CSE590b: Molecular and neural computation

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Administrative

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**Grading:**

30% class participation: ask questions. It’s more fun if it’s interactive.

30% Homework: Due at the end of class one week after they are handed out. Late policy: -10% each day for the first 3 days, then not accepted.

40% Class project: A small design project using one (or several) of the design and simulation tools that will be introduced in class.

**Books:** There is no single book that covers the material in this class. Any book on molecular biology and on neural computation might be helpful to dig deeper.

https://www.coursera.org/course/compneuro
Computation can be embedded in many substrates

Alternative physical substrates can be used to make computers

Computation controls physical substrates (output of computation is the physical substrate)
The molecular programming project

The history of computing has taught us two things: first, that the principles of computing can be embodied in a wide variety of physical substrates from gears and springs to transistors, and second that the mastery of a new physical substrate for computing has the potential to transform technology.

Another revolution is just beginning, one that will result in new types of programmable systems based on molecules. Like the previous revolutions, this “molecular programming revolution” will take much of its theory from computer science, but will require reformulation of familiar concepts such as programming languages and compilers, data structures and algorithms, resources and complexity, concurrency and stochasticity, correctness and robustness. With molecular programming, chemistry will become the new information technology of the 21st century.
Biological inspiration

DNA Genome

...GTGGTACAGGTG
AATTTGGGTTAGGCTA
AATTGTCCATAGTTT
ATGTGTGTGAATGAG
GGTGTATGGATGTTT
CTCAGAGATGGGTGTG
CAGCTGGAAGGGCGT
CCATTGTGCAAAACA
TATGCTGGAGAAGTT
GCCGGTTCATTCGTCG
TGTGGCGACCCCAGA
TTAATAAAAGGACTA
AGCCGAAAAGAAAAT
GAAACATATATATATAT
ATATATATAATAATAATATATATA

Regulatory Circuitry

Zebrafish Development

Can we learn how to write such a program?
Motivating question for this class

What abstractions, architectures and programming languages are appropriate for specifying spatial organization and differentiation of cells/matter such that we can synthesize a system as complex as the brain?
What I cannot create I do not understand (R. Feynman)

We’re taking a forward engineering/rational design approach to understanding biological computation.

Biological systems are evolved and may not provide an ideal blueprint for engineering. We still have no idea how to read/write biological “code.”

This is not a developmental biology class and also not a computational biology class.
Models of computation

- Cellular automata
- Register machines
- Chemical reaction networks (analog circuits)
- Digital logic circuits
- Finite state machines
- Neural networks
- ...
From molecules to the brain

**Topic 1: DNA nanotechnology and molecular programming:** The basic modules are programmable biomolecules

DNA: GTGGTACAGGTG
RNA: GGGCUGUUUUUC
Prot: MTYRLELNGKTL

**Topic 2: Synthetic biology (gene circuit engineering):** The basic building blocks are genes and their products

![Gene Circuit Diagram]

**Topic 3: Computation in the brain:** The basic building blocks are cells

![Neuron Image]
Topic 1: Molecular programming

a

b

c

Structural DNA nanotechnology
(images by Rothemund, Shih, Winfree, Yin and others)
Logic circuits and dynamical systems (images by Qian, Winfree and others)
Topic 1: Molecular programming

Detection stage
- mRNA target
- Probe binding sites
- Probes
- HCR initiators

Amplification stage
- Fluorescent metastable hairpins
- Triggered polymerization creates fluorescent amplification polymers

Imaging application
(Images by Pierce and Fraser)
Topic 2: Synthetic biology

A biological oscillator
(Hasty lab)
Topic 2: Synthetic biology

A synthetic pattern forming system (lab)
**Topic 2: Synthetic biology**

Installing a synthetic genome

- Synthetic genome: “new operating system”
- Host cell
- Install

**Step 1:** Complete synthesis of the genome from *Mycoplasma genitalium*, 580K basepairs

**Step 2:** Genome transfer from one cell to another (similar) cell

- *Mycoplasma mycoides capri*
- *Mycoplasma capricolum*

- Craig Venter
- Hamilton Smith
- and others
Application: Artemisinin synthesis (Keasling lab, )

Artemisinin is an anti-malarial drug that is difficult to synthesize chemically. Can we make it through biotechnology?

Challenges:
• Efficiently use resources
• Potentially toxic intermediates
**Topic 2: Synthetic biology**

![Graphs and images showing membrane potential and action potential propagation in cell networks.](image-url)
The brain is organized at multiple scales

Neurons

Columns

Maps

Areas

Jack Gallant, Berkeley
Cerebral cortex inhibitory axons only via infection with a brainbow virus

But what if we want to see all the connections?

Dawen Cai et al., 2013 & Luke Bogart, Takao Hensch

Jeff Lichtman, Harvard
Understanding computation in neuronal networks. Toward a mechanistic understanding of the biology computation

- What do different neuronal types contribute to computation?
- How do we go from neuronal details to global information processing and network function?

Adrienne Fairhall, UW
Characterizing neuronal computation

Adrienne Fairhall, UW
What can neurons compute? The dynamical systems properties of neurons lead to a range of different computational properties.

- Integrators or differentiators or fractional differentiators!
- Resonant at certain frequency band
- Distinct representations of information at different timescales
- Modulatable between different modes of operation
- Long timescale changes in operation

Computational character depends on input statistics  Adrienne Fairhall, UW