., a receptor) and catalysis of biological reactions by enzymes. The dynamic nature of the cellular skeleton and the workings of energy-transducing molecular motors (think about our muscles) is considered at the end.

Who can take this course: The course is catered to advanced undergraduate and starting graduate students in the biological sciences, engineering, and physical science. Since the focus is on molecules and molecular assemblies working in the context of a living cell, the engineering and physical science students are expected to be interested in questions related to the molecular aspects of biology. The workings of these biological molecules, however, are conceptualized using the mathematical language of thermal and statistical physics. Thus, the biology students are expected to be willing to use calculus and work with quantitative models. In some sense, this course is the advanced version of the first-year Science of Nature courses (NS 101 and NS 102) offered at Sabancı, in which students are expected to realize that the boundaries between physics, chemistry, and biology are largely artificial and counterproductive for the understanding of natural phenomena.

Evaluation:

Homework and quizzes	15 %
Midterm Exam (Apr 7)	25 %
Written report and oral presentation	25 %
Comprehensive final exam	35 %

Textbook:

PBoC Phillips, Kondev and Theriot, *Physical Biology of the Cell*, Garland Science, 2009.

Detailed Course Content:

I. The nanoworld of biological molecules

   A. Cells, molecules and numbers (**PBoC Chs. 1, 2**)

      1. The molecular machinery of cells
      2. Sizing up *E. Coli* and yeast cells
      3. Structure of biological molecules

   B. Thermodynamics and statistical mechanics

      1. Thermal and chemical equilibrium (**PBoC Secs. 5.2, 5.3, 5.4, 5.5**)
      2. Lattice models of protein folding and ligand binding (**PBoC Secs. 6.1, 6.2**)
      3. Discrete-state analysis of phosphorylation (**PBoC Sec. 7.2.3**)
      4. Statistical thermodynamics of mechanosensitive ion channels (**PBoC Sec. 7.1**)

   C. Thermal energy moves the nanoworld (**PBoC Chs. 13, 3**)

      1. Diffusion applied to chemoreception and flow through a channel
      2. Diffusion under force and the Smoluchowski equation
      3. The Nernst equation and the membrane potential (**PBoC Secs. 4.8.2, 17.1, 17.2, 17.3**)

II. Binding, conformational exchange, and catalysis

   A. Ligand binding and conformational transitions

      1. Chemical reactions and the chemical potential (**PBoC Sec. 6.3, 6.4**)
      2. Allostery and cooperative binding in Hemoglobin (**PBoC Sec. 4.2, 7.2.4**)
      3. Thermodynamics of binding and isothermal titration calorimetry
      4. Statistical thermodynamics of covalently bound signaling domains (**PBoC Sec. 19.4.2**)

   B. Enzymes

      1. Kinetics of binding and conformational exchange (**PBoC Sec. 15.2**)
      2. Catalytic strategies and stabilization of the transition state
      3. Fluctuating enzymes: Coupling of conformational exchange and catalysis

III. Cellular shape and intracellular transport

   A. The cytoskeleton

      1. Random walks and macromolecular structure (**PBoC Ch. 8**)
      2. Beam theory and cytoskeletal structure (**PBoC Ch. 10**)
      3. Dynamics of cytoskeletal polymerization (**PBoC Secs. 15.1, 15.3, 15.4**)

   B. Molecular motors (**PBoC Ch. 16**)

Reference Books:

- **BP** Nelson, *Biological Physics: Energy, Information, Life*, updated 1st edition, W.H. Freeman and Co., 2008.
- **MDF** Dill and Bromberg, *Molecular Driving Forces: Statistical Thermodynamics in Chemistry and Biology*, 1st edition, Garland Science, 2004.
- **WiL** Schrödinger, *What is Life?*, Cambridge University Press, 1992.
- **BNT** Goodsell, *Bio**nano**technology: Lessons from Nature*, Wiley-Liss, Inc., 2004.
- **MBoC** Alberts, Johnson, Lewis, Raff, Roberts, and Walter, *Molecular Biology of the Cell*, 5th edition, Garland Science, 2008.
- **Bioch** Berg, Tymoczko and Stryer, *Biochemistry*, 6th edition, W.H. Freeman, 2006.