Chemistry 163. Frontiers in Biophysics, Fall 2022
This interdisciplinary course will explore the physical interactions that underpin life: the interactions of molecules, macromolecular structures, and cells in warm, wet, squishy environments. Topics will include Brownian motion, diffusion in a potential field, mechanical, thermal and electrical properties of polymers and membranes. We will study nonequilibrium dynamics and fluctuations, with applications to biochemical signaling, action potentials and Turing patterns in morphogenesis. Numerical simulations in Matlab will be used extensively.

Primarily for advanced undergraduate students and graduate students with either biological or physical backgrounds.

Prerequisite: Chemistry 160 and 161 or equivalents, or permission of the instructor.

Tuesday, Thursday 9 – 10:15 am, Pfizer Lecture Hall (in the basement of Mallinckrodt, 12 Oxford Street)

- First class will be on Thursday Sept. 1

Professor: Adam E. Cohen, cohen@chemistry.harvard.edu,
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Teaching Fellow: Ryan McMillan, rmcmillan@g.harvard.edu

Office hours:
Adam Cohen, Mallinckrodt M115, Thursday 10:15-11:15 or by appointment.
Ryan McMillan, tbd

Section: Thursday 4:30 – 5:45 pm, Mallinckrodt 217

- First section will be on Thursday Sept. 8

Final project presentations: Dec. 7 and 8, 9 – 11 am (provisional)

COVID-19 Safety: Per University policy, masking is optional but strongly encouraged.

Textbooks:

- Phillips, Kondev, Theriot, Physical Biology of the Cell, Garland Science, 2009.
- Jonathon Howard, Mechanics of Motor Proteins and the Cytoskeleton, Sinauer, 2001.
- Eugene Izhikevich, Dynamical Systems in Neuroscience, MIT Press, 2007.

All are available as e-books from Harvard Library
If you wish to order via the COOP online, go to:
https://tinyurl.com/F22-PLACE-COOP-BOOK-ORDER-HERE

Other good resources:

- Jacob Israelachvili, Intermolecular and Surface Forces, Academic Press, 1991.
- Ken Dill, Molecular driving forces: statistical thermodynamics in biology, chemistry, physics, and nanoscience, Garland Science, 2003.

- Philip Nelson, From Photon to Neuron: Light, Imaging, Vision, Princeton University Press, 2017.

Homework (50%): 11 weekly problems sets will emphasize calculations and extensions of the ideas developed in class. Many of the problem sets will involve performing simulations or analyzing data in Matlab. You can discuss the problems with other students, but the work you submit should be your own. Please list any collaborators on your problem sets. Problem set grades will be docked 15% per day late.

Midterm (20%): An in-class midterm exam will test understanding of the key ideas in the course.

Final Projects (30%): Students will write a 5-8 page paper proposing a new physical approach to a problem in molecular or cellular biology. The paper may either propose a new experiment, or develop a new physical model for a known phenomenon. Students will then give a 15-minute presentation to the class. The paper should propose ideas not found in the published literature.

Schedule (subject to revision)
* Dates marked with an asterisk (*) will be pre-recorded lectures, with a separate OH to be scheduled for discussion.

Sept. 1 Introduction: Role of physics (and physicists) in biology. Examples of biological problems amenable to physical solution. Random walks, Brownian motion.
Reading: Hamming; PBOC Ch. 1; Robert Brown (optional); Einstein (optional).
HW 1 assigned.

Sept. 6 Statistics of Brownian Motion. Central limit theorem. Diffusion equation and its solutions; separation of variables.
Reading: Howard pp. 294 – 295, 296 – 298; PBOC Ch. 13.1 – 13.2

Sept. 8 Rotational diffusion and fluorescence depolarization. Diffusion with sources and sinks; first passage problems. Diffusion-limited reaction rates.
Reading: PBOC Ch. 13.3 – 13.4
HW 1 due; HW 2 assigned.

Sept. 13 Applications of Brownian motion: Chemotaxis in *E. coli*; limits on size of organisms; tumor growth; diffusion of excitons in the photosynthetic antenna complex; diffusion of photons in tissue.
Reading: Berg.

Sept. 15 Correlation functions and power spectra.
Reading: PBOC 140 – 142, 760 – 765
HW 2 due; HW 3 assigned.

Sept. 20 — Fluctuations spectroscopies: Fluorescence Correlation Spectroscopy (FCS).
Reading: Howard pp. 63 – 71, 295, 298 – 303.

Sept. 22 — Diffusion in a potential. Langevin, Smoluchowski, equations.
Reading: Howard pp. 49 – 63, 303 – 306.
HW 3 due; HW 4 assigned.

Sept. 27 — Diffusion in a parabolic well. Equipartition. Optical traps.
Reading: Block

Sept. 29 — Kinetics: Eyring model, Kramers theory.
Reading: McCann, Howard pp. 308 – 309.
HW 4 due; HW 5 assigned.

Oct. 4 — Two-state systems: Chemical equilibria, equilibria under external forces.
Reading: Howard Ch. 5

Oct. 6 — Membrane potential and Nernst Equation
Reading: PBOC Ch. 17.1-17.2.
HW 5 due; HW 6 assigned.

Oct. 11 — Ion channels and pumps. Electrogenetic transporters. Optogenetics.
Reading: Venkatachalam; PBOC Ch. 17.3.

*Oct. 13 — Electrophysiology in one variable. Cable equations. Rall models.
Reading: Izhikevich Ch. 1,2.
HW 6 due.

Oct. 18 — Electrophysiology in two variables. Bifurcations, oscillators, action potentials.
Reading: Izhikevich Ch. 3; PBOC Ch. 17.4.

Oct. 20 — **Midterm**
HW 7 assigned.

Oct. 25 — Reaction kinetics. Michaelis-Menten, bistability, cooperativity, oscillators
Reading: Julicher; PBOC Ch. 15, p. 747 – 758.

Oct. 27 — Reaction-diffusion equations: Krogh model, Fisher waves, Turing model.
Reading: Krogh, Turing, PBOC p. 759 – 760.
HW 7 due; HW 8 assigned.

Nov. 1 — Intermolecular forces: Coulomb, van der Waals, Keesom.
Reading: Israelachvili, Margenau (optional).

Nov. 3	Entropic forces. Depletion forces. Entropy-induced order. Hydrophobic effect. *Reading*: PBOC Ch. 14. **HW 8 due; HW 9 assigned.**
Nov. 8	Continuum mechanics of rods, cytoskeleton. Bending, twisting, buckling. *Reading*: Howard Ch. 3, pp. 312 – 315; PBOC Ch. 10; Fields.
Nov. 10	Polymers: persistence length, DNA and RNA stretching. *Reading*: Howard Ch. 6, Appendix 6.3; PBOC Ch. 8. **HW 9 due; HW 10 assigned.**
Nov. 15	Continuum mechanics of membranes. Stretching, bending. Membranes at finite temperature. Membrane tubes. *Reading*: PBOC Ch. 11.
Nov. 17	Electrostatics in solution: Poisson-Boltzmann, Debye-Hückel theory. Coagulation, flocculation, electrostatic forces. Cheese, and river deltas. *Reading*: Israelachvili; PBOC Ch. 9. **HW 10 due; HW 11 assigned.**
Nov. 22	Fluid dynamics: Poiseuille flow, Reynolds number, surface tension. Swimming vs. waiting. Blood flow. *Reading*: Purcell; PBOC Ch. 12.
Nov. 24	**No class, Thanksgiving**
Nov. 29	Quantum mechanics in biology: Magnetosensation *Reading*: Grissom, Hore. **HW 11 due.**
Dec. 1	Future challenges and opportunities in biophysics
Dec. 7, 8 9 – 11 am	Final presentations