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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  - 1 chosen by you from the **BIOREPS** (**Bio**physical **Re**search **P**roblem **S**et database). These were written by the previous year's class!

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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. Two undergrads from last year's class were supported on stipends this past summer.

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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 jigglings and wigglings of atoms.” — Richard Feynman

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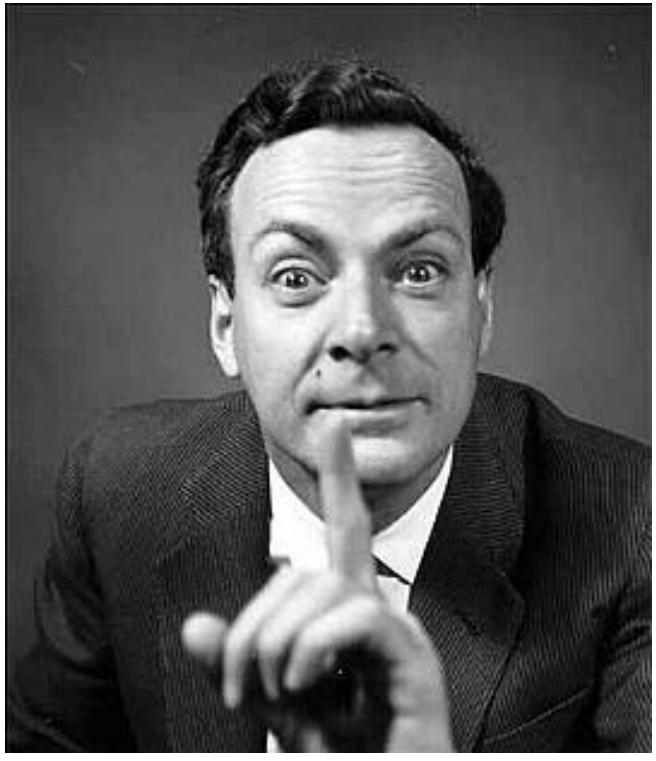

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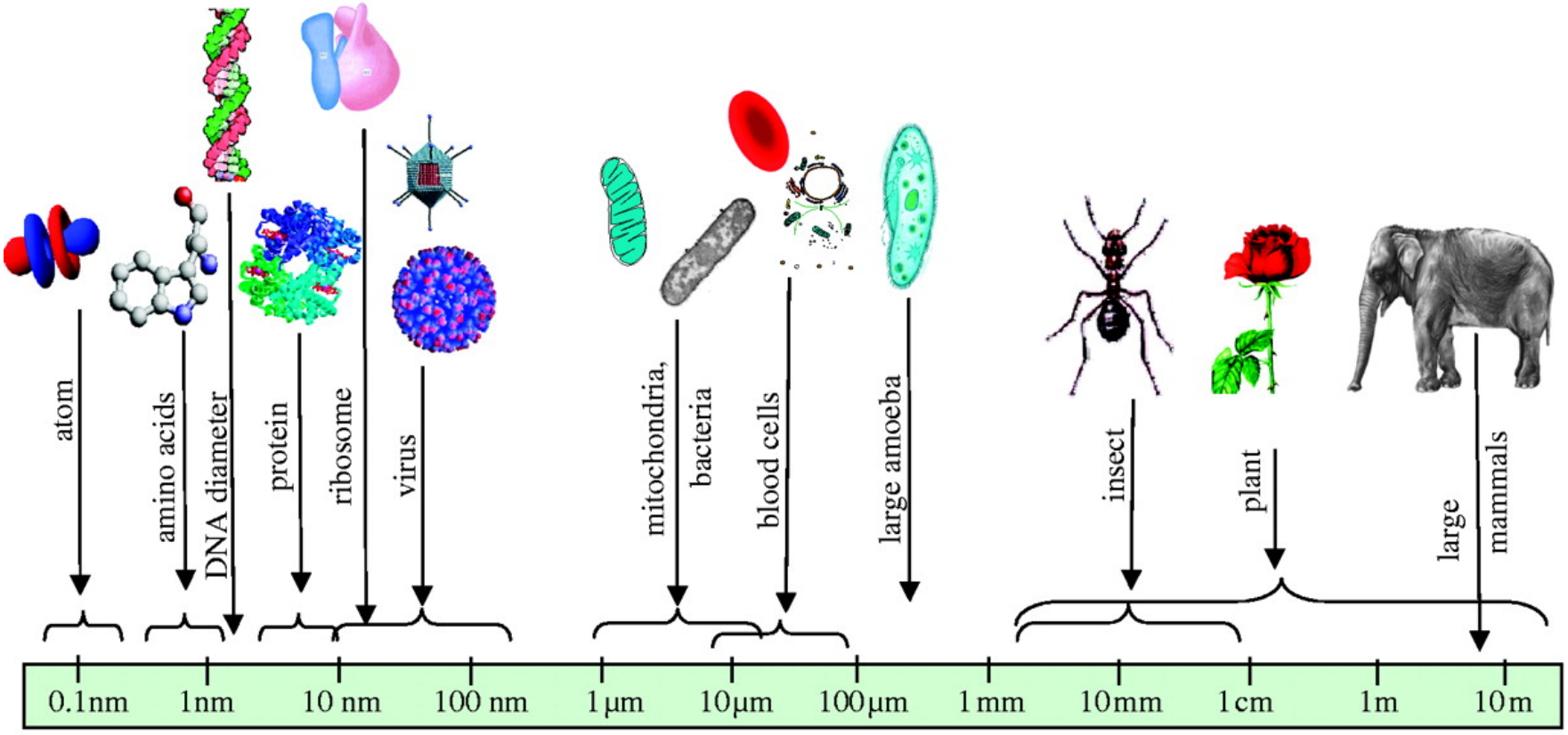
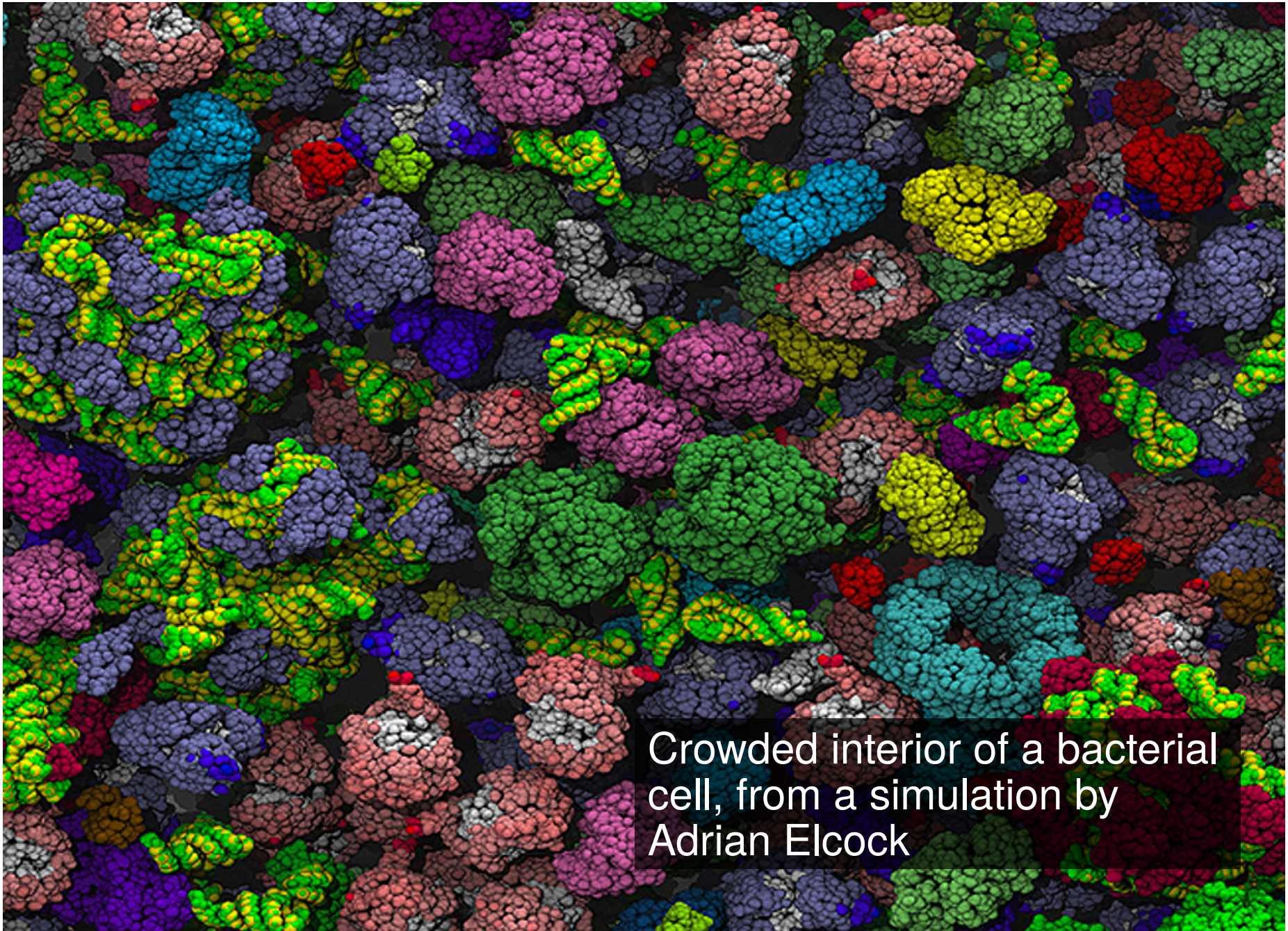
Fluctuations rule at scales below 1 μm



thermal fluctuations matter

The not-so-primordial soup



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

Shaken, not stirred...

Movie file on course website.

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

Central questions of the course

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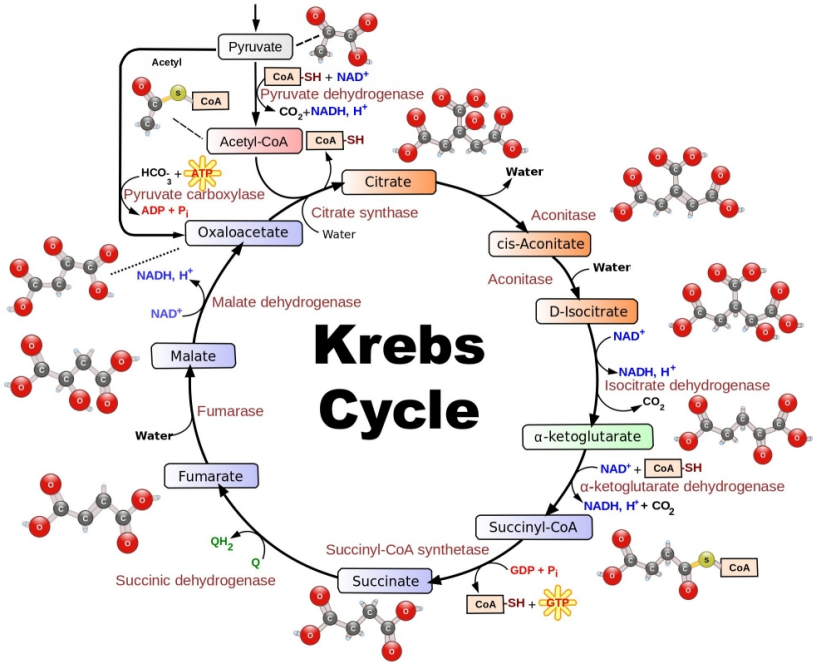
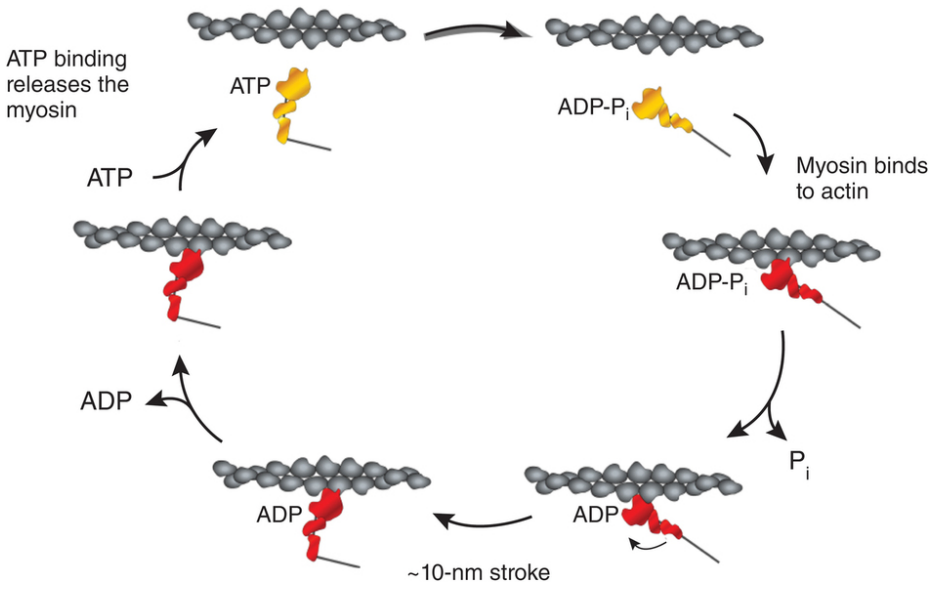
Biology provides a spectacular guide to the **how** of life. Can physics help provide a non-trivial answer to the **why**?

Finding a mathematical language for biological processes

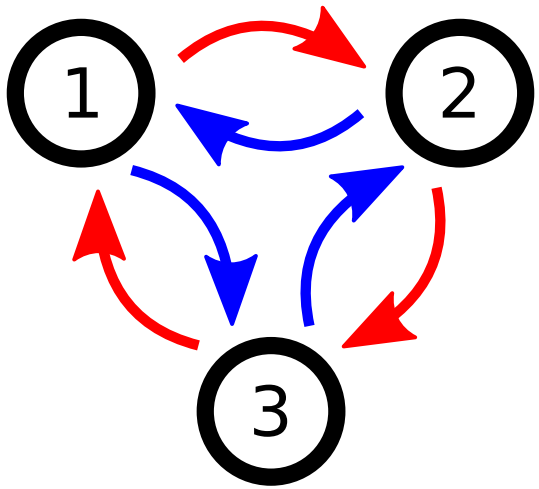
The bane of every intro bio course: cycles upon cycles...





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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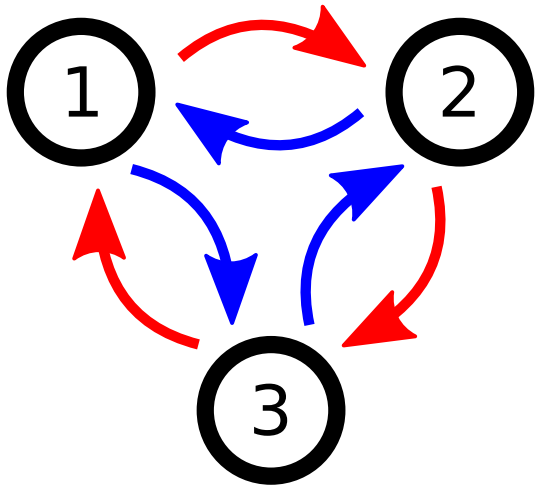

Versatility of the approach: the states can be molecule numbers in a chemical reaction, different structures of a protein, the populations of a genetic variant...

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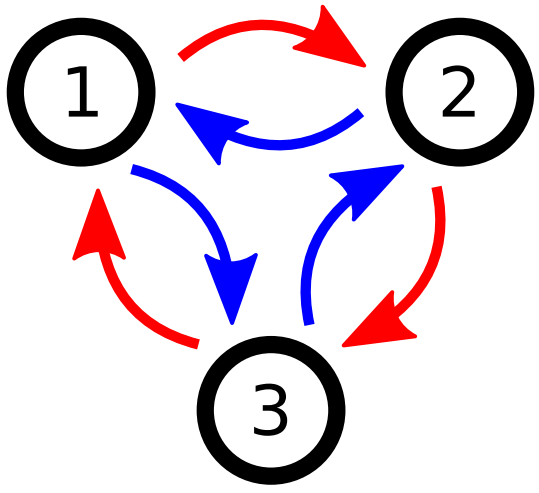

Two broad categories of transition networks:

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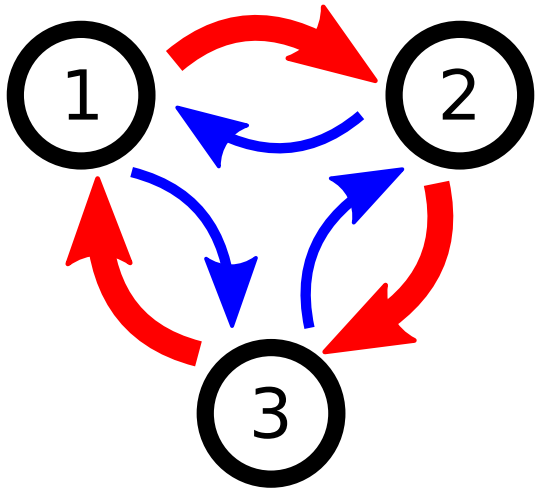


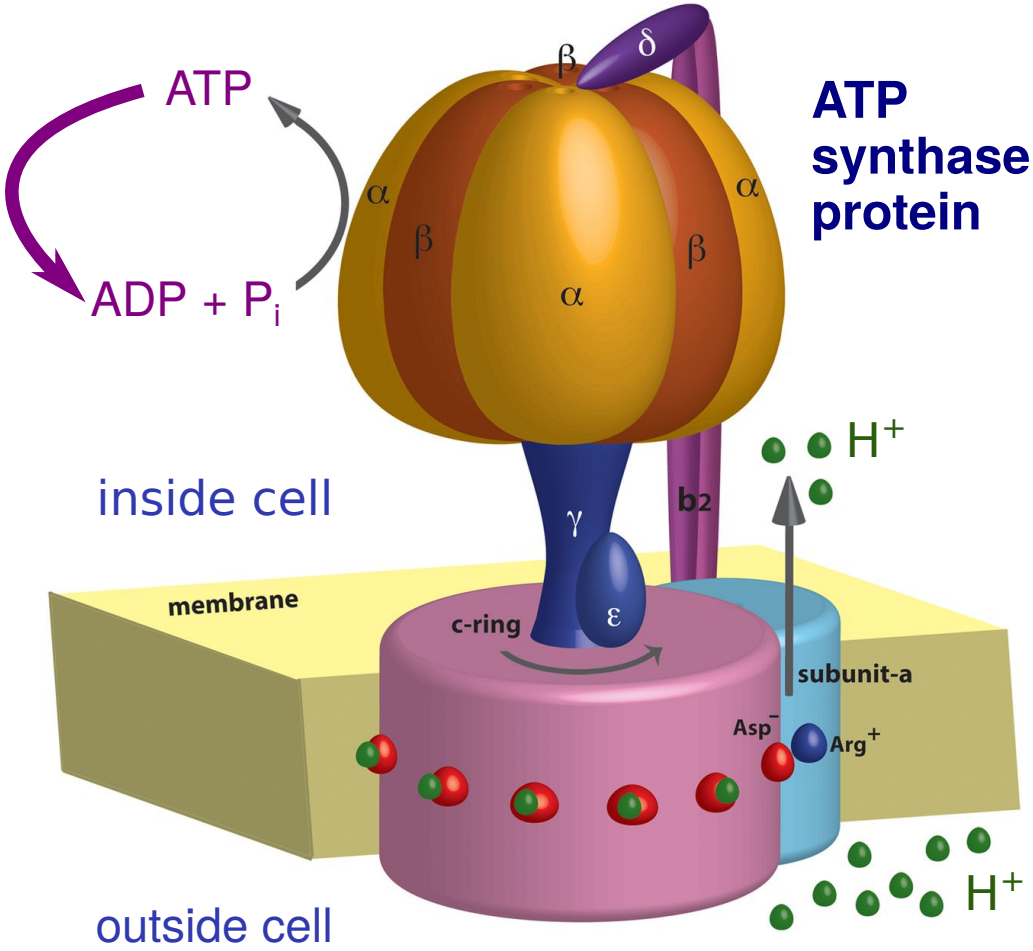
Two broad categories of transition networks:

- **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
...



ATP synthase protein

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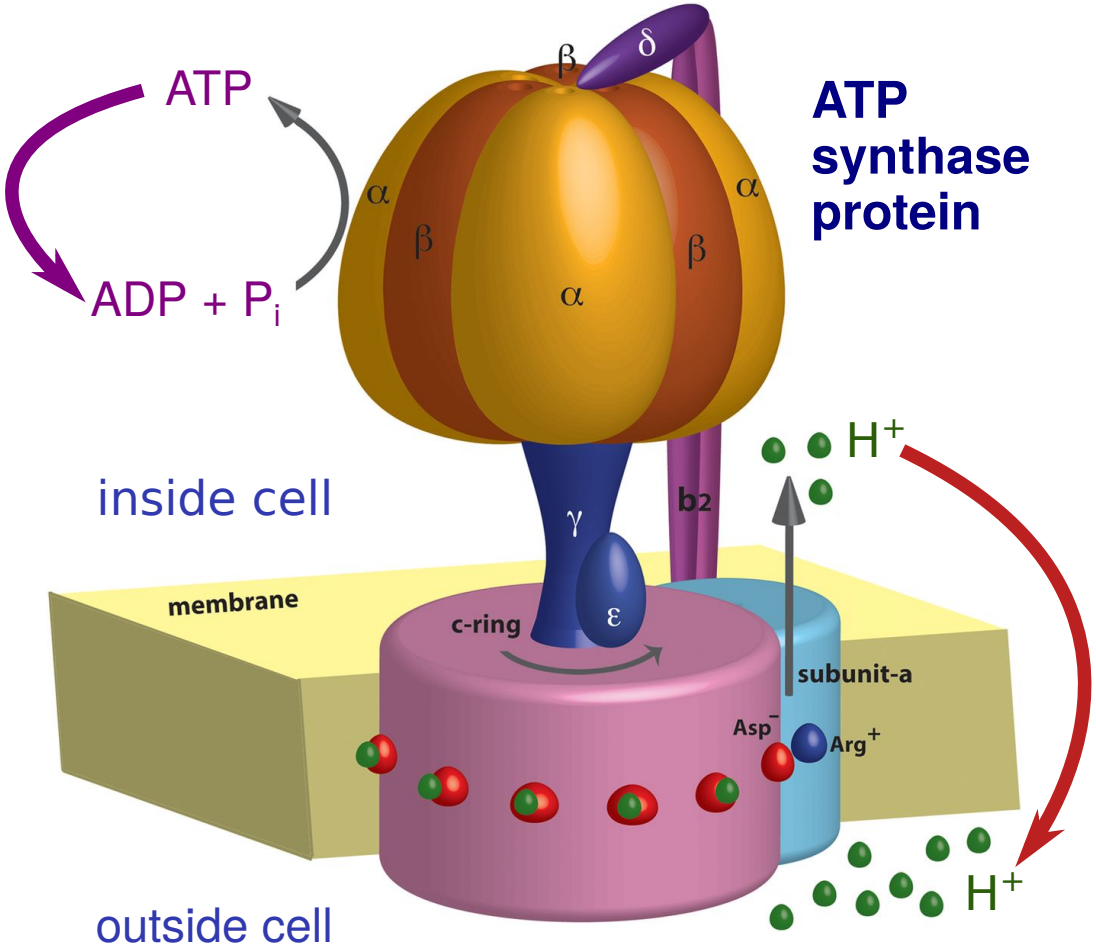
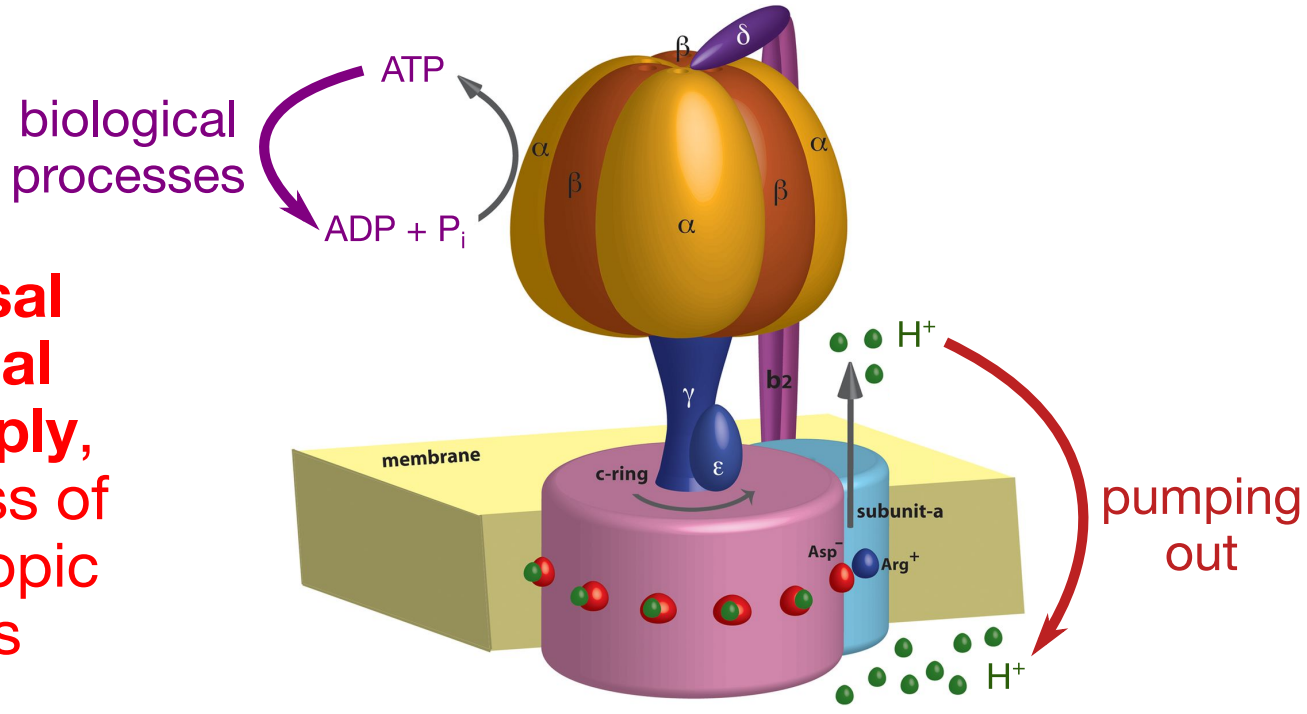


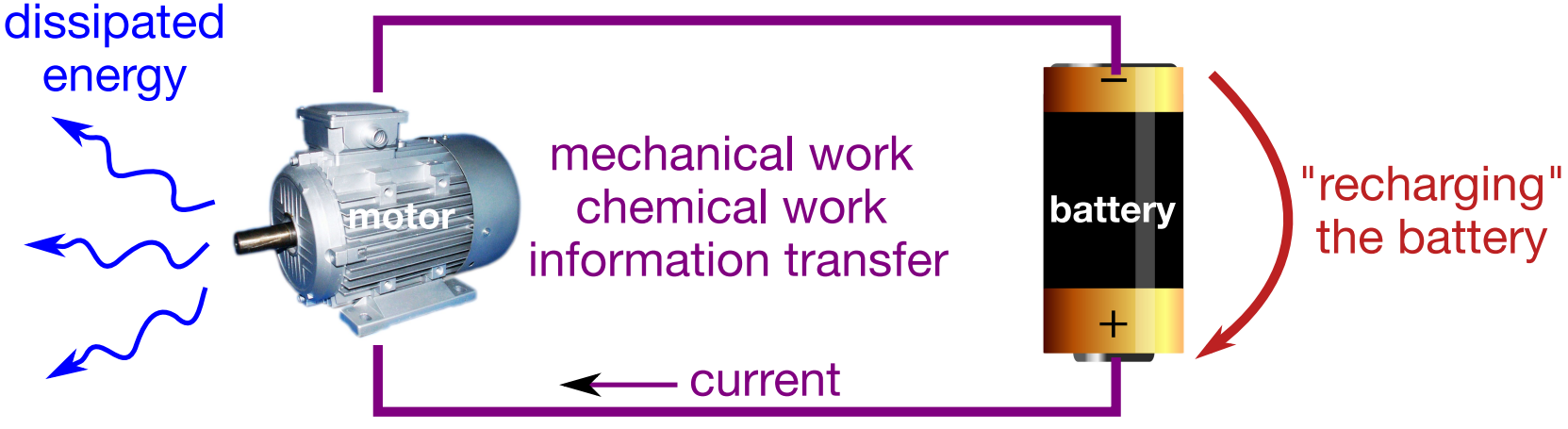
various mechanisms to pump H^+, maintaining imbalance: differ across branches of life

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

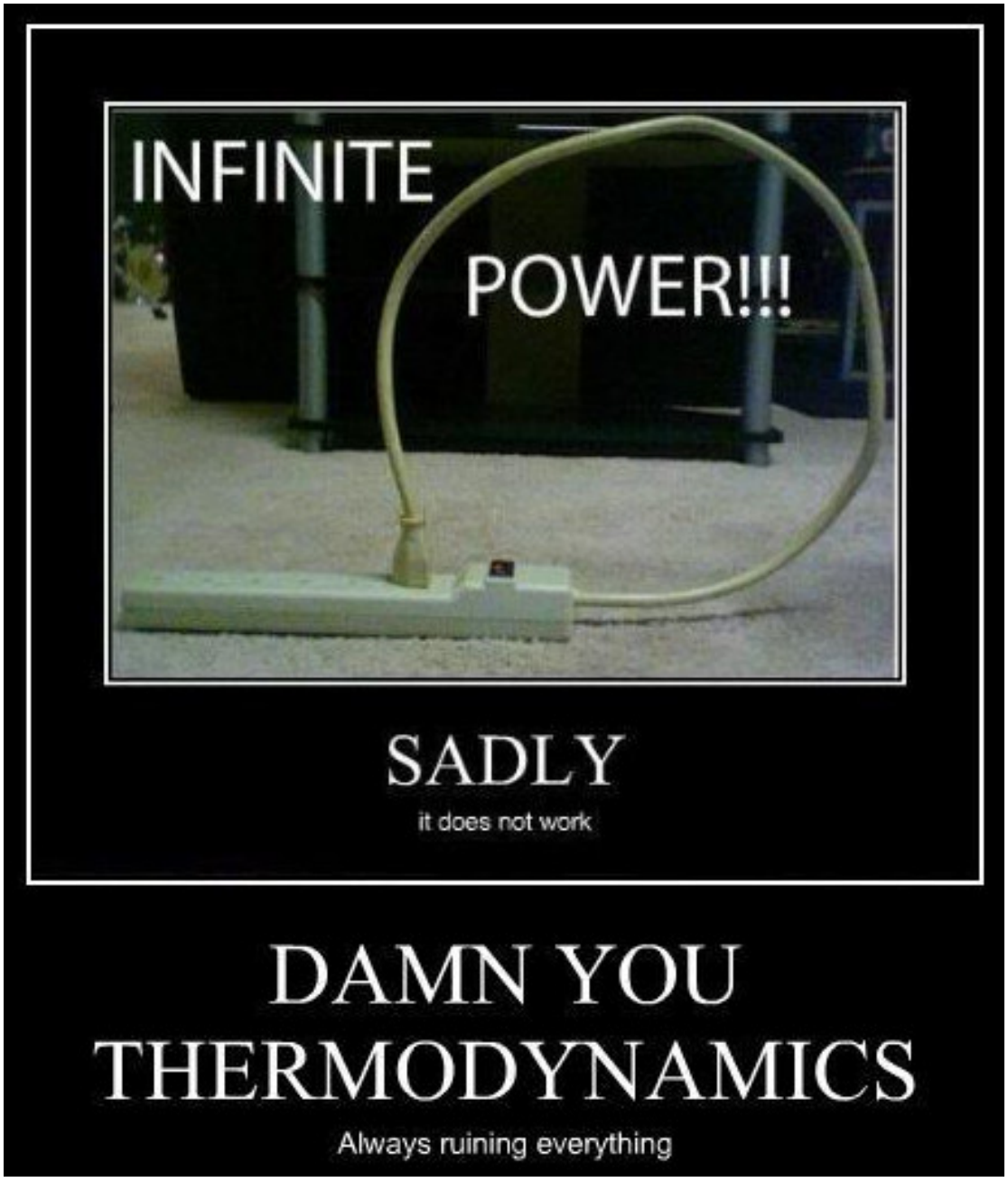
The role of physics: nonequilibrium thermodynamics

universal physical laws apply, regardless of microscopic details





The second law of thermodynamics



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

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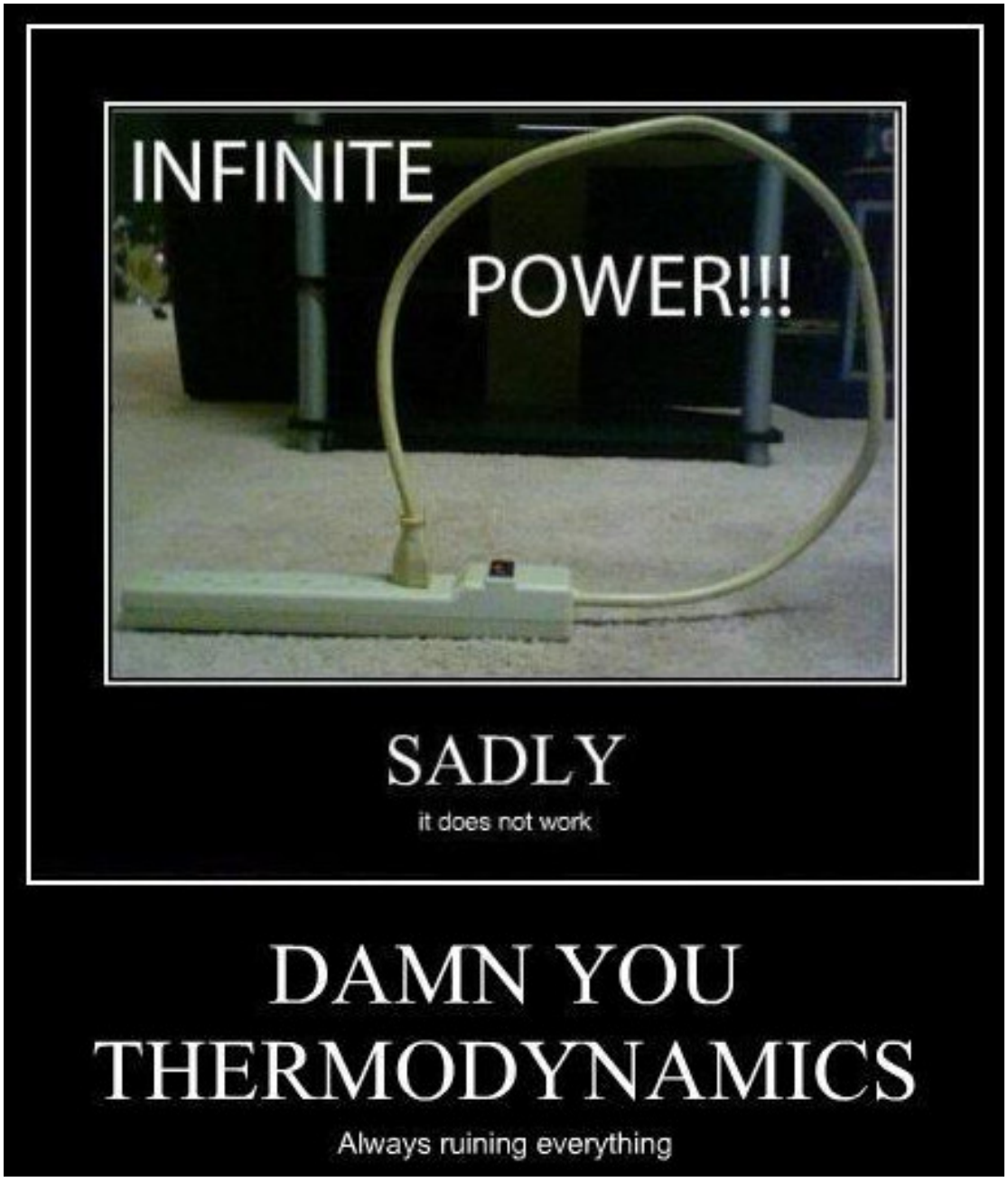

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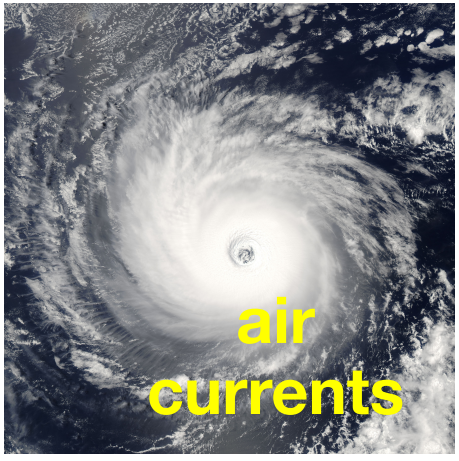
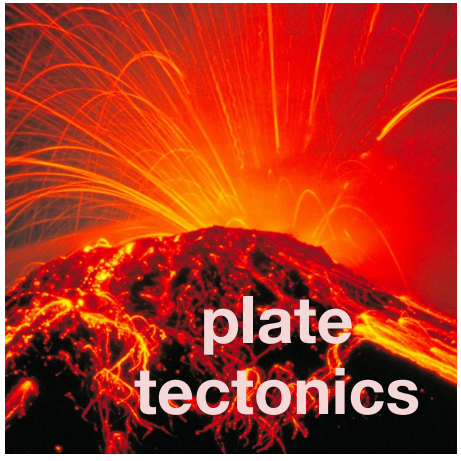
Every persistent imbalance in nature is driven by a more fundamental imbalance:

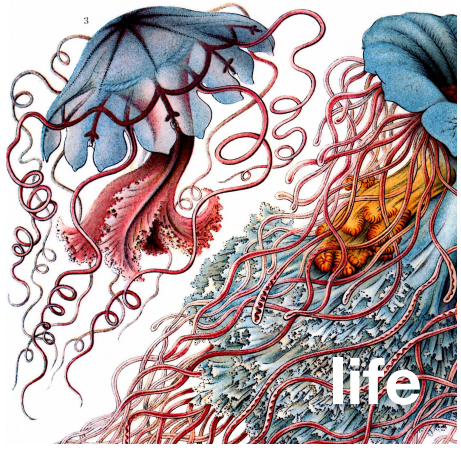
If you see a current, search for the power outlet.

The fundamental imbalances

All nonequilibrium processes on earth:







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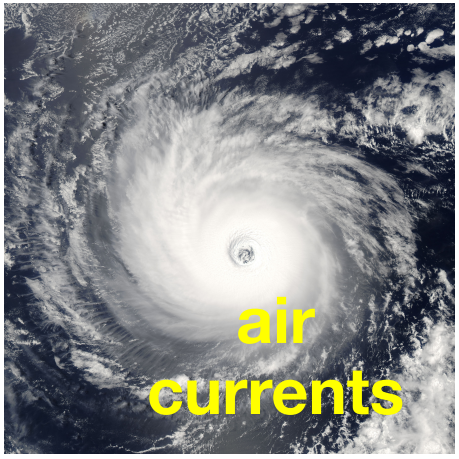

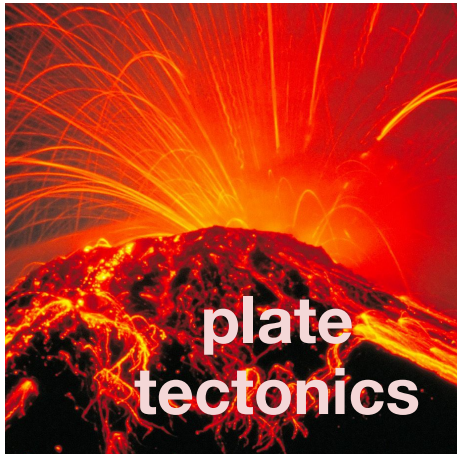

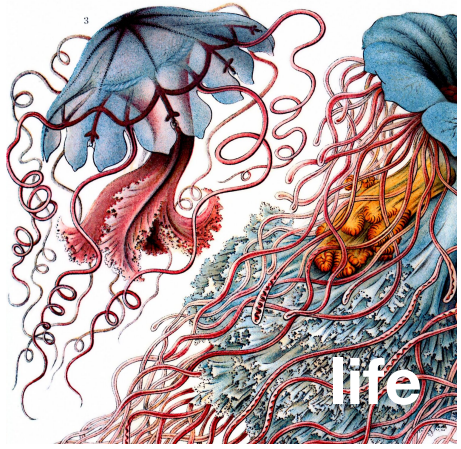

are ultimately “plugged into” two major imbalances:

Sketching out a “theory” of biology

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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.