Physics 2280: 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

Most students in this class are 2nd year or higher.

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.

Prerequisites:
PHYS 0101 (or higher), MATH1400 and [1410 or 1610]. Recommended:
previous or concurrent PHYS0102 or 0151; basic background in chemistry and
biology. We will use the computer-math package Python; no prior experience is
assumed.

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).
MW 1:45–3:15pm.

Office hours:
We'll arrange these to suit the class.

Computer lab sessions:
Time: during regular lecture hours.

Assessment:
See "course policies" document.

Books:
Paperback editions will be available at the Penn bookstore; e-book editions are
also available.
Nelson, *Physical Models of Living Systems* second edition (2021). If you find
any errors, 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* second
edition (2021), by JM Kinder and P Nelson (Princeton U Press).
press.princeton.edu/).
Other required readings will be posted on Canvas.

Computing
I recommend the free computing environment "Anaconda" from anaconda.com/
which runs on your own computer. See installation instructions available on
Canvas or Appendix A of the *Student's Guide*. You may, however, prefer
Anaconda's cloud facility or Google Collaboratory
(https://colab.research.google.com).

Tentative Outline

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

Prologue

"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 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. **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.

7. **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.

8. **Random walks on an energy landscape**
Biological question: How can pulling two things apart strengthen their bond?
Physical idea: Bond breaking is a first passage process, controlled by the lowest energy barrier, which can increase upon moderate loading.

9. **Representing experimental data**
Biological question: How can an experiment measure a parameter that you don't directly observe?
Physical idea: Maximum likelihood analysis as the basis for curve fitting.

Vistas

10. **Negative feedback control and homeostasis**
Biological question: How can we maintain a fixed population in a colony of constantly reproducing bacteria?
Physical idea: Negative feedback can stabilize a desired setpoint in a dynamical system by creating a stable fixed point..

11. **Positive feedback control and switching**
Biological question: How can you make decisions without a brain?
Physical idea: Cellular elements can implement logic circuitry and remember the answers by using bistability to create a separatrix (watershed)..

12. **Cellular clocks**
Biological question: How do the cells in a frog embryo know when it's time to divide?
Physical idea: Interlocking positive and negative feedback loops can generate stable, precise oscillation via a limit cycle..

13. **The role of superspreaders in pandemics**
Biological question: Why do some outbreaks of a communicable illness spread explosively, while others, in similar communities, fizzle after the first few cases?
Physical idea: A tiny subpopulation of superspreader individuals can introduce giant variations in the course of an epidemic..

14. **Bet hedging via phenotypic diversity**
Biological question: How does *B. subtilis* hedge against a wrong decision?
Physical idea: A trigger circuit can be driven by noise.

15. **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.