LS50: Integrated Science

Course overview

LS50 is a two-semester, double course that introduces the natural sciences as an integrated whole. Its goal is to teach students how to solve scientific problems by drawing methods and concepts from biology, chemistry, physics, and mathematics. The course uses examples from biology as an integrating theme, principles from physics and mathematics to reduce complex problems to simpler forms, and computer simulation to allow students to develop their intuition about the behavior of the dynamical systems that control the physical and biological universe. The course includes bootcamps to introduce students to biological experiments and the computer language, Matlab. Each semester will include a project lab, in which students will work in small teams to do original research on unsolved biological problems.

Natural science is a single intellectual enquiry into the universe of objects that surround us. Its components are linked by a common method: inducing hypotheses from a mixture of data and intuition, deducing predictions, and testing them by experiment and observation. The sciences depend on mathematics, from the simple act of counting to sophisticated methods required for computational chemistry and theoretical physics. The Integrated Science curriculum will introduce motivated freshmen to the concepts and methods needed to attack the life sciences in the 21st century. For both semesters, students will take the equivalent of two courses, meeting for formal instruction every day, performing hands-on, original research, and using modern computer methods to simulate scenarios and analyze data.

Darwin and Wallace's theory of evolution revealed that the living things have a purpose: their structure, function, and behavior are integrated to leave as many progeny as possible. For much of the 20th century, this difference, and the astonishing diversity of form and function, tended to separate biology from the other natural sciences: biology's complexity made it unappealing to many mathematicians, physicists, and chemists, and the "assume a spherical cow" flavor of theorists' simplifying assumptions made biologists skeptical about how useful theory was for understanding biology. Two advances have pushed biologists towards theorists and computer scientists: the need to test our understanding of biological processes by making explicit, mathematical models and the need to convert large datasets into information and, ultimately, knowledge.

We will teach students that the answer to "How will you solve this problem?" is "By any means necessary!" Our goal is to teach them how to find interesting problems, the means to solve them, and above all, the knowledge and courage to invent the new methods that make previously insoluble problems soluble. Coupling concepts and methods to problems that excite students and making them use these tools in their own research will embed the concepts in their working memory.

We will teach through iterated cycles of experiment and analysis, making use of experimental computation to simulate a system of interacting entities and explore the effect of parameter variation on the system's properties. Our goal is to complement the formal derivation of theorems, show the productive interplay between theory, simulation, and experiment, and show that computer systems and programs, like biological objects, have purposes. Mastering a restricted syntax to write algorithms will help students think about how biological systems use the restricted syntax of chemistry and genetics to accomplish tasks. Concepts like modularity, exploration with selection, error detection and correction, and recycling previous inventions are important in the function and evolution of both organisms and code. Six faculty will teach the course, working as three pairs of one life scientist and one physical scientist.

Students will use their knowledge to conduct original scientific research. To ensure that all the students start with abilities in laboratory experiments and computer simulations, we will have two, two week long boot camps, one in computation and one in experimentation. After the boot camps, students will perform original research in project laboratories. The project labs will be based on the research of and run by faculty and Bauer Fellows, independent scientists who spend five years at Harvard after their PhDs and run small research groups.

Class format

Lectures each weekday (M,Tu, W, Th, F) from 10-11:30 in Northwest Labs B108 (first basement level), 52 Oxford Street

Weekly discussion sections with teaching fellows, at locations and times to be determined based on student availability.

Weekly problem sets, to be submitted as indicated on each assignment.

Three in-class tests during semester, each covering the preceding month's worth of lecture material.

A four-week bootcamp that will introduce students to programming in Matlab and in experimental biology and will start on Monday, September 12th, in the teaching labs on the first basement level of Northwest Labs (52 Oxford Street). Labs will meet Tuesdays or Thursdays from 1:30-4:30 PM during the fall term beginning on September 19, 2016, beginning Bootcamps will include weekend sessions.

Post-bootcamp, research-based laboratory: students work on original research projects in small groups, with open access to a sophisticated modern research laboratory. Students are expected to spend 6 hr/week working on their projects. Labs will meet Tuesdays or Thursdays from 1:30-4:30 PM during the fall term beginning on September 19, 2016.

Faculty

Ben deBivort	OEB
Michael Desai	OEB
Sean Eddy	MCB
Cassandra Extavour	OEB
Erel Levine	Physics
Andrew Murray	MCB, Course Head

The year-long course will be divided into thirds, each team-taught by a pair of faculty, one from the physical and one from the life sciences.

Laboratory Heads

Nicolas Chevrier	Bauer Fellow
Dan Needleman	SEAS/MCB

The two lab heads will teach together in a course that will use a variety of techniques to investigate how cells of the immune system present antigens.

Teaching Fellows

Mariela Petkova	Biophysics	Early fall
Emma Nagy	MCB	Early fall
Ivana Cvijovic	Systems Biology	Late fall
Neil Peterman	Physics	Late fall
Sam Carlson	MCB	Early spring
Leo Blondel	OEB	Early spring
Cara Weisman	Biophysics	Late spring
Emily Hager	MCB	Late spring

Syllabus

Below we list the topics covered, week-by-week for the fall and spring semesters. Since the course will meet every day for two semesters, it will have roughly 120 lectures. As a result the description below is brief and lists weekly topics rather than those of individual lectures.

Fall Week	Topics
1	Intro and course overview. Biology as computation. Central Dogma. Inference, rules and errors.
2	Intro to probability and Bayesian analysis. Equilibria, energy, and steady state. The Lac operon as a paradigm for gene regulation.
3	Intro to differential equations. Intro to computation. Intro to linear algebra. Intro to the cell division cycle
4	Linear algebra. The cell division cycle.
5	Cell cycle checkpoints. Intro to principal component analysis and applications to microbial communities and face recognition. EXAM 1.
6	Cell cycle regulation. Symmetry breaking in cell polarization. Classical & molecular genetics. Chemistry: elements, quanta, atomic orbitals.
7	Molecular genetics. Chemistry: periodic table, molecular orbitals, bonding
8	Chemistry: macromolecules (proteins, nucleic acids), intermolecular forces, membranes. Gene regulation. Intro to neuroscience.
9	Math primer. Dynamical systems.
10	Neuroscience: modeling action potentials. Intro to thermodynamics. Entropy and temperature. EXAM 2.
11	Statistical physics: Boltzmann factor, partition function, pressure, volume, & free energy, chemical potential, Gibbs Free energy, equilibria, law of mass action.
12	The cellular energy budget. Cooperativity. Diffusion.
13	Diffusion. Fluorescence.
14	Diffusion-limited reactions. Reaction-diffusion systems. Precision in development. EXAM 3.

Spring week	
1	Intro to mechanics. Fluids. Fluid dynamics. Life at low Reynolds numbers.
2	Intro to structure and function. Membranes, channels, pumps. Electrostatics,

	capacitors, Debye screening. Photosynthesis & redox.
3	Chemiosmotic ATP synthesis. Structure: nucleic acids, proteins, protein folding. Self assembly.
4	Optics. X-ray crystallography. Microscopy. Enzyme catalysis.
5	Enzyme catalysis. Cell structure. Cytoskeleton. EXAM 1.
6	Probability & Bayesian statistics.
7	Graphs & networks. Inference & model selection. Biological applications.
8	Pattern recognition in biology and biological data.
9	Non-parametric methods of statistical analysis. Biological applications. EXAM2.
10	Stochastic phenomena in biology. Stochastic differential equations. Symmetry and symmetry breaking. Markov chains. Stochastic simulation. First passage.
11	Population genetics. Evolutionary thinking.
12	Modularity & modification. Molecular evolution of proteins. Evolution of development. Origin of life.
13	History of life. Diversity of life.

Assessment

Assessment will be based on five criteria:

In-class tests
We will administer three in-class tests, each 1.5 hours long and each covering the material presented in the preceding month. The question format and content will be similar to the weekly problem sets. Students can bring a single-sided 8.5 x 11 inch piece of paper, with any information they wish to remember to each exam and we will provide a sheet with key formulae and equations.

Problem sets
Weekly problem sets will review the topics covered in lectures and discussion sections. We highly encourage students to collaborate to solve the problems, which may include a comparison of scratch work, methods used, and numerical results. All submitted work should be written independently and reflect the students' own understanding. Students should not submit work that they would be unable to explain or reproduce on their own.

This policy reflects our intent in assigning the problem sets: to help you master the material under low-stress circumstances so they will not be blindsided by higher-stakes tests. While you should be wary of over-reliance, classmates are an excellent resource for help since they keep similar hours, live nearby, and remember their own learning process well enough to explain concepts appropriately. On the flip side, mentoring colleagues whenever possible is not merely kind and forward-thinking, but also helps crystallize your understanding and practice the mentorship and presentation skills needed for work in the scientific community.

Laboratory research
Students will be graded on the research projects they undertake, focusing on their ability to design and interpret experiments and their commitment to and engagement with their research more than on the quality of the results they produce (subject as these are to the whims of the

Gods). Approximately half of the grade from laboratory research will reflect weekly participation in lab, with the remainder attributed to a final lab report.

Participation
Students will be graded on their participation in class, which we expect to be highly interactive, weekly conferences, and the discussions associated with laboratory research.

These criteria will be accorded the following weights:

In-class tests	50%
Problem sets	20%
Laboratory research	20%
Participation	10%