Physics 280: Physical Models of Biological Systems

P. Nelson

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> "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 model, anyway?" and "How do we know when a simple, reductionistic modeling approach is appropriate/inappropriate?"

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 ideas involving probability. 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 Python. Whatever you may do in science after this course, the skills you get with Python will be useful to you.

Announcements: `http://canvas.upenn.edu/` Please log into Canvas now and check that you have access. Instead of the Canvas message system, I will send you e-mail to the address that the registrar has on file for you, or to any other address you like (but you'll have to tell me).
Grading: Will be based primarily on roughly 8 problem sets (25%), weekly short reading summaries (10%) two midterms (2×15%), and a comprehensive final exam (35%).
Time: MWF 2:00–2:50pm.
Computer lab sessions: Time: during regular lecture hours. These are short sessions, so be extra prompt and think about the assignment sheet 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 Python; no prior experience is assumed.

Books:

Required:
The main text will be Nelson, *From Photon to Neuron.* Other short required readings will be posted on Canvas. Known errata to this text are listed at `http://www.physics.upenn.edu/biophys/PtN/errata.html`. If you find any errors not on this list, please bring them to my attention so I can distribute to the class. Earn bragging rights!
We will also use *A Student's Guide to Python for Physical Modeling* Updated Edition, by JM Kinder and P Nelson. The bookstore could not promise to get us the brand-new Second Printing of this book, which reflects numerous minor changes to the language, so I got some hard copies and can supply them at my discounted cost.

Useful (on reserve in the library in DRL):
M. Denny and S. Gaines, *Chance in Biology* (Princeton Univ. Press, 2000).
R. P. Feynman, *QED: The Strange Theory of Light and Matter* (Princeton Univ. Press, 1985).
P. Nelson, *Physical Models of Living Systems* (W. H. Freeman and Co., 2015).

Computing
You will need to obtain the free Python computing environment for use on your own computer; see the updated installation instructions available on Canvas.
You can find printers in many places, including Math/Physics/Astro library (DRL 3d floor) and SAS Computing Multi-Media Services (basement of DRL).
For a summary of various public computing labs see:
`http://www.sas.upenn.edu/computing/instructional/labs.html`

Tentative Outline

We generally only cover about 2/3 of this material each year. See the course web site for each week's reading and homework assignments, and for online documents.

Prolog

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

1. **A stubbornly persistent illusion**
   Biological question: Why does red + green = yellow?
   Physical idea: All the brain can know about color is what's handed to it by the retina, and the retina *discards some information* about the incoming light.

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 Python**

3. **How to do better on exams, impress interviewers, and discover new physical laws**

4. **Rules of disorder**
   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. **Discrete distributions**
   Biological question: If you are your parents' genomes, then why does inheritance seem random?
   Physical idea: Meiosis and fertilization generate draws from two diploid sets of particulate traits.

6. **Continuous distributions**
   Biological question: Why does the Gaussian distribution fit so many phenomena?
   Physical idea: Any distribution looks like a Gaussian, if you add many independent measurements.

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

7. **Light is lumpy**
   Biological question: What sets the absolute limit to night vision?
   Physical idea: The spooky truth about photons.

8. **Poisson processes**
   Biological question: How do you detect an invisible step in a molecular motor cycle?
   Physical idea: The waiting-time distribution tells us about the mechanism.

9. **Devices that manipulate light**
   Biological question: If light really consists of particles, then how is focusing possible?
   Physical idea: Intensity as the probability of photon arrival; interference of probability amplitudes.

10. **Applications to microscopy**
    Biological question: If diffraction limits us to about two hundred nanometers, how can we see individual molecular motor steps?
    Physical idea: The *location* of a single spot can be measured to great accuracy, if we get enough photons.

11. **Vista: X-ray crystallography**

Vision

> "The sages of Chelm began to argue about which was more important: the Moon or the Sun. The reigning wise man ruled: 'The Moon *must* be more important, because without it, nights would be so dark we could not see anything. The Sun, however, shines only by day—which is when we don't need it!'" — Leo Rosten

12. **Animal eyes**
    Biological question: How can we sort out the many objects in our visual world?
    Physical idea: Limited depth of focus as a data-rejection tool.

13. **Image compression**
    Biological question: We have 10^8 photoreceptors, but only 10^6 neurons in our optic nerve. How can all the needed information reach our brains?
    Physical idea: The redundancy removal hypothesis.

14. **Vision in dim light**
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.

15. **Primary molecular events in vision**
Biological question: How are vision, olfaction, and taste the same?
Physical idea: The G-protein cascade.

Vistas

"Dazzling and tremendous how quick the sun-rise would kill me,
If I could not now and always send sun-rise out of me." — Walt Whitman

16. **Planetary climates**
Biological question: What is the biggest organism?
Physical idea: The Earth system is a self-regulating system with multiple feedbacks that hosts many other organisms—so let's explore its physiology.

17. **Valedictory**
Physical/biological question: Why did we spend our time studying mere specifics?
Physical/biological idea: There's no truth without the details. But if you look in the right places, you do see universality.