EE 193/COMP 150: Computing with Biological Parts
Spring 2019

Class meeting time: TuTh 3:00-4:15pm
Instructor: Joel Grodstein. Office hours: 1 hour before class or by appointment.
Teaching assistant: TBD, but we likely will not have one.

Prerequisites: junior status or above, and see below

***Course Overview*:**

Living organisms must adapt and compete in a constantly-changing environment. Thus the motto – *compute or die* – is an imperative for almost all living organisms, from humans down to bacteria. The class will cover ways in which living biological systems compute. Furthermore, as recombinant-DNA technology gives us the ability to alter DNA (the "software" of biology), we will explore what might be the results of altering organisms' computational processes.

After giving a backgrounder in biology, we will cover two specific areas of computation:

- Computing with bioelectricity. The most obvious example of bioelectrical computing is, of course, our brains. In fact, increasing evidence suggest that most of our cells work together, computing and signaling with bioelectricity, as a sophisticated image-processing computer to help our bodies grow from an embryo to our desired final shape, and then to maintain that shape.
- Computing with DNA. It is a surprising fact that humans and puffer fish have mostly the same genes; what separates us is the complex network of control logic that turns our genes on and off at various times. We will learn how this control logic works, how to analyze it in engineering terms, and how to use synthetic biology to build our own desired control logic instead.

***Course Objectives*:**

Upon completion of the course, students will be familiar with:

1. The basics of DNA, RNA, proteins, genes and cells
2. How bioelectricity works, how it is used in neurons, and how it may control body shape.
3. What gene-regulatory networks are, and how they control which genes turn on at any given time.
4. The use of synthetic biology to change the functions that gene-regulatory networks and bioelectricity compute.

Why should you care?

- The intersection of biology, computing and engineering may be poised for transformative applications, in medicine and elsewhere. The ability of recombinant DNA technology and drugs to subtly change the way that cells compute is extremely powerful. The potential applications of these technologies may be transformative, and are currently mostly still unrealized. Particular technologies may succeed or fail – understanding the basic computational abilities should not only be interesting, but should give you a better understanding of what types of computations living organisms are capable of.

- The microprocessor inside of your cell phone likely contains almost a billion logic gates. By contrast, current technology can place roughly a dozen gates inside of a bacteria. On the other hand, your cell phone cannot swim inside of your bloodstream and replicate a million billion copies of itself in 24 hours on a diet of sugar water. The medical consequences of this are already starting to appear, and may be far reaching – or not.

What this course isn't:

- We will cover some very new areas; some of them may not pan out.
    - Synthetic biology (the altering of DNA to build synthetic organisms that better suit our own purposes) is a fairly new and rapidly-growing field. It has seen several successes, launched an ever-increasing parade of startups, and may be poised for transformative successes – or not.
    - Morphogenesis is one of the black mysteries of biology; we know very little about how an embryo grows into a full body, and how the body can repair itself. The course will cover, in some detail, one particular hypothesis that is being worked at the Tufts Allen Discovery Center. This hypothesis, which supported by growing evidence, has by no means reached the status of fact. Even if it eventually is disproved, bioelectricity is a rapidly growing field with numerous medical applications (from neuroscience to electroceuticals).
- All of our experiments will be done on computers using simulators. We will *not* do any actual lab work with any organisms (though we may arrange a visit to one of the Tufts labs).

Rough course sequence:

1. Introduction to biology. The central dogma: what are DNA, RNA and proteins and cells and why we care. Morphogenesis – the march from a single-celled embryo to a fully-formed body. Synthetic biology – altering DNA sequences for our own purposes (1.5 weeks).
2. Introduction to bioelectricity: how a cell creates a voltage inside of itself and controls that voltage. Neurons and the brain. Gap junctions – how cells communicate bioelectrically (1.5 weeks).
3. Morphogenesis: how we progress from a single cell to fully-formed bodies (4 weeks). The magic of planaria (an organism that regenerates itself so well that it is essentially immortal). Building coordinate systems from bioelectricity, so that we know where to put different organs. Building neural networks with bioelectricity so as to recognize body shapes.
4. Gene regulatory networks (GRNs), 5 weeks. What purpose GRNs serve in biology. Modeling simple pieces of GRNs. Building and analyzing simple gates, latches and oscillators. Altering GRNs – the medical applications of altered computing.
5. Final project (1 week).

***Programming Assignments**:*

There will be at roughly eight programming assignments throughout the term. Depending on the composition of the class, we may have the actual coding for all assignments done individually or via pair programming. In either case, you can (and should) talk about ideas with other students.

Exams

There will not be a midterm or final exam. However, there will be a quiz after each section (roughly matching the programming assignments). They are expected to take about 15 minutes or so.

Final project:

The course will have a final project. You may work in teams of 1-3 people, and choose any project that is related to the course materials. A selection of potential topics will be given in class.

Resources:

- *An Introduction to Systems Biology: Design Principles of Biological Circuits*, Uri Alon. An excellent introduction to the field of systems biology, with a bit of synthetic biology and morphogenesis thrown in. Particularly, Chapters 2-6 cover much of the material on GRNs that we cover in class. The book is on reserve at Tisch.
- *Molecular biology of the cell* is an excellent first textbook in molecular biology. It covers everything you would need for this class, and in substantially more detail than we will. However, I've found it to usually be quite readable.
- The best introduction to bioelectricity I've found is *"Biological Physics: Energy, Information, Life"* by Philip Nelson. It's the textbook for PHYS 25, and so the bookstore may have some copies left. Tisch has two copies (one of which I've placed on reserve).
- *Modeling Planarian Regeneration: A Primer for Reverse-engineering the worm*, Lobo and Levin 2012. A very readable overview of the computational problems that planaria seem to solve effortlessly as they regenerate themselves.
- *Gap junctional blockade stochastically induces different species-specific head anatomies in genetically wild-type Girardia dorotocephala flatworms*, Emmons-Bell 2015. Another paper describing the wild and wooly feats that planaria are capable of.
- http://neuralnetworksanddeeplearning.com , by Michael Nielsen.
- There are numerous books on Python programming. Two that are available free online are
  - http://greenteapress.com/thinkpython2/thinkpython2.pdf
  - https://automatetheboringstuff.com

Prerequisites

- This is an extremely interdisciplinary course, covering parts of biology, physics, computing, electrical engineering and programming. It is expected that very few people will enter the course being competent in all of the above areas, and we thus are not being strict about prerequisites. Obviously, the more areas you have to learn, the more work you will have. With that in mind…
- While we will cover a fair amount of biology, the course is intended to be self-contained in that respect; we will cover all of the biology that we absolutely need. Of course, you will find it easier if you already have some biology background – especially in molecular biology and genetics. Nonetheless, my expectation is that only perhaps half the class will be in this category.
- We will be doing a nontrivial amount of programming in Python. In all cases, you will be given an existing simulation framework and you will "merely" need to write enough code to use it. If you're reasonably competent in Python, you will have no trouble. If you're competent in a similar language (e.g., Matlab), you should be able to pick up Python without much trouble. If you've never done any programming at all, then this may not be the class for you unless you're willing to put in some work catching up.
- We will be learning about bioelectricity. Having learned something about electricity (e.g., with PHYS 2 or 12) will give you quite a leg up.
- One semester of calculus is listed as a prerequisite.

Grade Formula

As with the course material, the number of assignments will be adapted to what best works for our mix of students. The grading formula will adapt with it. One possible mix might be:

- Programming assignments – 60%
- A few quizzes – 15%
- Final project – 15%
- Class participation – 10%

The course will probably not have a formal midterm or final.

Late Assignments:

Late assignments will be penalized by 10% per day. Any extensions due to extenuating circumstances (illness or family emergencies) must be arranged ahead of time with the instructor before the original due date.

Collaboration policy

Learning is a creative process. Individuals must understand problems and discover paths to their solutions. During this time, discussions with friends and colleagues are encouraged—you will do much better in the course, and at Tufts, if you find people with whom you regularly discuss problems. But those discussions should take place in English, not in code. If you start communicating in code, you're breaking the rules. When you reach the coding stage, therefore, group discussions are no longer appropriate. Each program, unless explicitly assigned as a pair problem, must be entirely your own work. Do not, under any circumstances, permit any other student to see any part of your program, and do not permit yourself to see any part of another student's program. In particular, you may not test or debug another student’s code, nor may you have another student test or debug your code. (If you can’t get code to work, consult a teaching assistant or the instructor.) Using another’s code in any form or writing code for use by another violates the University’s academic regulations. Do not, under any circumstances, post a public question to Piazza that contains any part of your code. Private questions directed to the instructors are OK. Suspected violations will be reported to the University's Judicial Officer for investigation and adjudication. Be careful! As described in the handbook on academic integrity, the penalties for violation can be severe. A single bad decision made in a moment of weakness could lead to a permanent blot on your academic record. The same standards apply to all homework assignments; work you submit under your name must be entirely your own work. Always acknowledge those with whom you discuss problems! Suspected violations will be reported to the University's Judicial Officer for investigation and adjudication. Again, be careful

Additional resources

Tufts University values the diversity of our students, staff, and faculty, and recognizes the important contribution each student makes to our unique community. Tufts is committed to providing equal access and support to all qualified students through the provision of reasonable accommodations so that each student may fully participate in the Tufts experience. If you have a disability that requires reasonable accommodations, please contact the Student Accessibility Services office at Accessibility@tufts.edu or 617-627-4539 to make an appointment with an SAS representative to determine appropriate accommodations. Please be aware that accommodations cannot be enacted retroactively, making timeliness a critical aspect for their provision. Tufts and the teaching staff strive to create a learning environment that is welcoming to students of all backgrounds. If you feel unwelcome for any reason, please let us know so we can work to make things better. You can let us know by talking to anyone on the teaching staff. If you feel uncomfortable talking to members of the teaching staff, consider reaching out to your academic advisor, the department chair, or your dean.