BE/APh 161: Physical Biology of the Cell

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Course description and objectives

Contemporary research in cell biology increasingly relies on physical concepts. Quantitative measurements, and models to design and interpret them, are essential as we build our understanding of phenomena such as cytoskeletal mechanics, functioning of ion channels, packaging and replication of nucleic acids, pattern formation, biochemical regulation, membrane structure and dynamics, and cellular motility, to name just a few of many. Despite the diversity of these phenomena, they can be well-described with just a few governing physical principles. This course introduces these principles and applies them to quantitatively model exciting case studies in cellular structure and dynamics.

Rough course outline

The course will consist of three broad sections. A more detailed lecture schedule follows.

- **Biology by the numbers.** In this section, we perform simple estimates of the size, speed, and numbers of cells and cellular components. In addition to being illuminating in their own right, such estimates provide a grounding for more precise experiments and theories.
- **The stuff of cells.**
  1. **Molecules.** Nearly all cellular processes at the molecular level occur with energy close to the thermal energy. Therefore, statistical mechanics is therefore an exceptionally useful modeling tool. In this section, we will cover some basic concepts of statistical mechanics and use them to study molecular interactions, including regulation of gene expression.
  2. **DNA.** We will study the physics of DNA as it is packaged and transported by cells and viruses.
  3. **The cytoskeleton.** The cytoskeleton imparts the mechanical integrity of eukaryotic cells, and we will study its principle components, actin and microtubules. We will look at their assembly and mechanical properties.
  4. **Membranes.** We will investigate the physics of membranes and vesicles, taking a look at their composition, their mechanics, and how they form.
- **Cells in their environment.** In this section of the course, we will study how cells interact with their environment and with neighboring cells.

This is but a tiny slice of the giant pie of topics in physical cell biology. We just barely touch the topics we cover and completely exclude important topics such as photosynthesis, gene regulation networks, and electrical biology, to name just a few. Nonetheless, I hope that at the end of this course, your interest will be piqued and you will be armed with enough knowledge to penetrate into the literature and expand and deepen your knowledge.

Textbook and references

The main text for the course is *Physical Biology of the Cell, 2nd Ed.*, by Rob Phillips, Jané Kondev, Julie Theriot, and Hernán Garcia, Garland Science, 2012. I will use *PBoC2* as shorthand for this book. I also ask you to read material from a book in progress, *Cell Biology by the Numbers*, by Ron Milo and Rob Phillips. This is essentially a second text for the course, and we will refer to it as *CBBTN*. I will also refer to classic and contemporary research papers throughout the course. In addition, the following books serve as useful auxiliary references. All are on reserve in Sherman Fairchild Library.

- *Essential Cell Biology, 4th Ed.*, by Bruce Alberts, et al., Garland Science, 2013.
- *Random Walks in Biology*, by Howard Berg, Princeton University Press, 1993.
- *Mechanics of the Cell, 2nd Ed.*, by David Boal, Cambridge University Press, 2012.
- *Molecular Driving Forces: Statistical Thermodynamics in Chemistry and Biology, 2nd Ed.*, by Ken Dill and Sarina Bromberg, Garland Science, 2010.
- *Mechanics of Motor Proteins and the Cytoskeleton*, by Jonathon Howard, Sinauer Associates, 2001.

An additional note about reading

I will assign substantial reading from *PBoC2*, *CBBTN*, and from the literature. I cannot stress enough how important it is that you do this reading. It will help you tremendously throughout the course. Perhaps more importantly, the reading assignments will help give you the foundation of knowledge you need to learn more after the course is over.

That said, I do not want the reading to be stressful for you. I invite you to take a relaxed approach. Try to enjoy the reading and use it to develop your own thinking and perspectives about the topics of the course and physical cell biology in general.

Homework

There will be weekly homework assignments related to lecture and reading material. The homeworks will not always have "right answers," but are always aimed at making you think about the central concepts of the course. We will not have any exams. Homework assignments are posted on the website. The due date and time, usually one week after posting, is indicated on the website and on the homework PDF. Following are homework policies.

- Homeworks must be handed in as a hard copy unless prior arrangements have been made with the instructor or TAs.

- No late homeworks will be accepted after the due date and time unless you have a note from someone like a doctor or dean. There are no exceptions to this rule.

- All homeworks must either be typed or written in legible handwriting. You will lose points for illegible homework. Mathematical expressions must be clearly presented with all variables defined.

- You are encouraged to discuss the homework with your classmates, but your explanations and derivations must be your own.

- You may not refer to homework problems from previous editions of this course. You also may not refer to solutions manuals, etc., for problems assigned from textbooks. In general, "homework by Google" is ill-advised. Slogging through a tough problem is often the best way to learn a concept, which is the whole point of the homework.

- The logic and *significance* of the results in your homeworks must be discussed in clear English.

- If you are asked to "sketch" a plot, you may (and should) draw it by hand. If you are asked to "plot" something, you must use a plotting program, such as Matlab, Gnuplot, Matplotlib, etc., to generate the plot.

- Graded homeworks are returned one week after they are submitted.

Lecture schedule and topics

There are twenty scheduled lectures in the term. Following is a tentative lecture schedule. The timing and topics are subject to change as I see fit during the course, but this should serve as a rough guide.

- **Biology by the numbers.**

  L1: Why biology is a quantitative science; course overview; biology by the numbers I

  L2: Biology by the numbers II; principles of estimation

  L3: Dimensional analysis; mathematizing cartoons

- **The stuff of cells.**

  L4: Statistical mechanics of molecular interactions

  L5: Two-state models

  L6: Allostery and the Monod-Wyman-Changeux model

  L7: States and weights I: application of statistical mechanics to regulation of gene expression

  L8: States and weights II: dynamics of regulation of gene expression and genetic switches

  L9: Introduction to biopolymers; beam theory and the wormlike chain

  L10: DNA packaging in nuclei and viruses

  L11: Fluid properties of cytoplasm; diffusion and transport in cells

  L12: Introduction to actin and microtubules; nucleation, polymerization, and length control

  L13: Molecular motors: active transport and force generation

  L14: The actin cytoskeleton and cellular integrity; viscoelasticity

  L15: Microtubules: dynamic instability and spindle formation

  L16: Introduction to biological membranes: composition and mechanics

- **Cells in their environment.**

  L17: Intercellular signaling

  L18: Adhesion and crawling

  L19: Bacterial swimming and chemotaxis

  L20: Bacterial quorum sensing; course recap

Prerequisites and assumed background

Mathematics. Courses in ODEs and PDEs are a prerequisite for the course, as we will be analyzing some differential equations. We will also be applying concepts from probability and statistics. That said, if you feel like your mathematical background is shaky, do not worry. Mathematical rigor is not the central thrust of this course, and the TAs and I will assist you with mathematical difficulties.

Programming. Some of the problem sets will ask you to write short programs to do simulation or analysis. The calculations will not be computationally intensive, and may be written in a high-level language. You can use tools such as Python, Matlab, Mathematica for this purpose. As these skills are needed, we will provide tutorials and handouts to help you along.

Lecture policies

Lecture attendance is mandatory. We will be having discussions and doing exercises together during lecture, so it is important that you be there. I understand that you may miss a lecture from time to time, for graduate school visits, etc., but I ask that you make every effort to come to class. If you are concerned that you may out of necessity miss too many lectures, please talk with me and we can try to work out arrangements.

Lectures are a very important time for me to interface with you. As we have discussions in lecture, we both learn, and I get a good idea of how you are doing with the material. I therefore often find it distracting when students use laptops in lecture. Nonetheless, I do not what to take away your preferred method of note-taking, if that is the case, so laptops are allowed in lecture. **I do ask that you use laptops and tablets strictly for note-taking purposes.** Cell phones must be completely silenced and put away.

Lectures may not be recorded without my permission. If you miss a lecture, I invite you to discuss what you have missed with a classmate, your TAs, or with me.