

biophysics

PHYS 320 / 420: Intro to Biological Physics



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- ▶ **Problem sets:** 65% 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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Groups that do a good job will have their problem sets published in the **BIOREPS** open online database. You will be given full credit by name for your work, and it will be published under a Creative Commons license as a resource both to future students and the larger research community. Website: biotheory.phys.cwru.edu/bioreps

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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 for the next five years, including [financial support for undergrad research projects](#) that grow out of the group work. So far three undergrads from the course over the last two years received summer stipend support.



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As a condition of that support, NSF requests a quantitative assessment of our CURE (course-based undergraduate research experience). There will be a pre-course survey and post-course survey (each 10-15 minutes, administered at an external link you will receive in your e-mail). Completing these surveys counts for **5% of your total grade.**

The arrogance of physicists



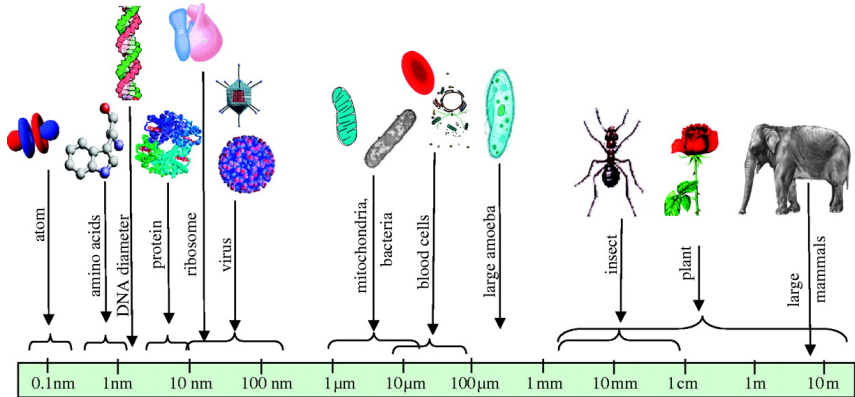
“...everything that living things do can be understood in terms of the jiggings and wiggings of atoms.” — Richard Feynman

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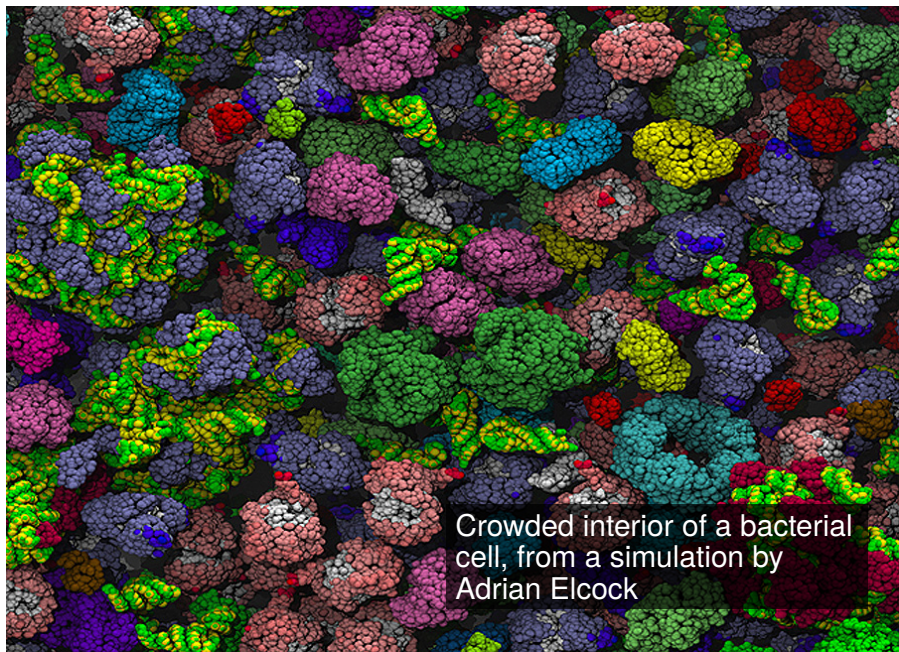
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Fluctuations rule at scales below 1 μm



thermal fluctuations matter

The not-so-primordial soup



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

Shaken, not stirred...

See inner_clip.mp4 file on course website.

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

See capsid_assembly.mp4 file on course website.

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?

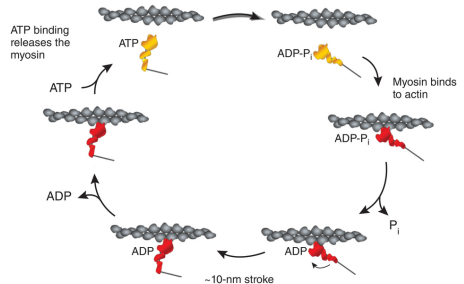
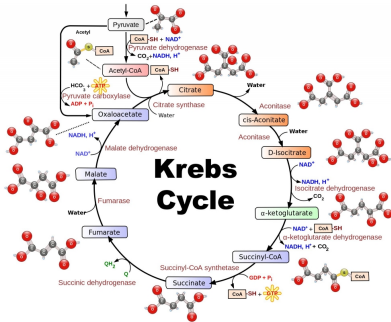
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Biology provides a spectacular guide to the **how** of life. Can physics help provide a non-trivial answer to the **why**?

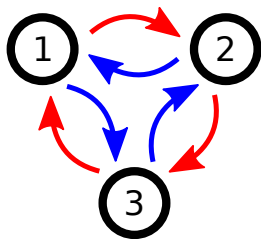
Finding a mathematical language for biological processes

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



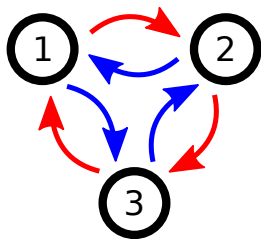
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For us, all these will be specific cases of a **universal mathematical framework**: Markov state models, describing stochastic transitions between states.



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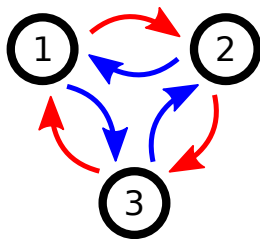
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Versatility of the approach: the states can be molecule numbers in a chemical reaction, different structures of a protein, the populations of a genetic variant...

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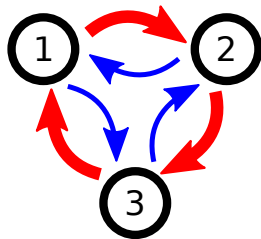


Two broad categories of transition networks:

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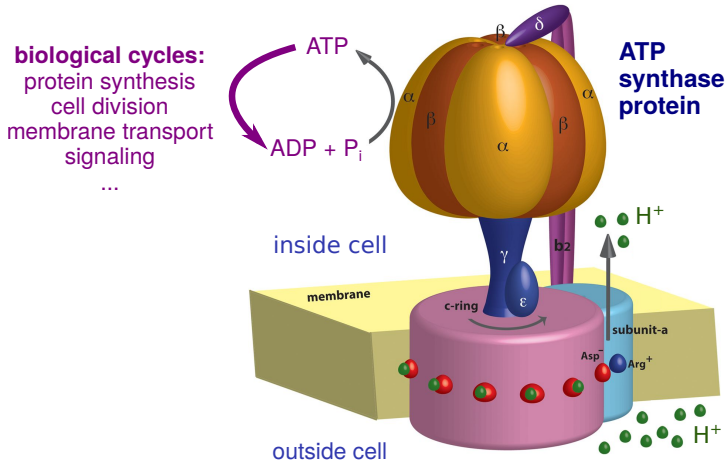


Two broad categories of transition networks:

- ▶ **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!)

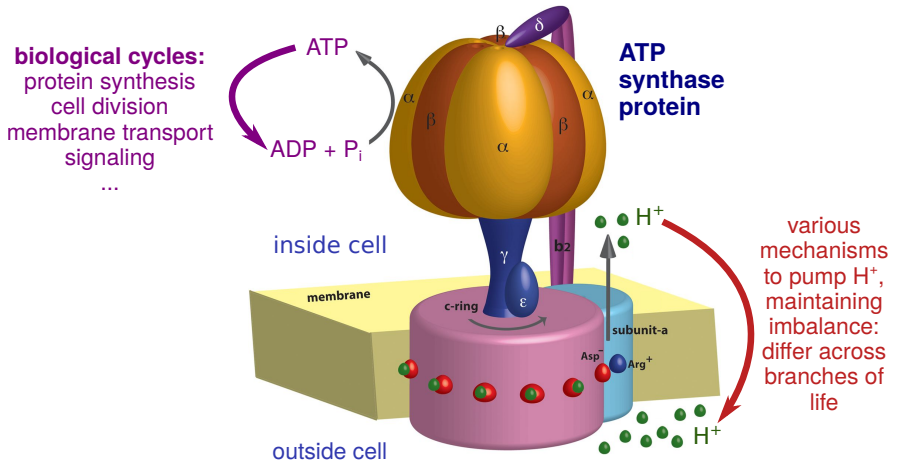
Non-equilibrium driving in living systems: ATP

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



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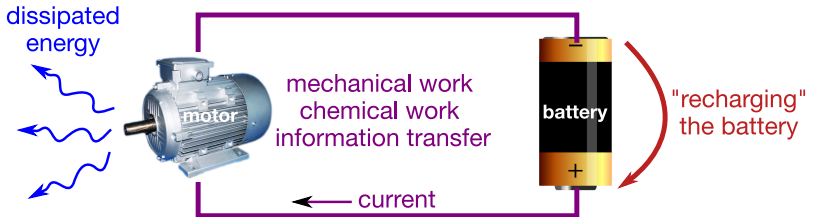
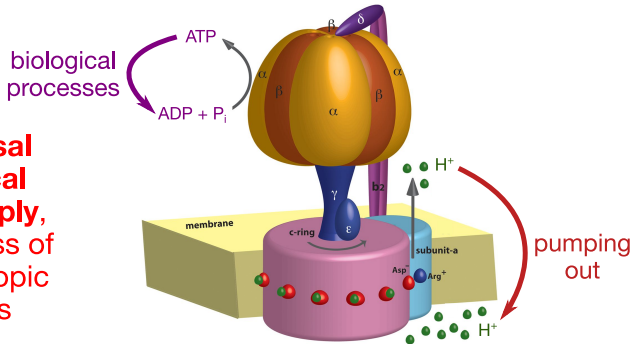
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Synthesizing ATP is a **nonequilibrium** process, driven by ion imbalances.

The role of physics: nonequilibrium thermodynamics

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



The second law of thermodynamics



SADLY

it does not work

DAMN YOU
THERMODYNAMICS

Always ruining everything

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

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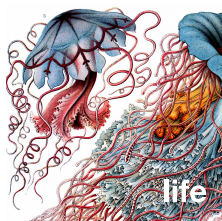
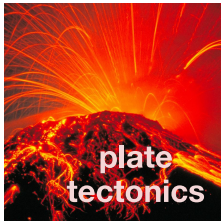
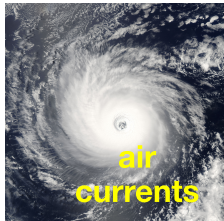
Self-recharging batteries cannot spontaneously arise from an equilibrium primordial soup.

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

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

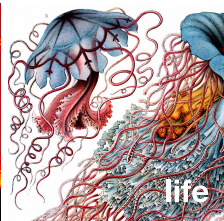
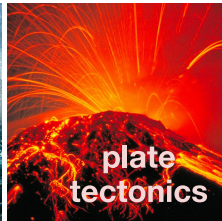
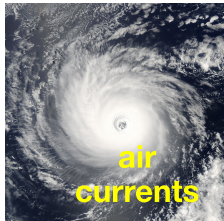
The fundamental imbalances

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are ultimately “plugged into” two major imbalances:



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

