

Physics 280: Physical Models of Biological Systems

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“We all know that Art is not truth. Art is a lie that makes us realize the truth.” — Pablo Picasso

“Nature uses only the longest threads to weave her patterns, so each small piece of her fabric reveals the organization of the entire tapestry.” — Richard Feynman

“Seek simplicity, and distrust it.” — Alfred North Whitehead

Every week we hear some highly-placed pundit announcing the end of the qualitative era in life science, and the need to train future scientists in mathematical modeling methods. Normally missing from such pronouncements are issues like “What is a physical model, anyway?” and “How do we know when a simple, reductionistic modeling approach is appropriate/inappropriate?” We also hear a lot of pundits announcing the era of “Integrated Systems Biology,” but never defining that phrase.

Our goal in this course is to study some classic case studies of successful reductionistic models of complex phenomena, emphasizing the key steps of (1) making estimates, often based on dimensional analysis, (2) using them to figure out which physical variables and phenomena will be most relevant to a given system, and which may be disregarded, and (3) finding analogies to purely physical systems whose behavior is already known. The cases we’ll study involve basic biological processes, in the light of ideas from physics.

A model is a distillation of the known relevant behavior of a system into just a few rules. A good model can help us see the forest for the trees; in Picasso’s phrase, it is “the lie that makes us realize the truth.” But as scientists, we want to take our existing models and poke them, looking for soft spots. We want to look for biologically relevant, incompletely tested aspects of the model. We want to find its falsifiable predictions, then devise uncluttered experiments that bear as directly as possible on those predictions. Quantitative predictions are often the sharpest tool for poking a model.

This course will develop many statistical ideas. But it’s not a course on descriptive statistics, the design of clinical trials, and so on. Rather we’ll look at case studies where important insights into biological systems emerged from an appreciation of the intrinsically random nature of the interactions in complex systems. Along the way we introduce some of the key ideas of biological physics, for example the concept of random walks.

Long ago, in a course like this we'd have to be content with me telling you what faraway people had done; you couldn't roll up your sleeves and do the actual science yourself, because it was too difficult to make computers do anything. Luckily all that has changed. We will be learning and using a general purpose computer-math package called *Matlab*. Whatever you may do in science after this course, the skills you get with *Matlab* will be useful to you.

Announcements: <http://courseweb.library.upenn.edu/> Please log into courseweb now and check that you have access, and that it's using your preferred e-mail address, as this is the address I'll use to contact you.

Grading: Will be based primarily on roughly 10 problem sets (25%), short reading summaries (10%) two midterms (2×15%), and a comprehensive final exam (35%).

Time: We meet MWF 2-3pm in DRL room A7.

Computer lab sessions: Sep 12, 19. Location: Multi-Media Services, DRL (Basement), room BS3. Time: during regular lecture hours. These are short sessions, so be extra prompt and think about the task in advance.

General policies: see separate handout.

Prerequisites:

PHYS 101 (or higher), MATH 104 and [114 or 115]. Recommended: previous or concurrent PHYS 102; basic background in chemistry and biology. We will use the computer-math package *Matlab*; the labs will introduce this useful tool.

Books (more are listed in a separate Book List):

Required:

M. Denny and S. Gaines, *Chance in biology* (Princeton, 2000).

If you find any errors in the text, please bring them to my attention so I can distribute to the class (and to the authors).

Many other short required readings, including lecture notes, etc. will be posted on Courseweb.

Supplemental (on reserve in the library in DRL):

H. Berg, *Random walks in biology* 2d ed. (Princeton UP, 1993).

R. P. Feynman, *QED*.

P. Nelson, *Biological Physics: Energy, Information, Life*, updated first edition (W. H. Freeman, 2008).

Matlab:

Penn has a site license for this software, and there are many places on campus where you can use it, including: SAS Computing Multi-Media Services (basement DRL), Undergraduate Data Analysis Lab (104/108 McNeil Building), The Weigle Information Commons (Van Pelt Library).

For a summary of various public computing labs see:

<http://www.sas.upenn.edu/computing/instructional/labs.html>

<http://www.upenn.edu/computing/view/labs/lablist.html>

Or you can purchase *Matlab* for use on your own computer.

To get started using *Matlab*, I suggest you spend a couple of hours with the tutorial “Intro to Matlab for dynamic modeling,” available on Courseweb.

Matlab itself comes with various tutorials. Other sources include

http://www.mathworks.com/academia/student_center/tutorials/launchpad.html

<http://www.math.ufl.edu/help/matlab-tutorial/matlab-tutorial.html>

<http://www.physics.byu.edu/Courses/Computational/phys330/phys330.pdf>

Rudra Pratap, *Getting started with MATLAB 7: A quick introduction for scientists and engineers* (Oxford University Press, 2006).

Tentative Outline

See Courseweb for each week's reading and homework assignments, and for online documents. "D+G" refers to the main text.

Prolog

"The objective of physics is to establish new relationships between seemingly unrelated, remote phenomena." — L. D. Landau

1. **A breakthrough on HIV**

Biological question: Why did the first antiretroviral drugs succeed briefly, then fail?

Physical idea: Steady state is not the same as equilibrium.

Tools and concepts

"The generation of random numbers is too important to be left to chance." — Robert R. Coveyou, Oak Ridge National Laboratory

2. **Hello Matlab**

2a **How to do better on exams, impress interviewers, and discover new physical laws**

3. **Rules of disorder**

Biological question: How can an inherited feature skip a generation, then reappear?

Physical idea: The discovery of particulate, diploid inheritance.

4. **Discrete distributions**

Biological question: How can we make definite statements about *random* processes?

Physical idea: The distribution can be definite even if individual samples are unpredictable.

5. **Application: Bacterial genetics**

Biological question: How do bacteria become resistant to a drug or virus that they've never encountered?

Physical idea: Models can be tested via their statistical predictions.

6. Continuous distributions

Biological question: Why does the Gaussian distribution fit so many phenomena?

Physical idea: Any distribution look like a Gaussian, if you add many independent measurements.

7. Representing experimental data

Biological question: Do your data reflect a 1-step or multi-step process?

Physical idea: Maximum likelihood analysis as the basis for curve fitting.

Light and life

“Query 30: Are not gross Bodies and Light convertible into one another, and may not Bodies receive much of their Activity from the Particles of Light which enter their Composition?” — Isaac Newton

8. Light is lumpy

Biological question: What sets the absolute limit to night vision?

Physical idea: The spooky truth about photons.

9. Animal eyes

Biological question: Why bother focusing light? And how is it even possible, if light consists of particles?

Physical idea: Intensity as the probability of photon arrival; interference of probability amplitudes.

10. Monochrome vision

Biological question: Why can't you see the stars during the day? They're still there!

Physical idea: The contrast threshold can be predicted from experiments done in the dark.

11. Color vision

Biological question: Why does a mixture of red and green light appear yellow?

Physical idea: Color as a 3-dimensional linear vector space.

12. Primary molecular events in vision

Biological question: Why is dim-light vision slower than bright-light vision?

Physical idea: The G-protein cascade.

Switches in cellular control networks

“Whenever I’m faced with a choice between two evils, I like to choose the one I haven’t tried yet.” — Mae West

13. **Bacteria have feelings, too**

Biological question: How well can bacteria smell?

Physical idea: The Berg–Purcell limit.

14. **Gene expression and genetic switching in bacteria**

Biological question: How can you make decisions without a brain?

Physical idea: Cellular elements can implement logic circuitry.

15. **A developmental genetic switch**

Biological question: How does *Xenopus* know when it’s time for a change?

Physical idea: Bifurcations in a control system.

Neural coding

“The Analytical Engine *weaves algebraical patterns*, just as the Jacquard loom weaves flowers and leaves.” — Ada, countess of Lovelace, 1815–1853

16. **Spike world**

Biological question: What is the internal language of the brain?

Physical idea: The action potential idea.

17. **Visual coding**

Biological question: What’s the “best” way to send a lot of information down the optic nerve?

Physical idea: The best choice of coding depends on the nature of the typical signals to be encoded.