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 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. Five faculty will teach the course, working in 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 JHDSF Fellows, independent scientists who spend five years at Harvard after their PhDs and run small research groups.

Class format

Lectures M, Tu, Th, F from 10-11:30 am, in the Northwest building room B108 (NWB108).

Wednesday activities, W, 10-11:30 am. These will be of various types, including lectures on faculty research and discussion of scientific papers and careers. Mid-terms will occur on Weds. and, on those days, we will scheduled class of 10:00 am-noon to allow 2 hrs for a 1.5 hr midterm.

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 each semester, each covering the preceding month's worth of lecture material.

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 3-6 hr/week working on their projects. Labs will meet at times to be determined, probably Tuesdays and Wednesdays from 1-4:00 pm (students choose which day they'll attend).

Faculty

Ben de Bivort	OEB
Michael Desai	OEB
Sean Eddy	MCB
Cassandra Extavour	OEB
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

Kristin Koenig	John Harvard Distinguished Science Fellow
Paul Shamble	John Harvard Distinguished Science Fellow

Teaching Fellows

Mariela Petkova	Biophysics	Early fall
Emma Nagy	MCB	Early fall
Severine Atis	Physics	Late fall
David Jacobowitz	Systems Biology	Late fall
Cara Weisman	Biophysics	Early spring
TBN	TBN	Early spring
Mike Jin	Systems Biology	Late spring
Eli Weinstein	Biophysics	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 100 lectures. As a result the description below is brief and lists weekly topics rather than those of individual lectures. A full schedule is on the course website.

Fall Week	**Topics**
1	Intro and course overview. Biology as computation. Central Dogma.
2	Intro to probability and Bayesian analysis. Equilibria, energy, and steady state. The Lac operon as a paradigm for gene regulation.
3	Classical and molecular genetics.
4	Math primer. Introduction to computation and differential equations.
5	Linear algebra. The cell division cycle.
6	Linear algebra. The cell division cycle. EXAM1
7	Introduction to thermodynamics, entropy, temperature.
8	Statistical mechanics. Chemistry of bonding.
9	Statistical mechanics. Chemistry of cellular molecules.
10	Statistical mechanics. Cellular energy budget. Cooperativity. EXAM 2
11	Diffusion. Gene regulation.
12	Diffusion. Gene regulation. Membranes.
13	Reaction-diffusion systems. Electrostatics. Thanksgiving!
14	Capacitors. Photosynthesis, oxidation, reduction. ATP synthesis. EXAM 3.

Spring week	
1	Graphs & networks. Sequence alignment.
2	Sequence search algorithms. Finding sequence motifs.
3	Bayesian inference, probability & Markov models.
4	Phylogenetic trees. Computational grammar. Gene finding.
5	Determining protein and nucleic acid structure. EXAM 1.
6	Protein structure. Enzyme mechanism. Dynamical systems.
7	Enzyme mechanism. Dynamical systems. Cell structure.

8	Dynamical systems. Cell structure. Neuroscience
9	Facial recognition. Population genetics. EXAM2.
10	Population genetics. Stochastic phenomena in biology. Symmetry breaking.
11	Simulating stochastic processes. Evolutionary thinking. Evolution of development.
12	Evolution of development. History & origin of life.
13	Watch this space! EXAM3.

Matlab

We assume no prior experience in writing computer programs, but a major goal of the course is to teach scientific computation, using the language Matlab. Students will participate in a Matlab boot camp run by Adam Cohen and colleagues. Information can be found here: https://wiki.harvard.edu/confluence/display/fasmatlab (you need a Harvard key to access). Problem sets will have questions that depend on your ability to use Matlab but we will increase their difficulty gradually so as not penalize those encountering a computer language for the first time.

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. Questions will be designed to take 90 min, but exams will be scheduled for 2 hrs. 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%