Biophysics 4251

When? TTh 9:30-10:45 PM

Where? Howey N210

Where (virtual)? http://simbac.gatech.edu/biophys17

Who? JC Gumbart

Who? Howey W202

Who? (404) 385 0797

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Textbooks

(for when my lectures just aren’t enough for you)

Physical Biology of the Cell (2nd Ed.)
by Phillips, Kondev, Theriot, & Garcia

Physical Models of Living Systems
by Philip Nelson
Grading

- Homework (50%)
- Class Participation (10%)
- Papers (10%)
- Project/Presentation (30%)

Note: for grad students, project and homework become 40% and 40%

**NO TESTS**: haven’t you suffered enough by now?

Participation: up to **two** absences will be accepted without penalty

Papers: we will read four papers together; turn in summary before discussion in class
Project

The class project will take one of two forms:

1) computationally/mathematically model a specific biophysical phenomenon, e.g., modeling neurons as an excitable system

2) use molecular dynamics to simulate a protein and analyze the resulting trajectory data with VMD
Project steps

1) *research the chosen subject*

2) *design an approach to model it*, i.e., build a mathematical model or a simulation system

3) *implement the model*, either in code (Matlab, python, etc.) or by running the simulation

4) analyze the model for its connection to real biological behavior

5) present the background, model, and results in class

6) write a paper in a form suitable for publication
What is biophysics?
Two basic goals in biophysics

describe biological processes mechanistically

protein folding

fluorescence microscopy

develop and apply physical methods to studying biology
The Inner Life of the Cell (Biovisions, Harvard)

Somewhat idealized (too dilute, not enough noise), but still compelling and relatively accurate molecular visualizations

https://www.youtube.com/watch?v=wJyUtbn0O5Y
Biophysics takes many forms, especially here at Tech
Biophysics from atoms to ants at Georgia Tech

Jennifer Curtis
mechanics of phagocytosis

Dan Goldman
animal locomotion

JC Gumbart
bacterial systems

Joshua Weitz
viral dynamics/evolution

Flavio Fenton
cardiac dynamics

Harold Kim
transcriptional dynamics

Simon Sponberg
physiology of animal motion
“Everything that living things do can be reduced to wiggling and jiggling of atoms.”

Richard Feynman (1963)

50 years later…

But we are far from done!

The Nobel Prize in Chemistry 2013

The Nobel Prize in Chemistry 2013 was awarded jointly to Martin Karplus, Michael Levitt and Arieh Warshel "for the development of multiscale models for complex chemical systems".
Can we realize this ultimate reductionism?

Maybe.... bacterium (10 billion atoms)

molecular dynamics simulation but it wouldn’t be very useful!

“It is nice to know that the computer understands the problem. But I would like to understand it, too.”

Eugene Wigner

the computer is just a tool to help us think!
We aim to derive physical principles that apply to biological systems.

Biophysical simulations reveal the secrets of photosynthesis from electrons to entire organisms.
But… “can biological phenomena be understood by humans?”*

biological systems exhibit unimaginable complexity, compromising traditional physics approaches

It depends on what the definition of “understand” is!

Transcriptional regulatory network of *Mycobacterium tuberculosis*

protein function emerges from its sequence

MLEFIAH…

Maybe “engineering” biology is enough?

Does the computer scientist look for a simplified equation that explains how a processor works?

A COMPUTATIONALLY DESIGNED INHIBITOR OF AN EPSTEIN-BARR VIRAL BCL-2 PROTEIN INDUCES APOPTOSIS IN INFECTED CELLS

If we can measure and quantify the behavior of various proteins, we can, for example, design novel ones to carry out new and interesting functions.
Biology requires a different way of thinking from physics...

...but that doesn’t mean we throw away everything we know!
Biology requires a different way of thinking from physics

Fundamental “laws” of biology largely non-existent - why?
  - probabilistic nature (e.g., “errors” not only tolerated but often necessary!)

  - emergent biological behavior is the result of context-dependent evolution: different context would give different results!

  - every rule has an exception, e.g., non-mendelian inheritance

  - instead, have organizing principles such as evolution

The mantra of biophysics

Seek simplicity -
and distrust it.

early 20th century mathematician and philosopher, Alfred North Whitehead
“Nothing in biology makes sense except in the light of evolution”* (T. Dobzhansky 1973)

*except in Georgia

But evolution is blind!

neutral mutations can even lead to increased complexity with no apparent selective advantage

Consequences of evolution: biological systems are not perfect, they just happen to be good enough.

two solutions to the same problem

minimize errors...

...or have correcting mechanisms in downstream process

Biology is robust
Consequences of evolution: biological systems don’t fight disorder - they harness it

Thermal energy

\[ kT = 0.6 \text{ kcal/mol} = 4 \text{ pN.nm} \]

* same scale as many molecular processes

Diffusion can bring reactants together

Fluctuations allow systems to spontaneously find new states

Molecular machines spend energy to *redirect* thermal noise, *not* to fight it, like in man-made machines
Consequences of evolution: cells are crowded!

“Dilute” conditions don’t apply - 20-30% of cell volume is dry material!
-effects are numerous: diffusion rates, association/dissociation equilibria, folding, thermostability, etc.
-crowding hypothesized to also be an evolved trait, to maximize reaction rates