

biophysics

PHYS 320 / 420: Intro to Biological Physics



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- ▶ **Problem sets:** 70% of the course grade. Each problem set will be based on a recent paper in the literature, and consist of two parts: an intro explaining why the topic is important and interesting, and then a guided, step-by-step walk through some calculations in the paper (either analytical or numerical). *Working in groups is fine (even encouraged), but please hand in your own write-up.*

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Each group will include 1-2 graduate students, who will also do a 20 minute presentation on the problem set to the whole class as part of the project.

BIOREPS

The entire **BIOREPS** initiative is being supported by NSF through 2022, including [financial support for undergrad research projects](#) that grow out of the group work. So far each year 1-2 undergrads from the course have received summer stipend support. If you are interested after the end of the course, reach out to me!



The arrogance of physicists



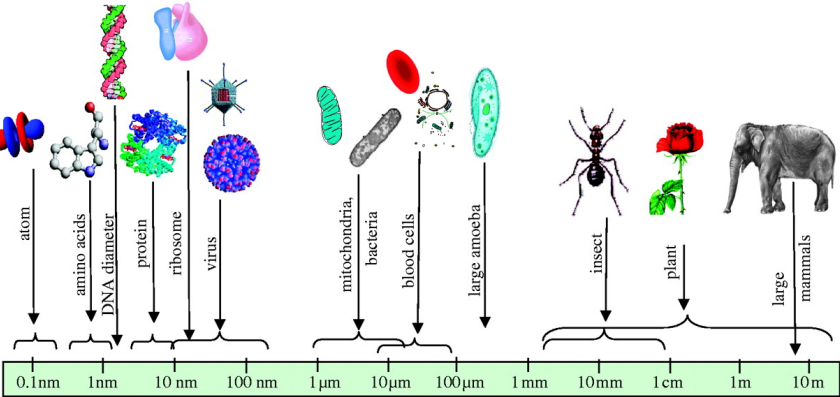
“...everything that living things do can be understood in terms of the jiggings and wiggings of atoms.” — Richard Feynman

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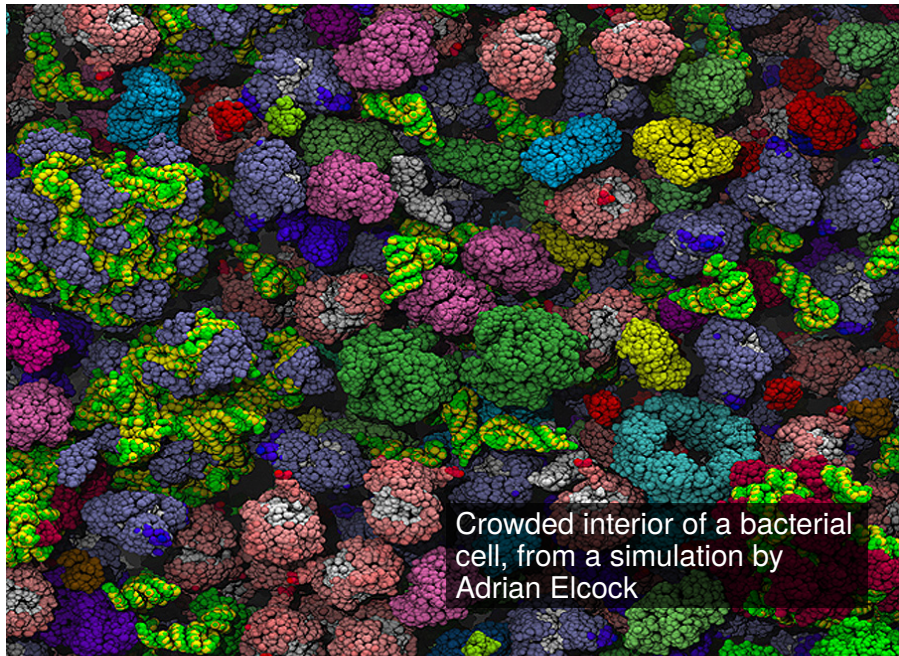
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Fluctuations rule at scales below 1 μm



thermal fluctuations matter

The not-so-primordial soup



Crowded interior of a bacterial cell, from a simulation by Adrian Elcock

Shaken, not stirred...

See lecture video for movie.

Virus assembly [Perlmutter *et al.*, eLife (2013)]

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Central questions of the course

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- ▶ Are there fundamental physical laws governing the speed of these processes, the work they can carry out, the information they can transmit?
- ▶ What do these laws tell us about the trajectory of evolution and the necessary conditions under which life arose? To what extent are living things “optimized” under these physical constraints?

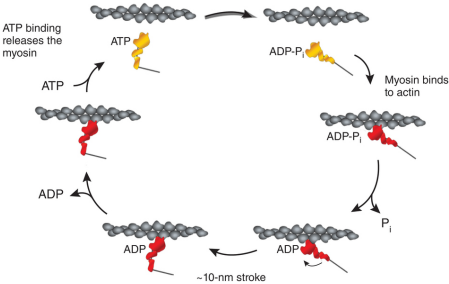
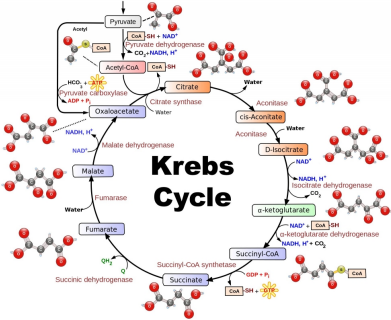
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Biology provides a spectacular guide to the **how** of life. Can physics help provide a non-trivial answer to the **why**?

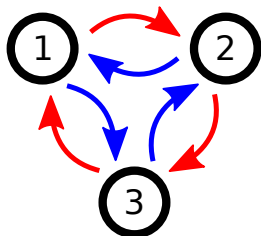
Finding a mathematical language for biological processes

The bane of every intro bio course: **cycles upon cycles...**



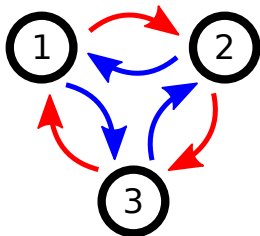
Finding a mathematical language for biological processes

For us, all these will be specific cases of a **universal mathematical framework**: Markov state models, describing stochastic transitions between states.



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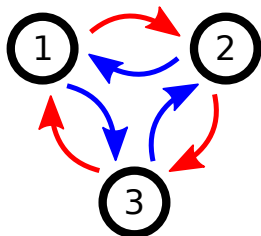
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Versatility of the approach: the states can be molecule numbers in a chemical reaction, different structures of a protein, the populations of a genetic variant...

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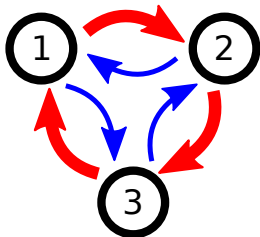


Two broad categories of transition networks:

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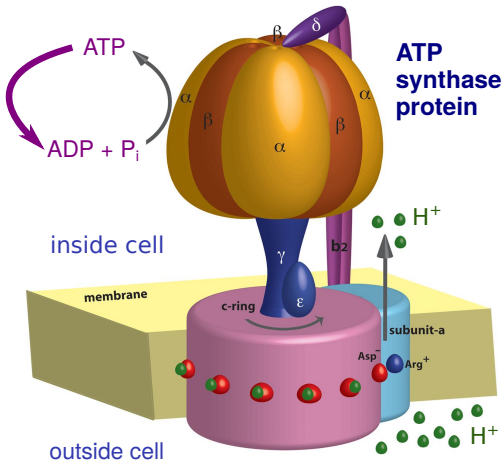
Two broad categories of transition networks:

- ▶ **equilibrium**: any random path on the network and its reverse are equally likely
- ▶ **non-equilibrium**: the symmetry between paths and their reverses is broken \Rightarrow **requires external fuel source** (we will prove this!)

Non-equilibrium driving in living systems: ATP

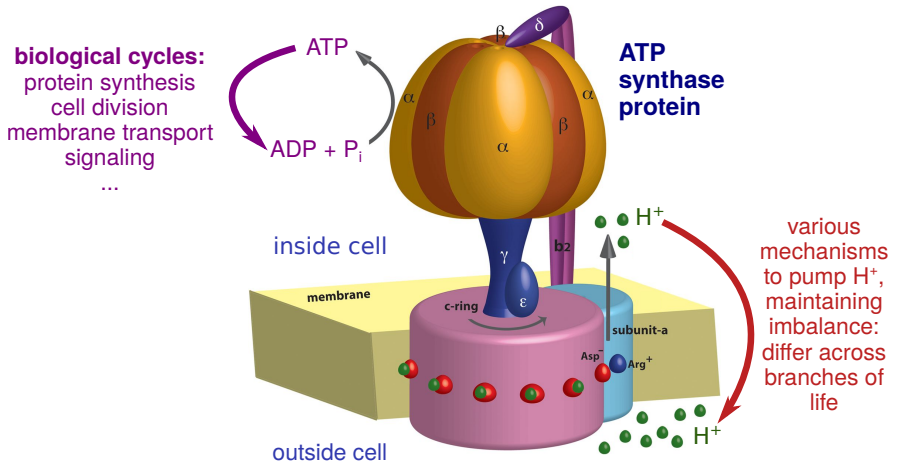
ATP as the prime biological fuel source is as universal as the genetic code.

biological cycles:
protein synthesis
cell division
membrane transport
signaling
...



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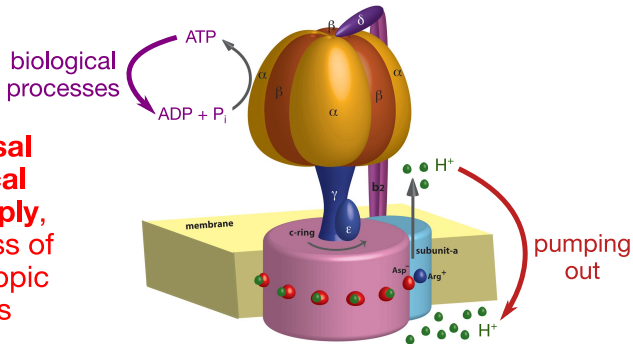
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Synthesizing ATP is a **nonequilibrium** process, driven by ion imbalances.

The role of physics: nonequilibrium thermodynamics

**universal
physical
laws apply,
regardless of
microscopic
details**



dissipated
energy



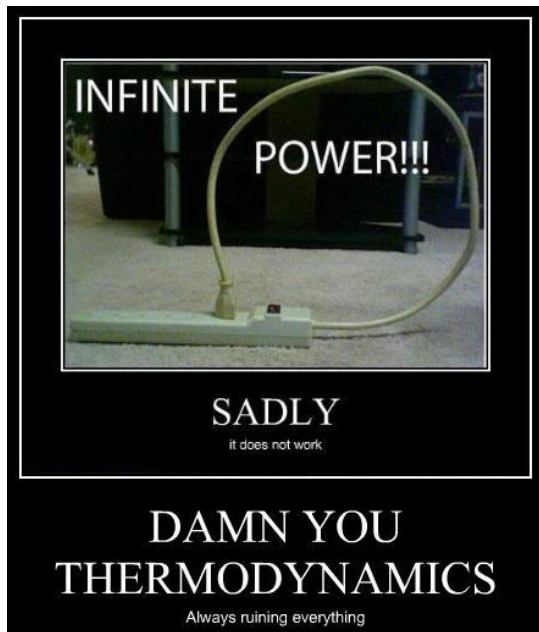
mechanical work
chemical work
information transfer

current



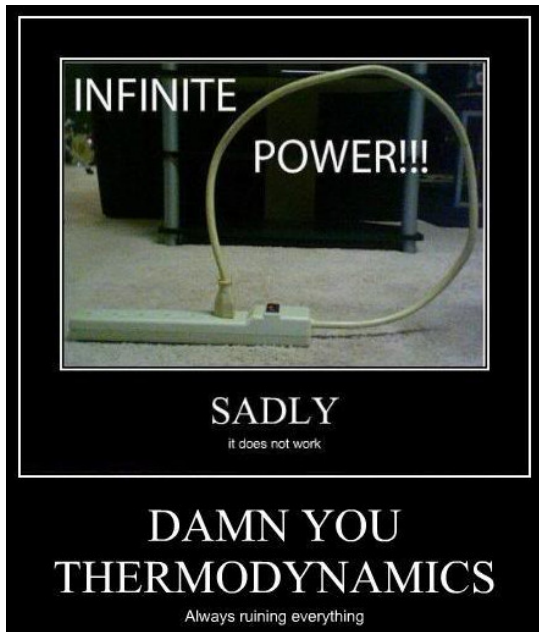
"recharging"
the battery

The second law of thermodynamics



Evolutionary conundrum:
Self-recharging batteries
cannot spontaneously
arise from an equilibrium
primordial soup.

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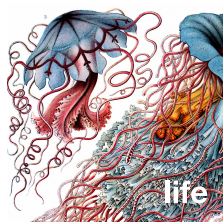
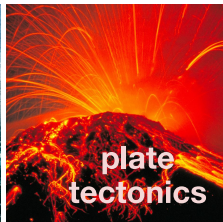
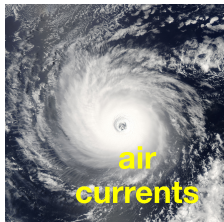
Evolutionary conundrum:
Self-recharging batteries cannot spontaneously arise from an equilibrium primordial soup.

Every persistent imbalance in nature is driven by a more fundamental imbalance:

If you see a current, search for the power outlet.

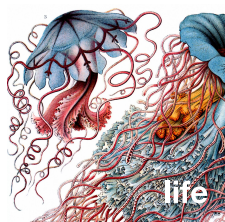
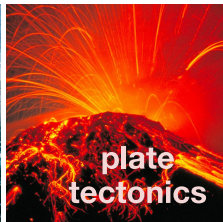
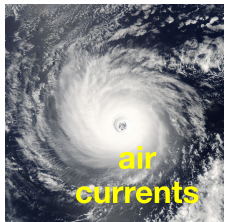
The fundamental imbalances

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are ultimately “plugged into” two major imbalances:



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(The really hard part!)

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True universality: The molecular details of potential life-forms on exoplanets will be different, but the constraints of nonequilibrium physics will be the same.

