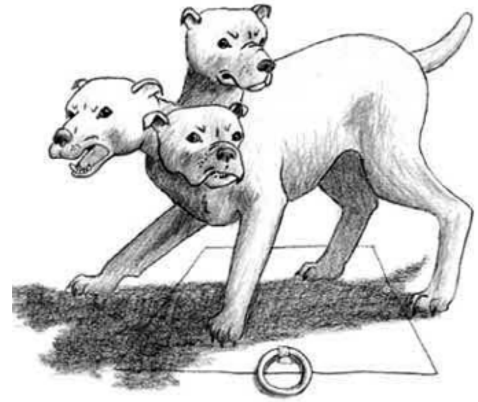


Boltzmann's Dog and Darwin's Finch:

The statistical thermodynamics of self-replication and evolution

Jeremy England
Department of Physics
Massachusetts Institute of Technology
Tuesday, January 7, 2014

The meaning of life

In biology we focus on

Behavior
Function
Survival
Reproduction
Heredity

We start by fiat: “That’s life.”

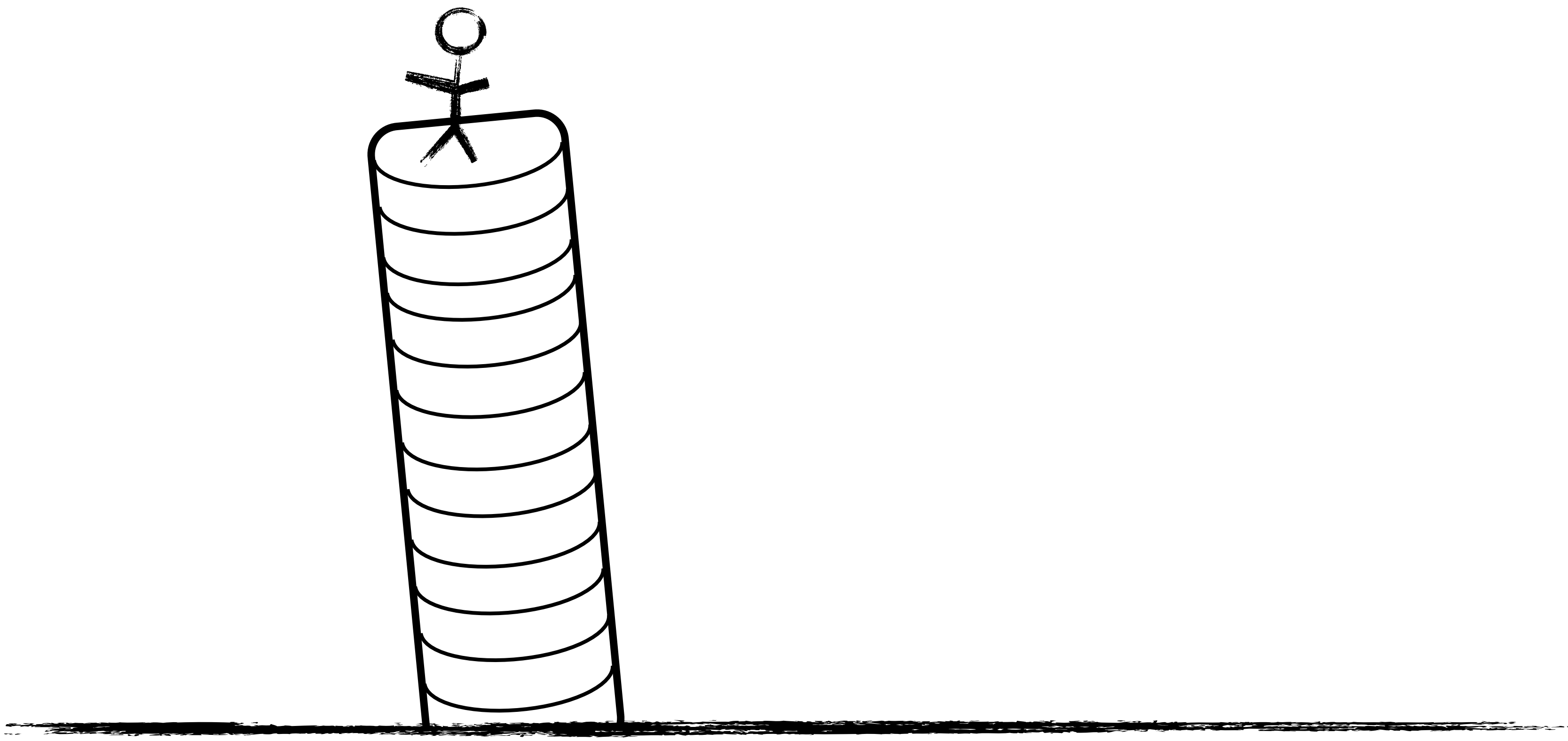
The meaning of measurement

In physics we focus on

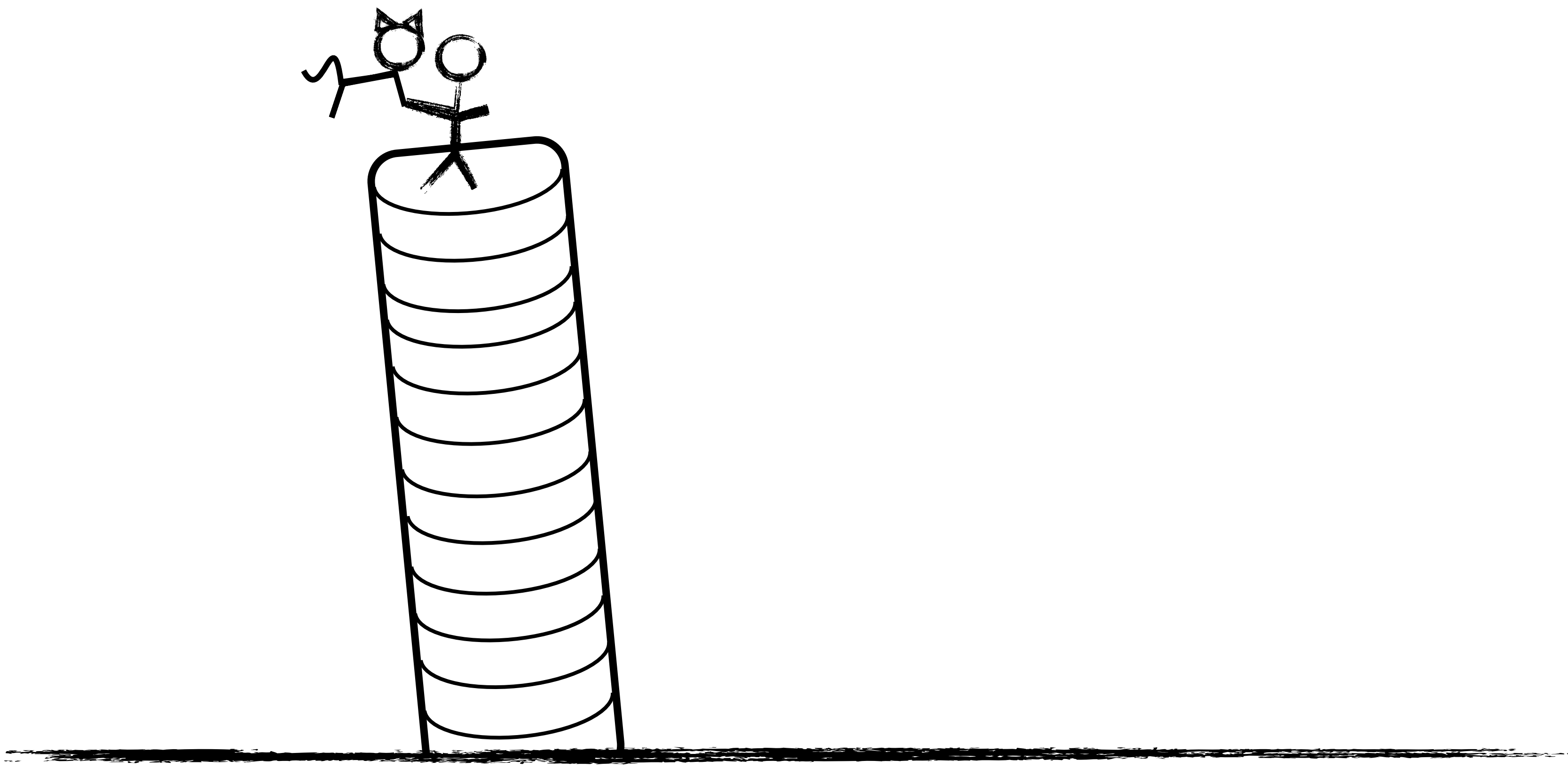
Distance (location)
Time
Number of particles
Energy
Temperature

A priori, life is absent from the physical description

The art of translation



The art of translation



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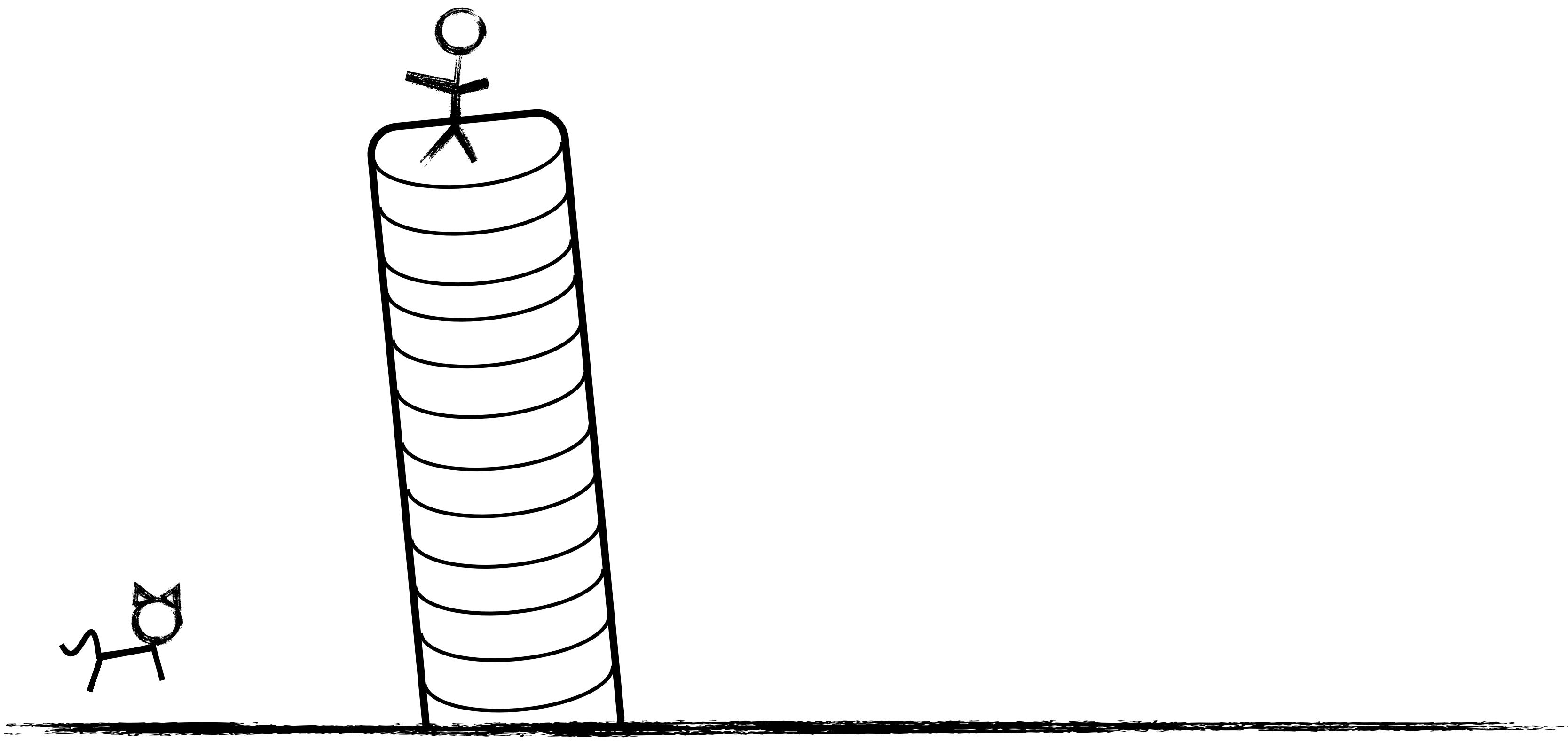

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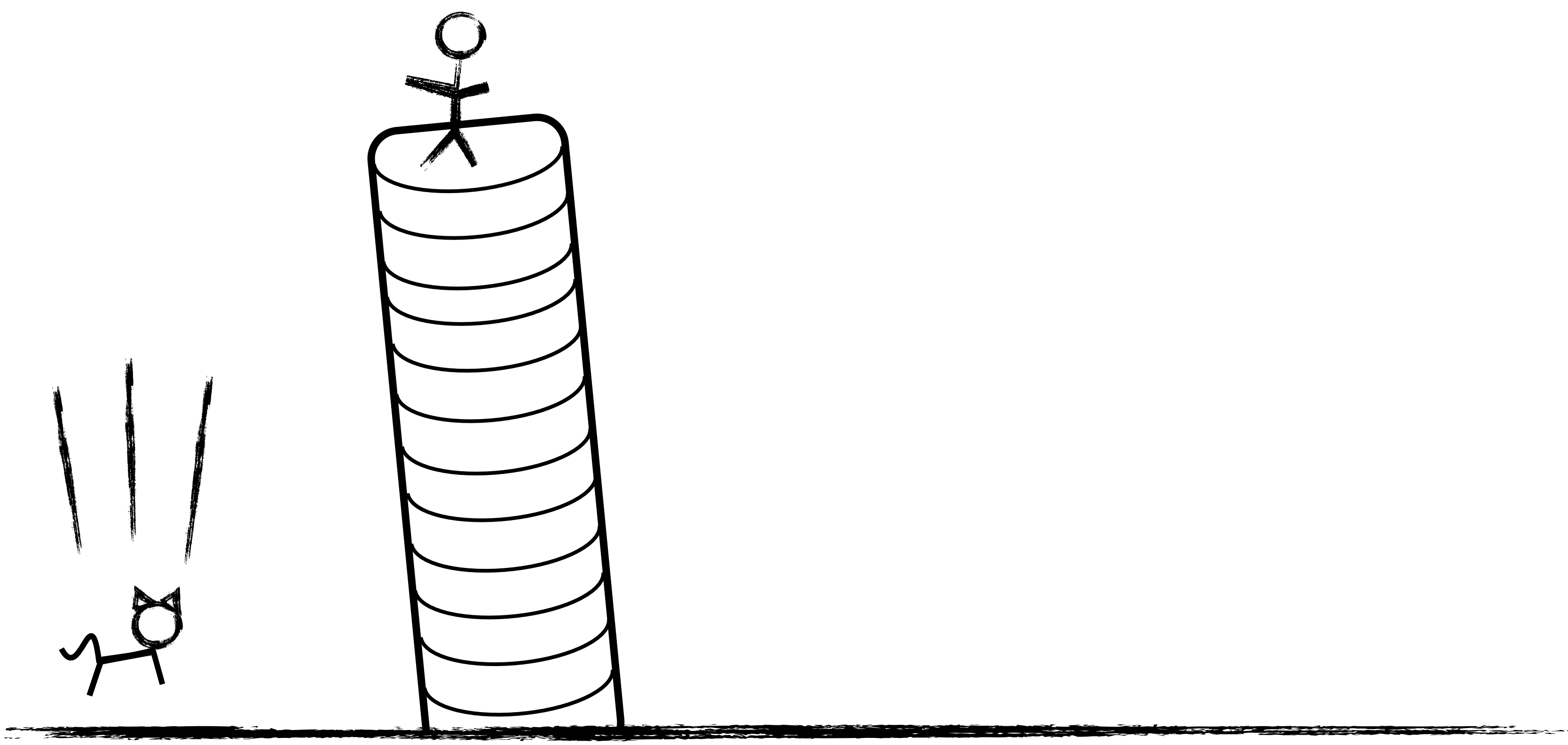
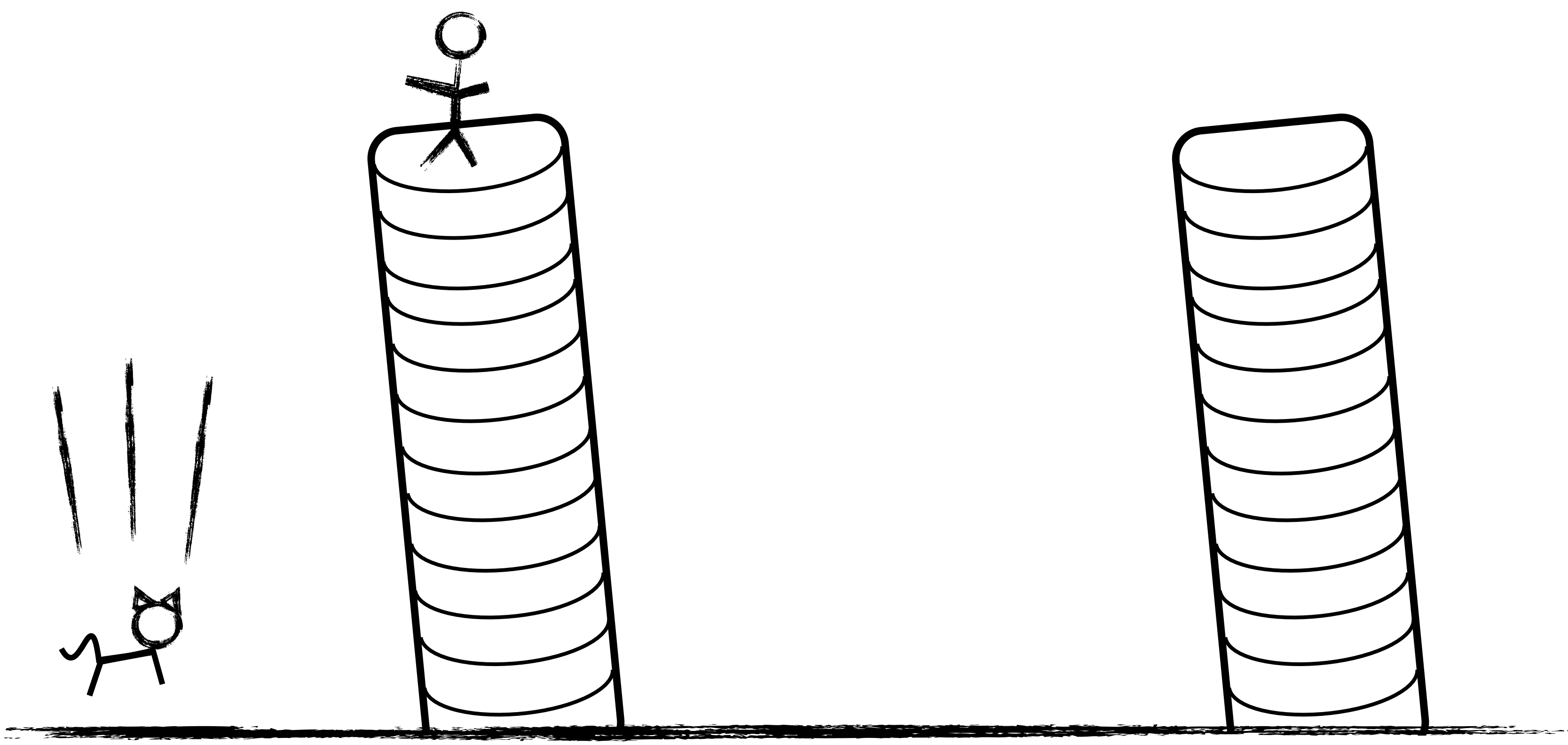


mv^2?

The art of translation



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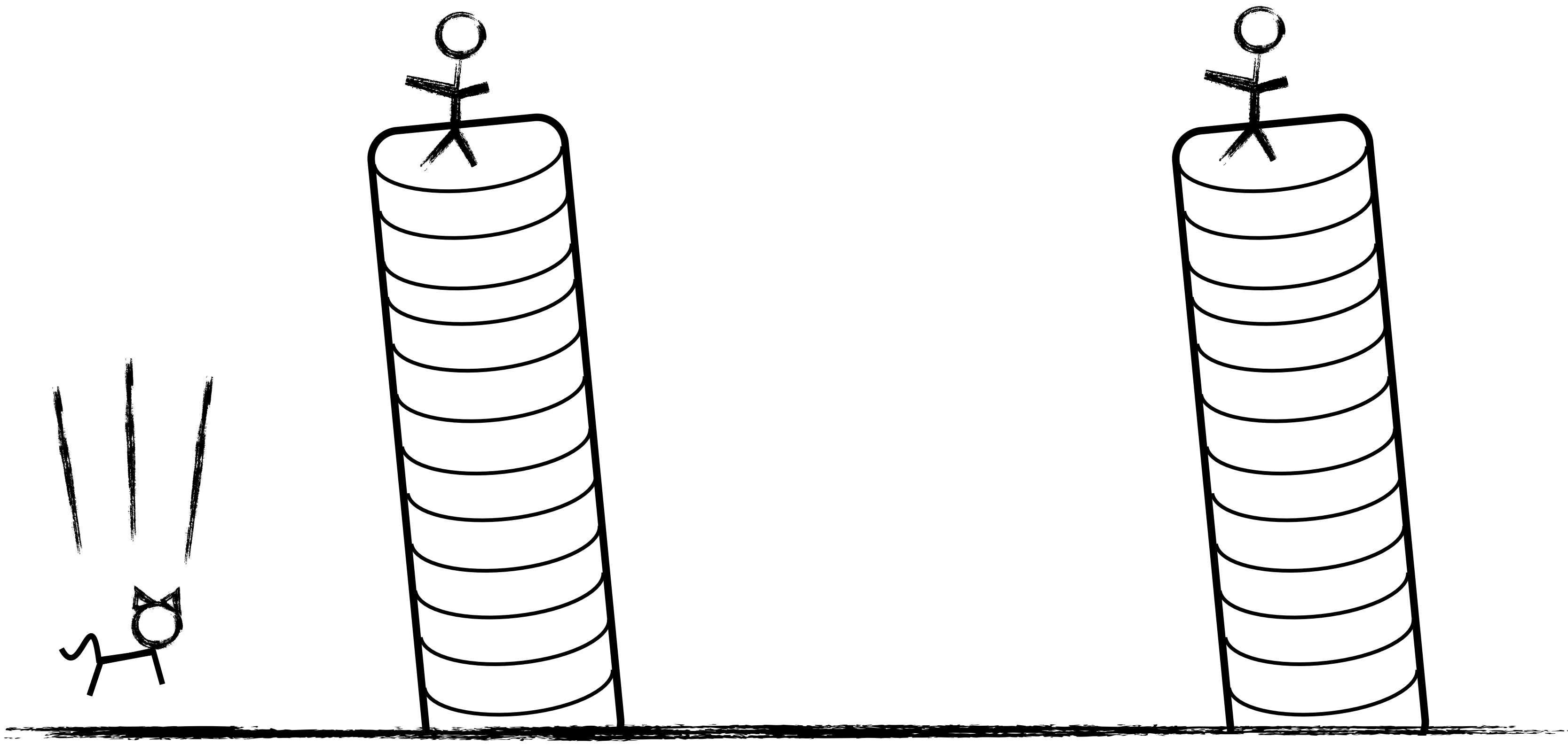

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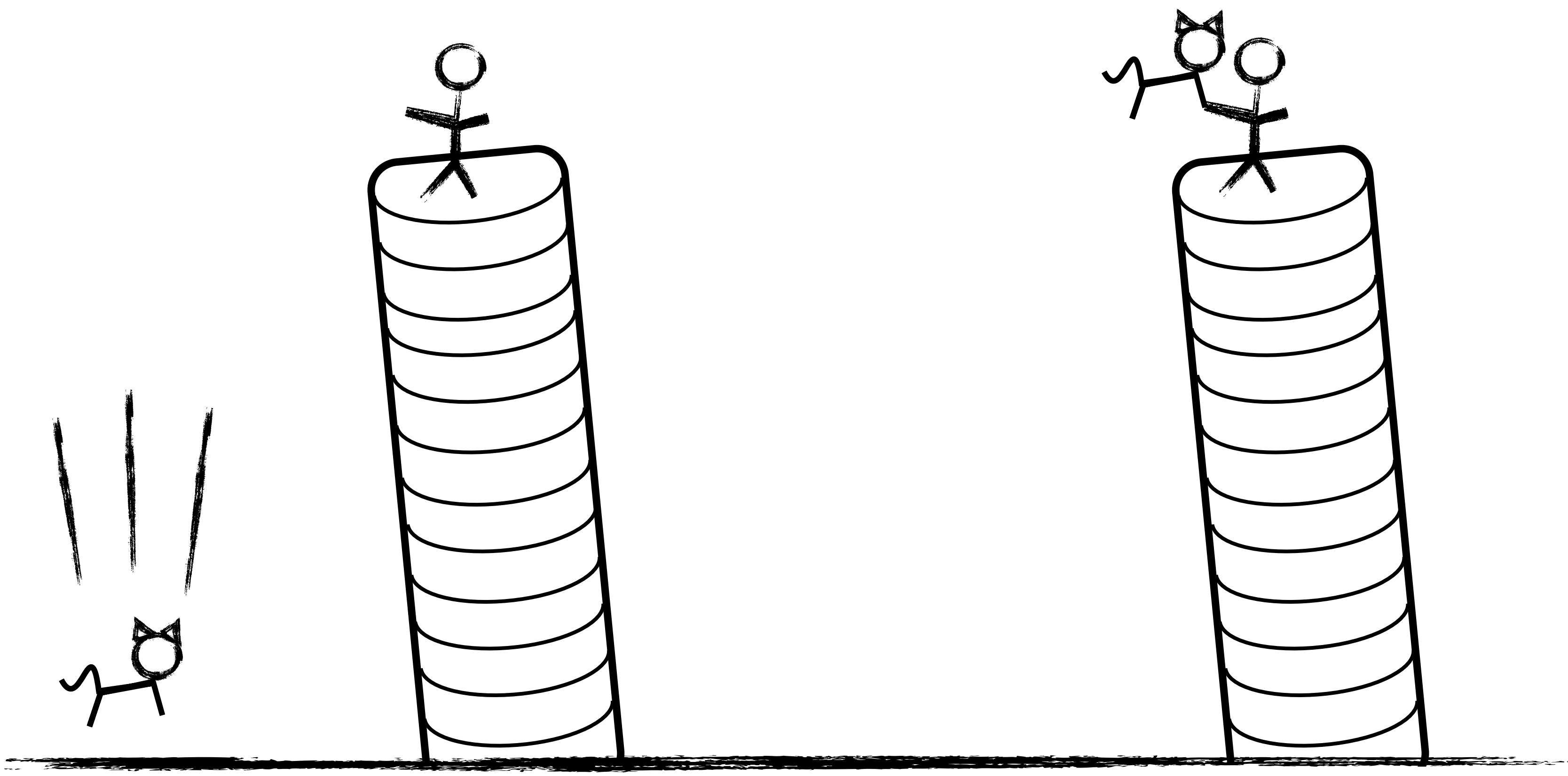
The art of translation



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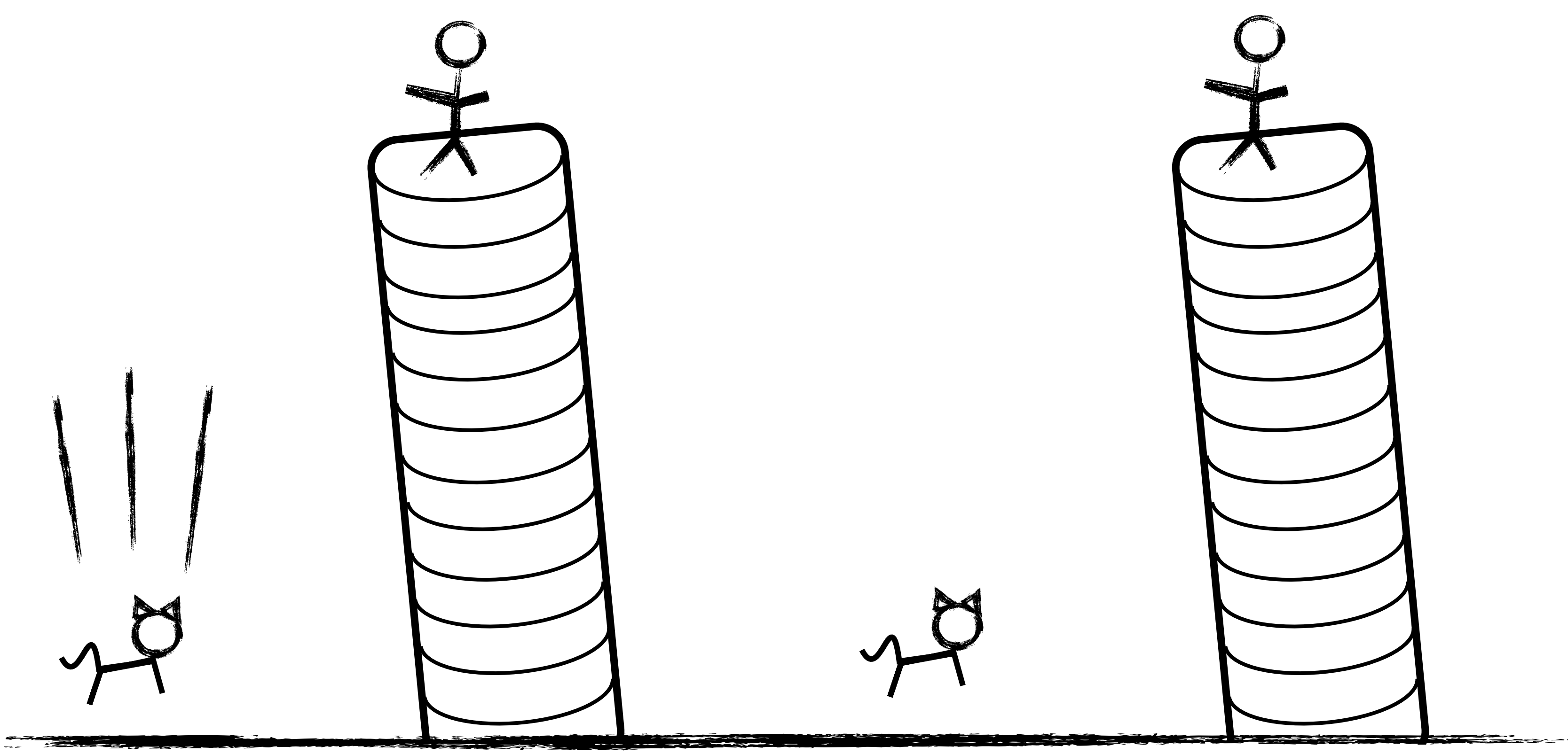
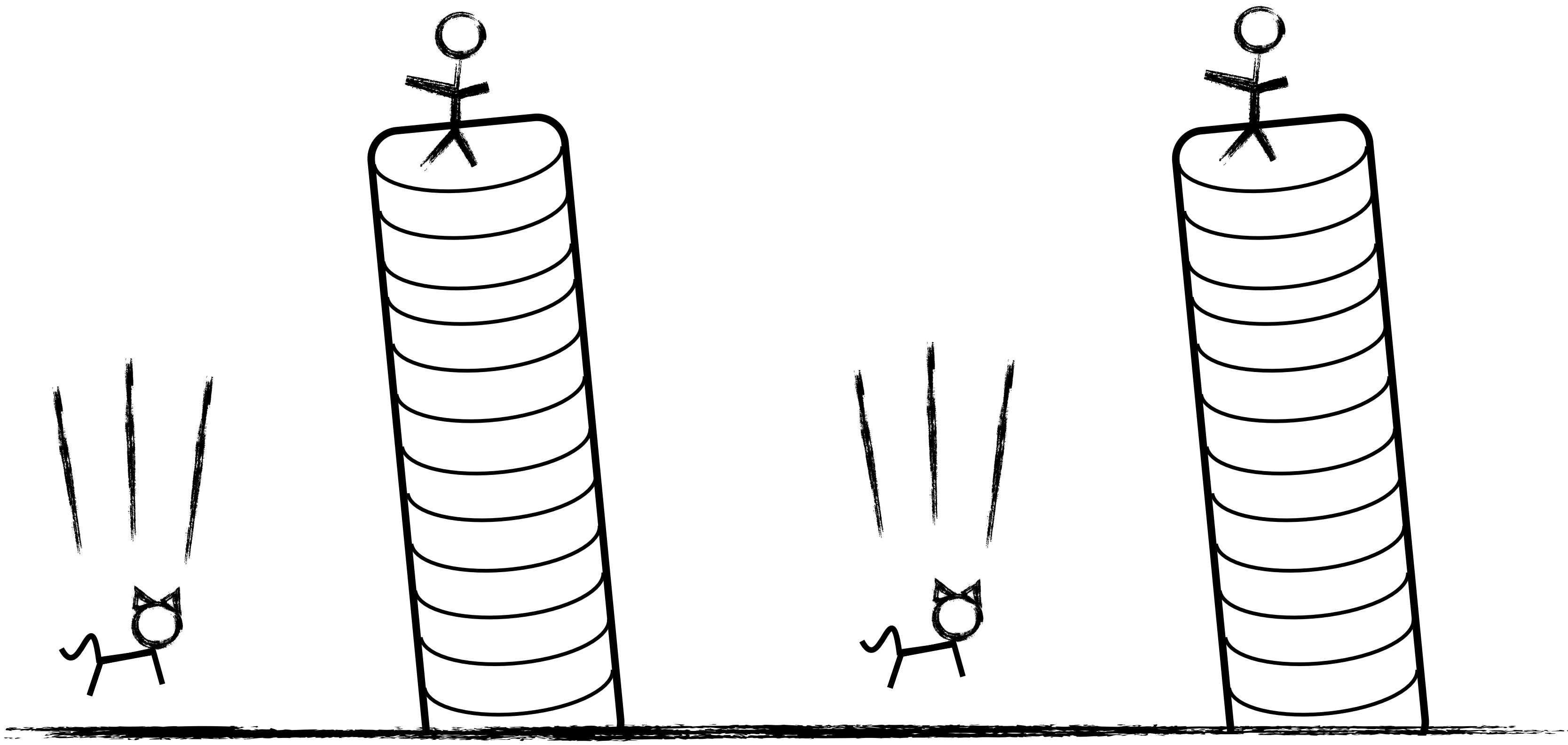


mv^2?

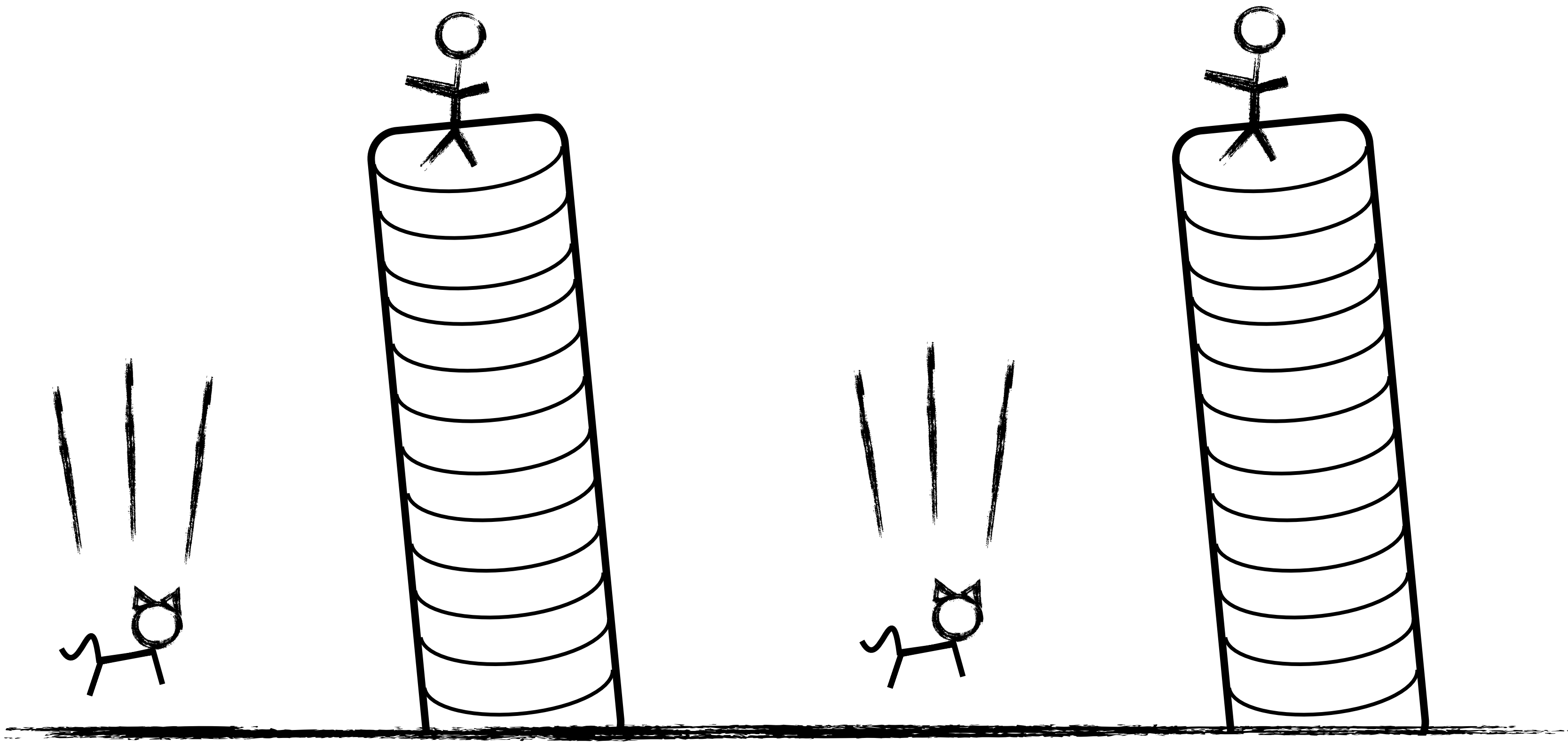
The art of translation



mv^2?

meow?

The art of translation



mv^2?
physics

Sometimes the link is clear

meow?
biology

A physics of living systems?

Living things . . .

. . . are made of matter (so cats fall)

(can we be more specific, though?)

. . . exchange particles with surroundings
. . . exchange heat with surroundings
. . . propagate exponentially

Sounds like a job for stat mech . . .

A physics of living systems?

Living things . . .

(let’s be even more specific . . .)

. . . tend towards ‘low’ internal entropy

. . . are ‘durable’ on growth timescale

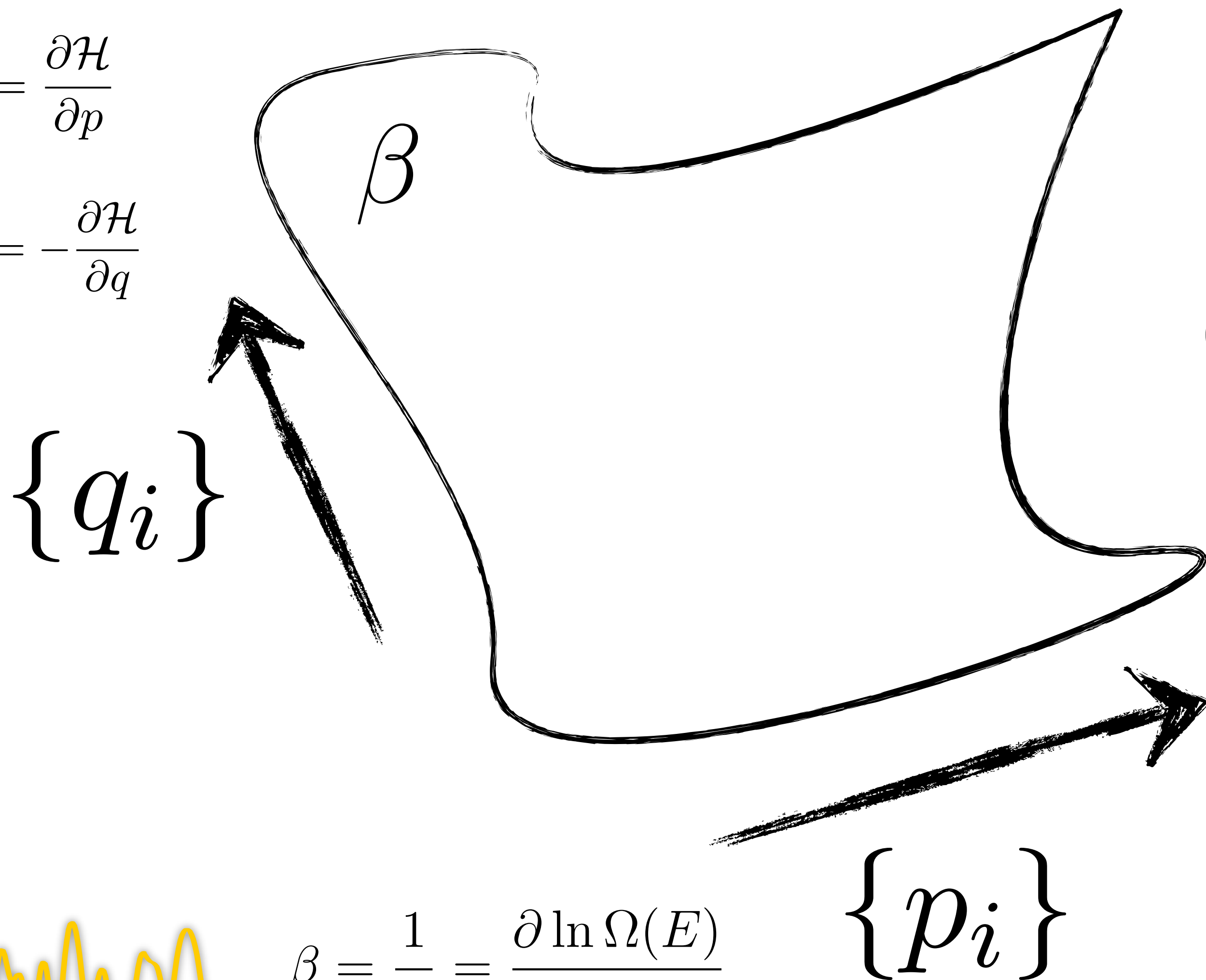
. . . get the environment to do work on them, and then dissipate it back

Definitely a job for stat mech!

Hamiltonian dynamics

$$\dot{q} = \frac{\partial \mathcal{H}}{\partial p}$$

$$\dot{p} = -\frac{\partial \mathcal{H}}{\partial q}$$



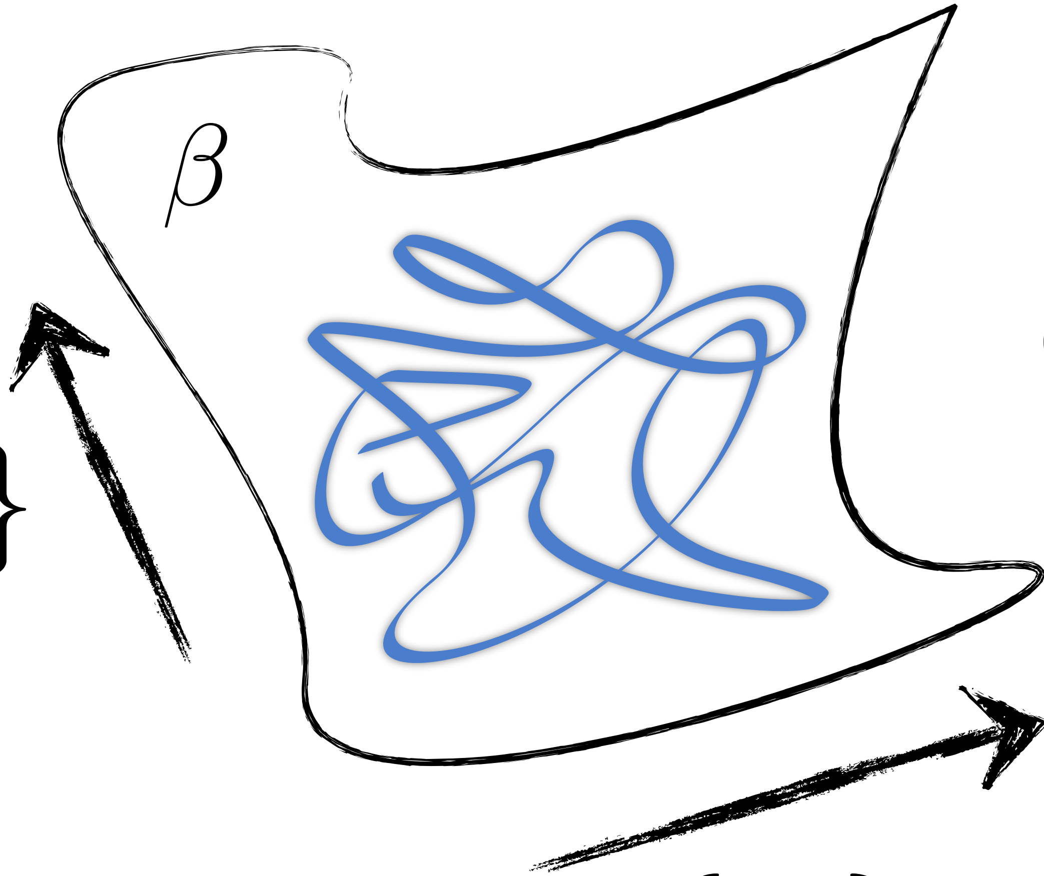
We explore a constant energy surface in phase space

$$\beta = \frac{1}{T} = \frac{\partial \ln \Omega(E)}{\partial E}$$

Hamiltonian dynamics

$$\dot{q} = \frac{\partial \mathcal{H}}{\partial p}$$

$$\dot{p} = -\frac{\partial \mathcal{H}}{\partial q}$$



$\{q_i\}$

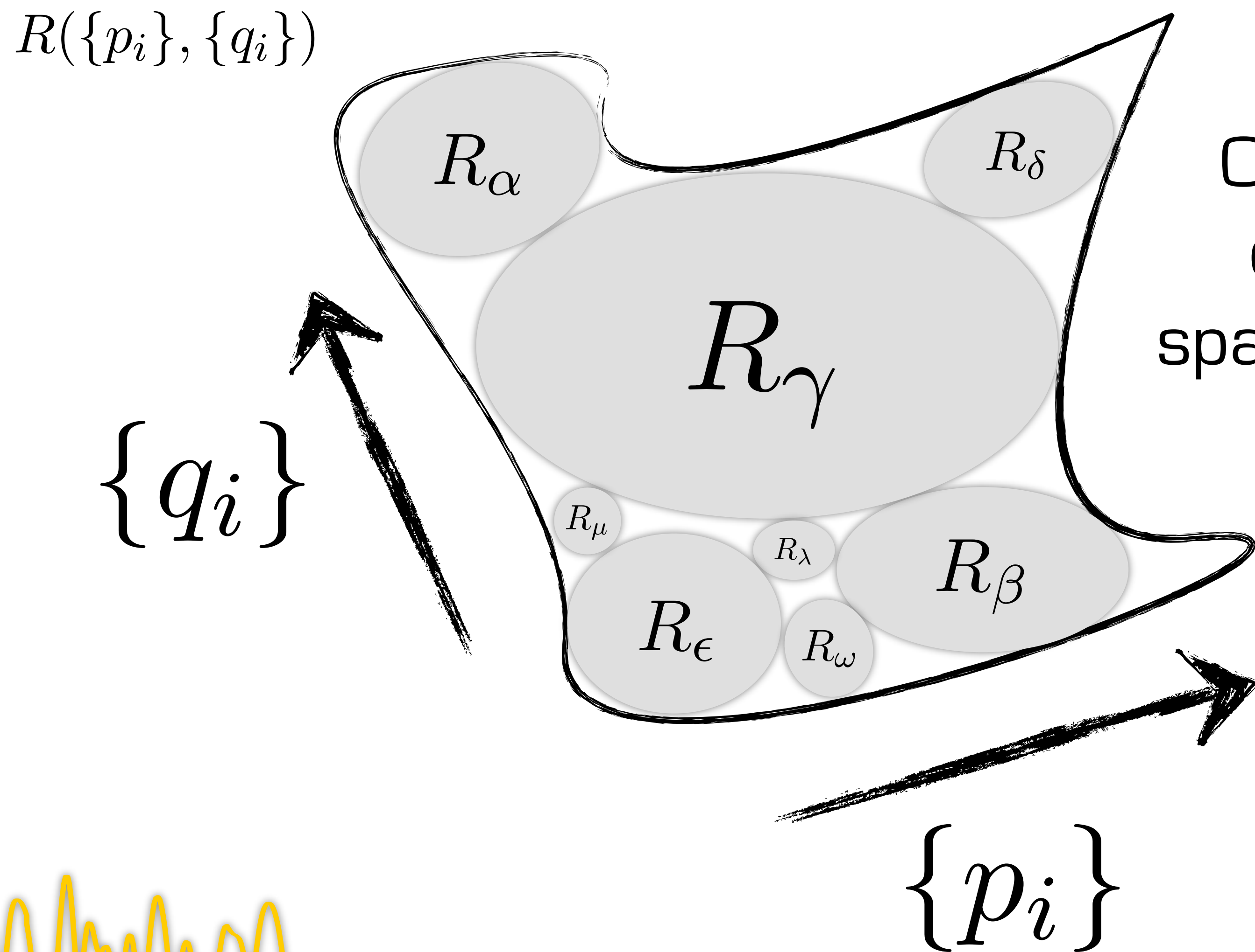
β

$\{p_i\}$

We explore a constant energy surface in phase space

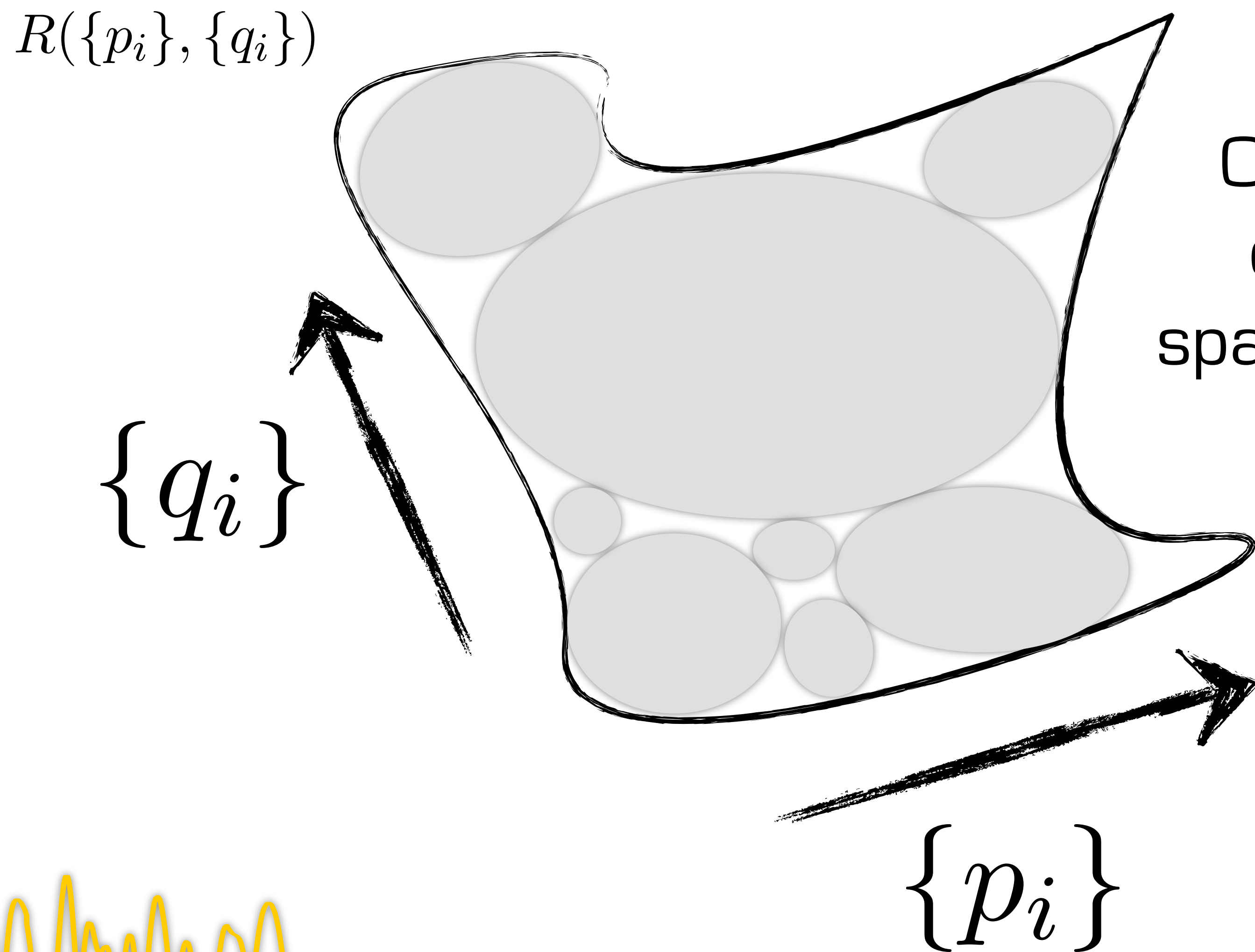
$$\beta = \frac{1}{T} = \frac{\partial \ln \Omega(E)}{\partial E}$$

Coarse-graining phase space



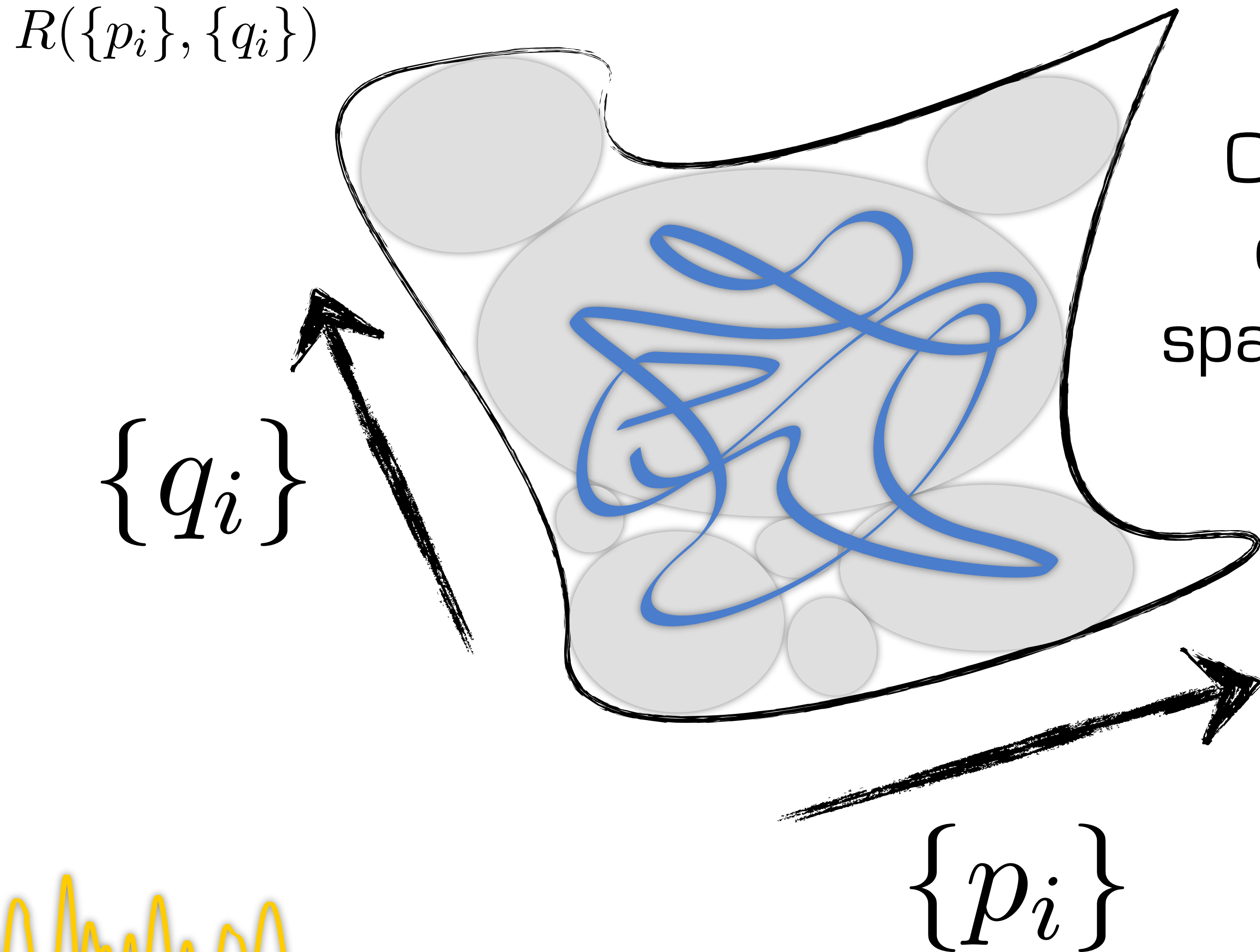
Our observable divides phase space into different sub-volumes

Coarse-graining phase space



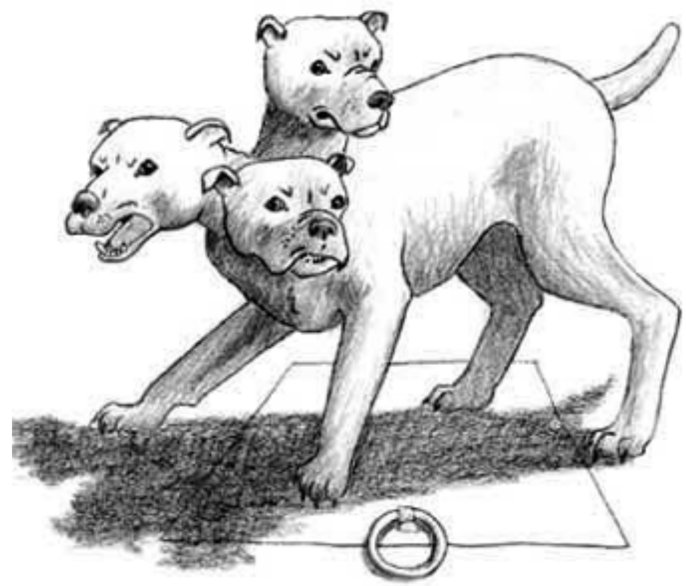
Our observable divides phase space into different sub-volumes

Coarse-graining phase space

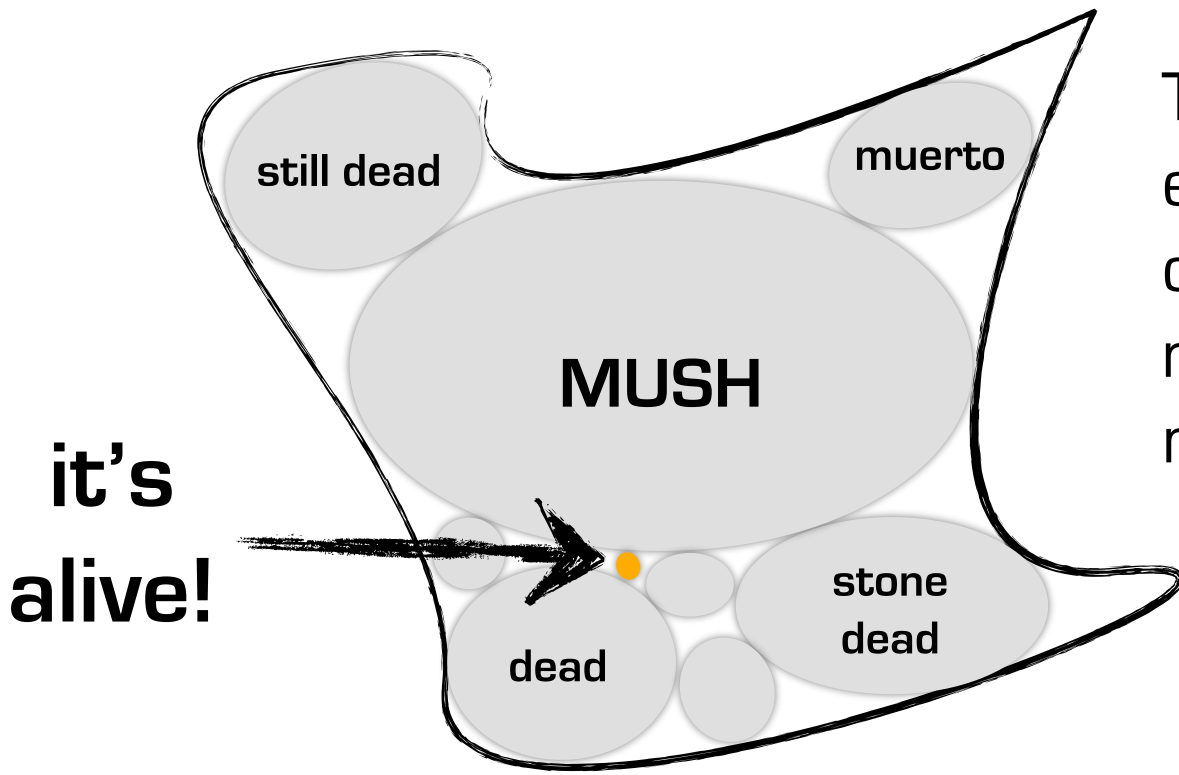


Our observable divides phase space into different sub-volumes

Boltzmann’s Dog



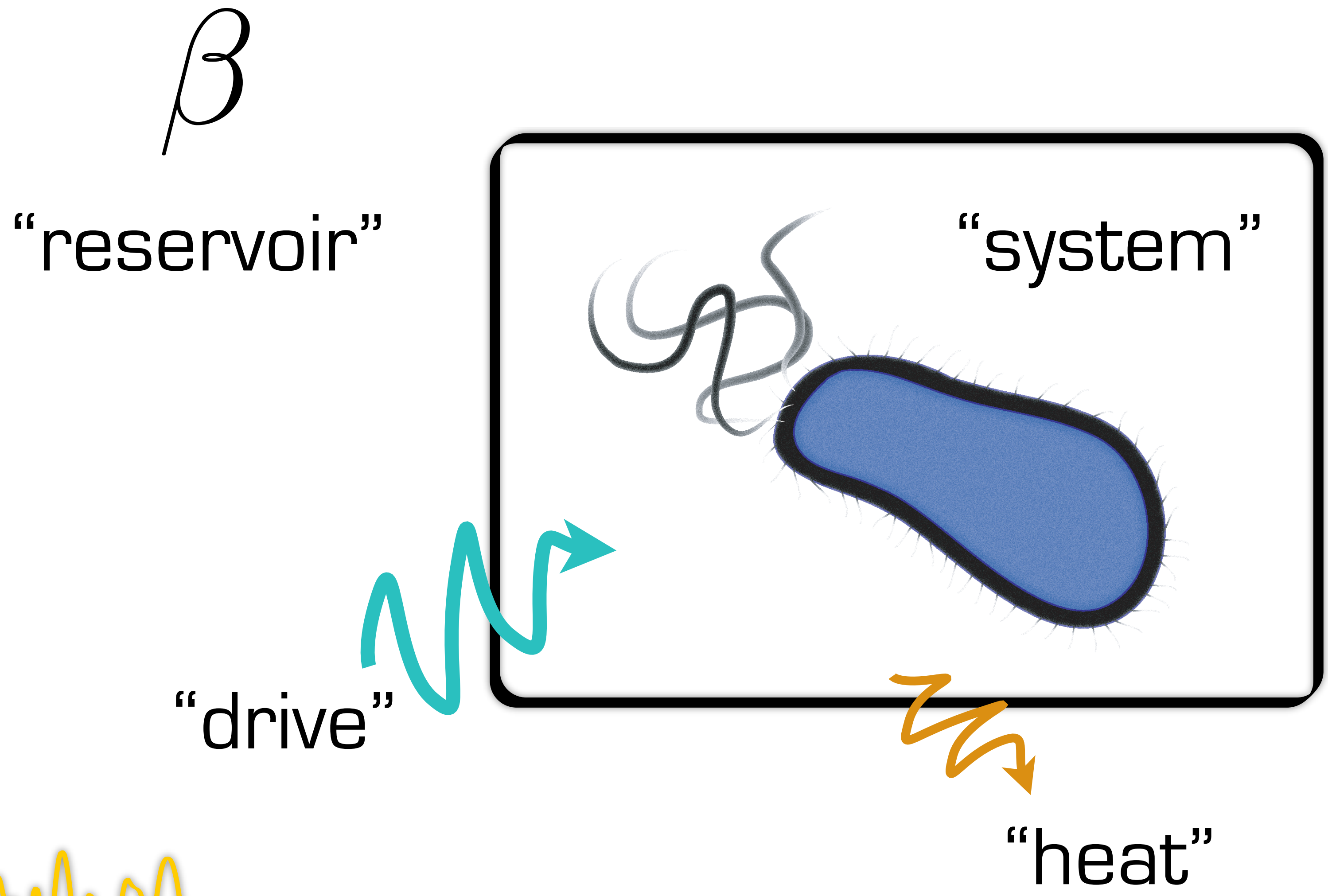
Boltzmann's Dog



The statistical equilibrium in a closed system is not going to be remotely alive

If living things are not at equilibrium then what can stat. mech. tell us?

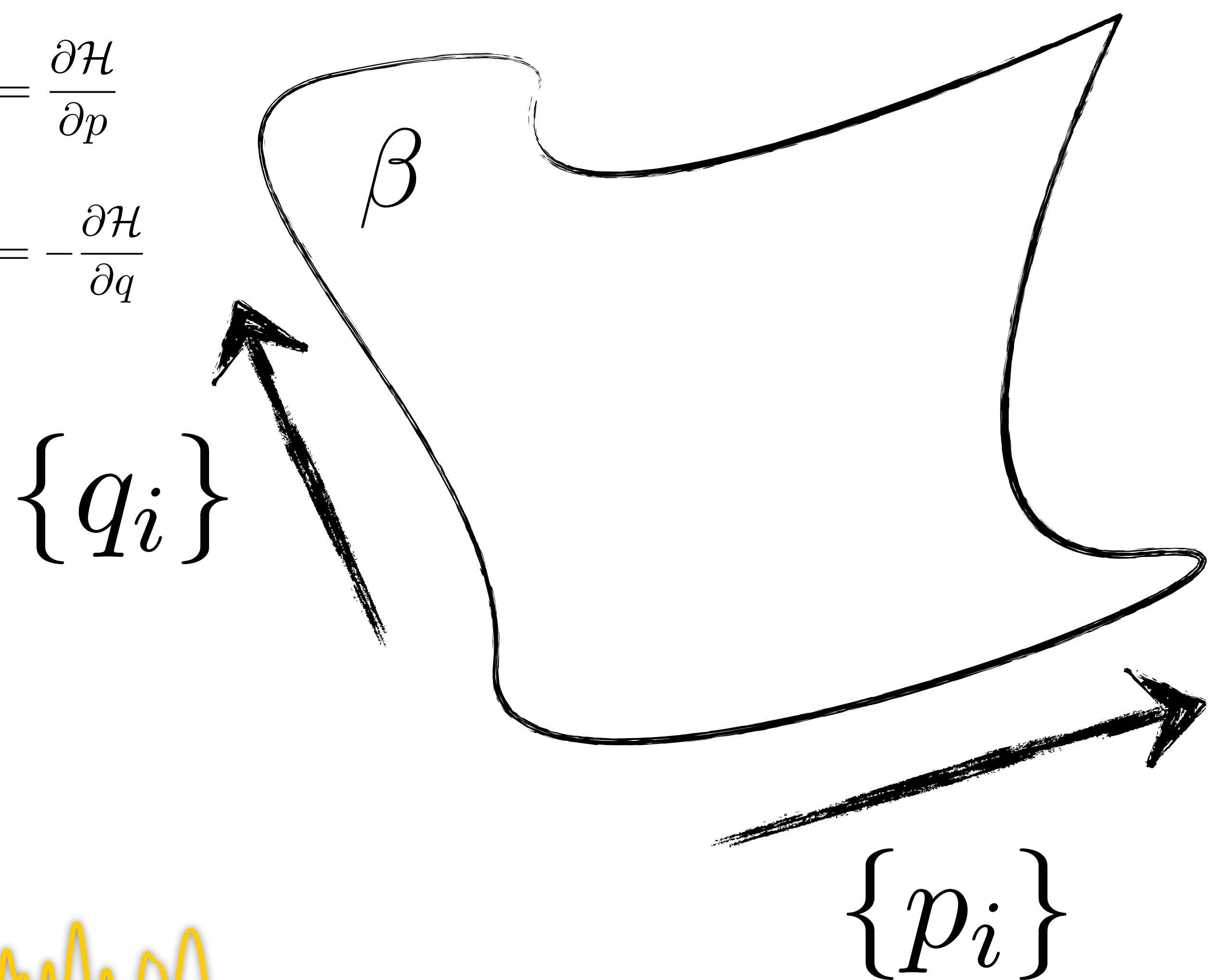
Reservoir dogs



Running backwards

$$\dot{q} = \frac{\partial \mathcal{H}}{\partial p}$$

$$\dot{p} = -\frac{\partial \mathcal{H}}{\partial q}$$

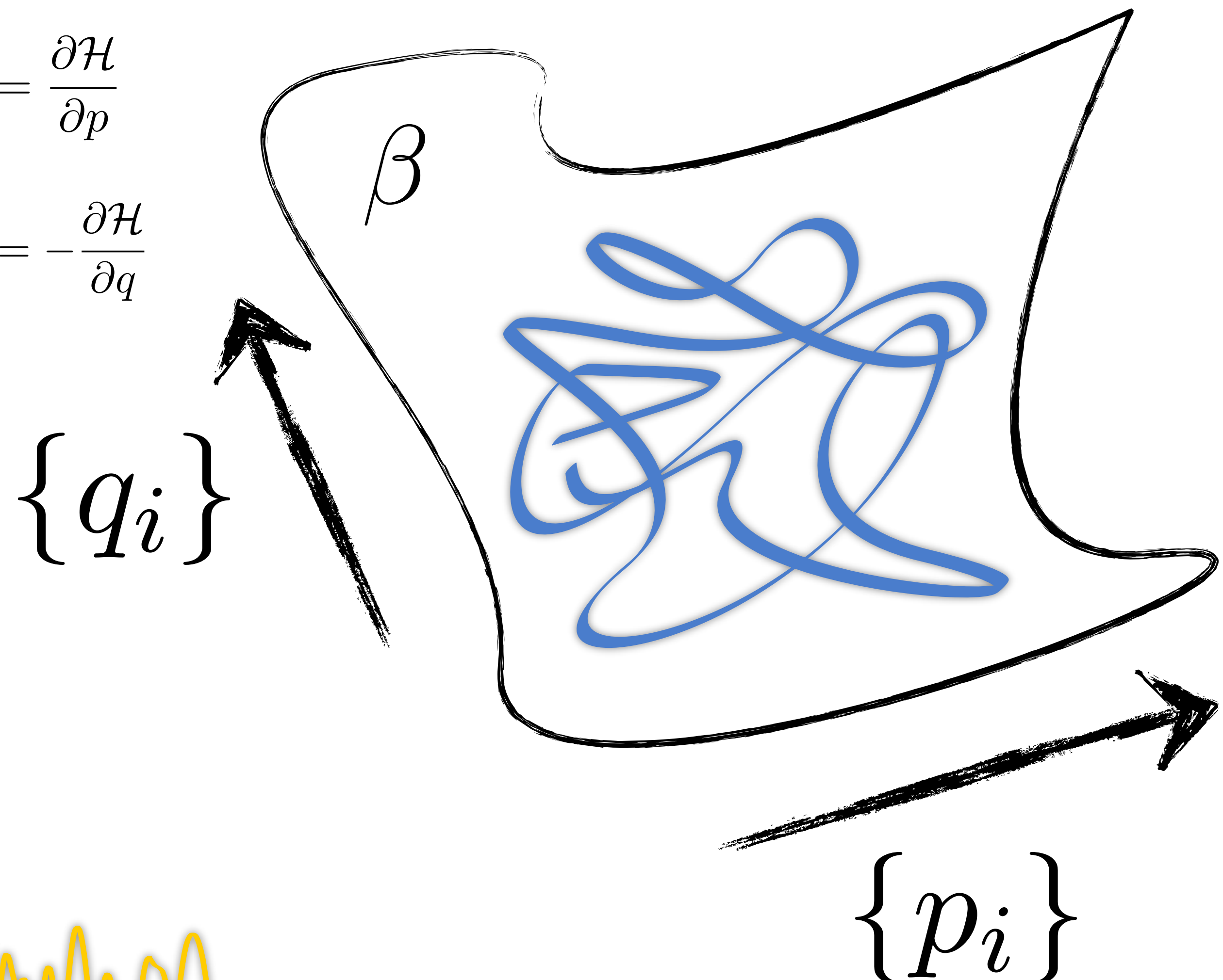


Underlying equations of motion have time-reversal symmetry

Running backwards

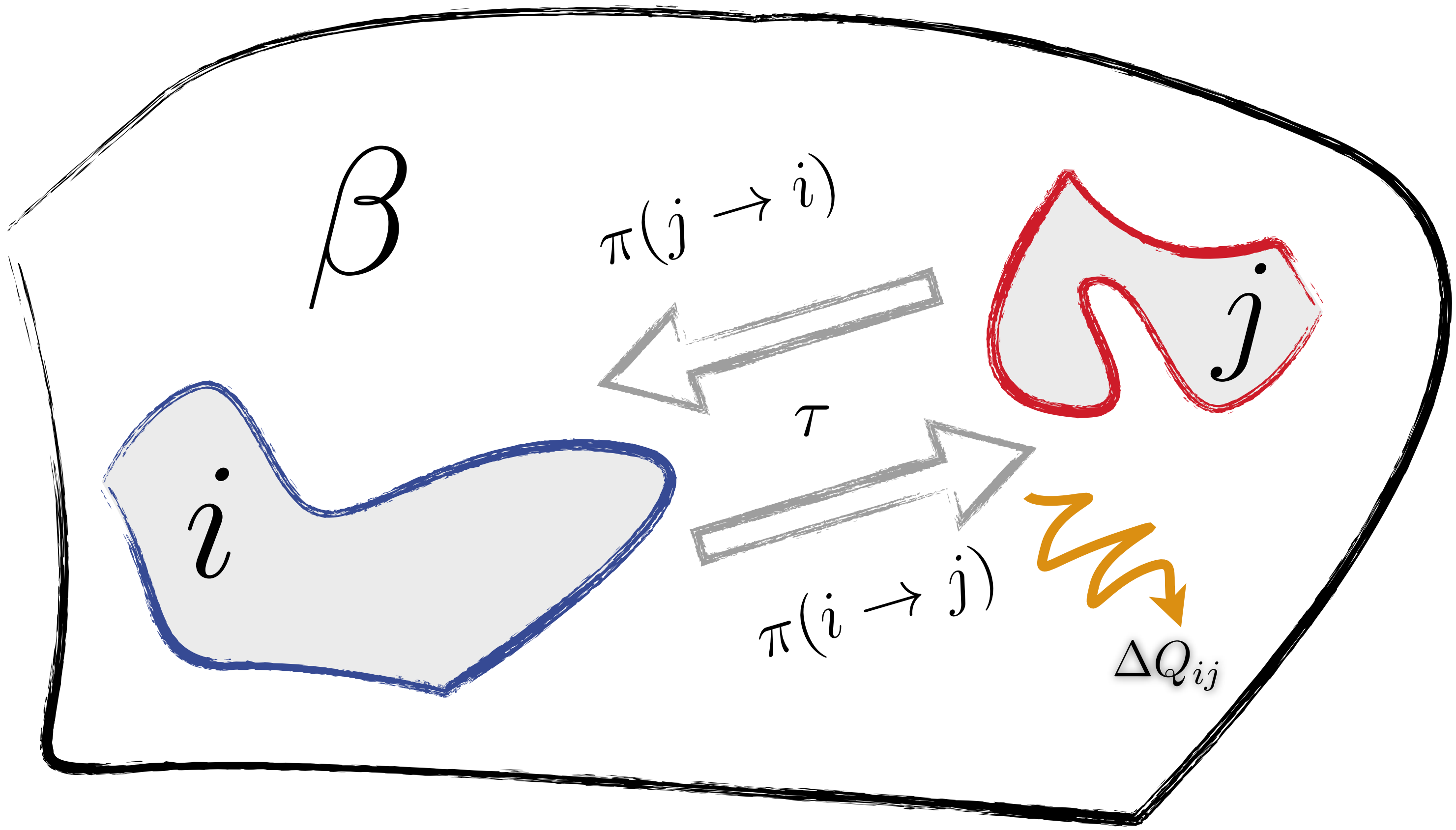
$$\dot{q} = \frac{\partial \mathcal{H}}{\partial p}$$

$$\dot{p} = -\frac{\partial \mathcal{H}}{\partial q}$$



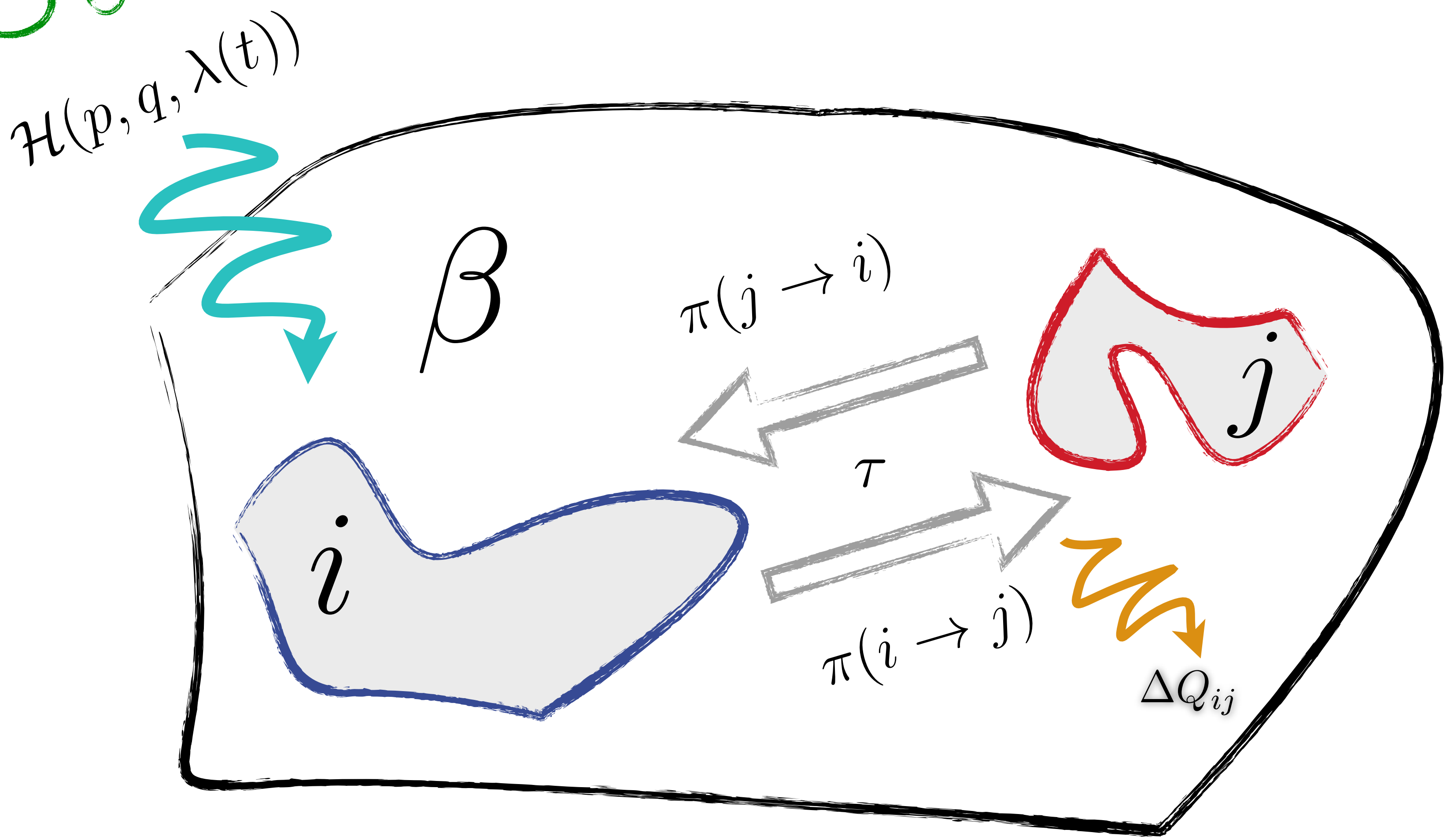
Underlying equations of motion have time-reversal symmetry

Detailed balance



$$\frac{\pi(j \to i)}{\pi(i \to j)} = \exp[-\beta(E_i - E_j)] = \exp[-\beta \Delta Q_{ij}]$$

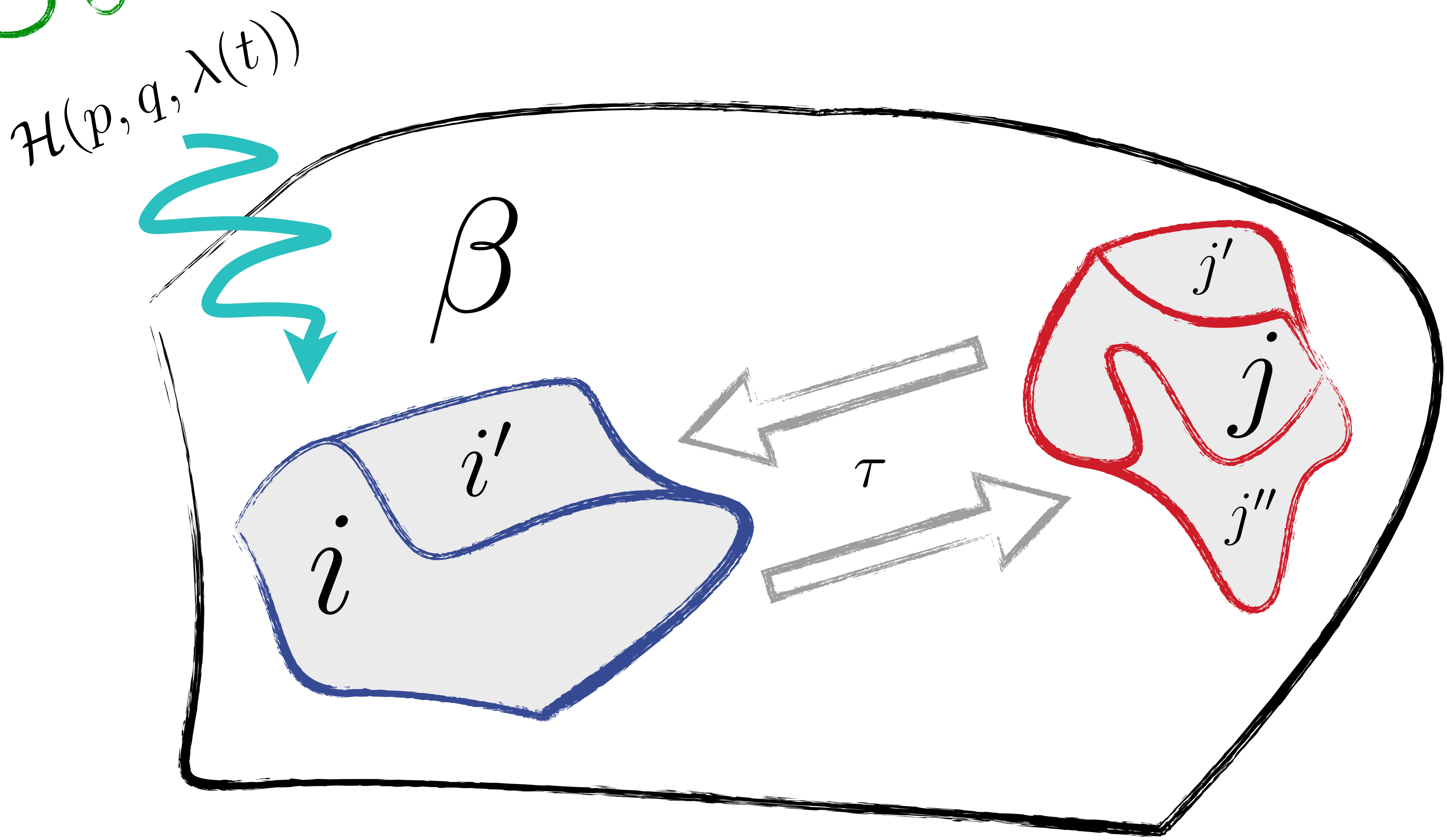
Crooks balance



$$\frac{\pi(j \to i)}{\pi(i \to j)} = \langle \exp[-\beta \Delta Q_{ij}] \rangle_{i \to j}$$

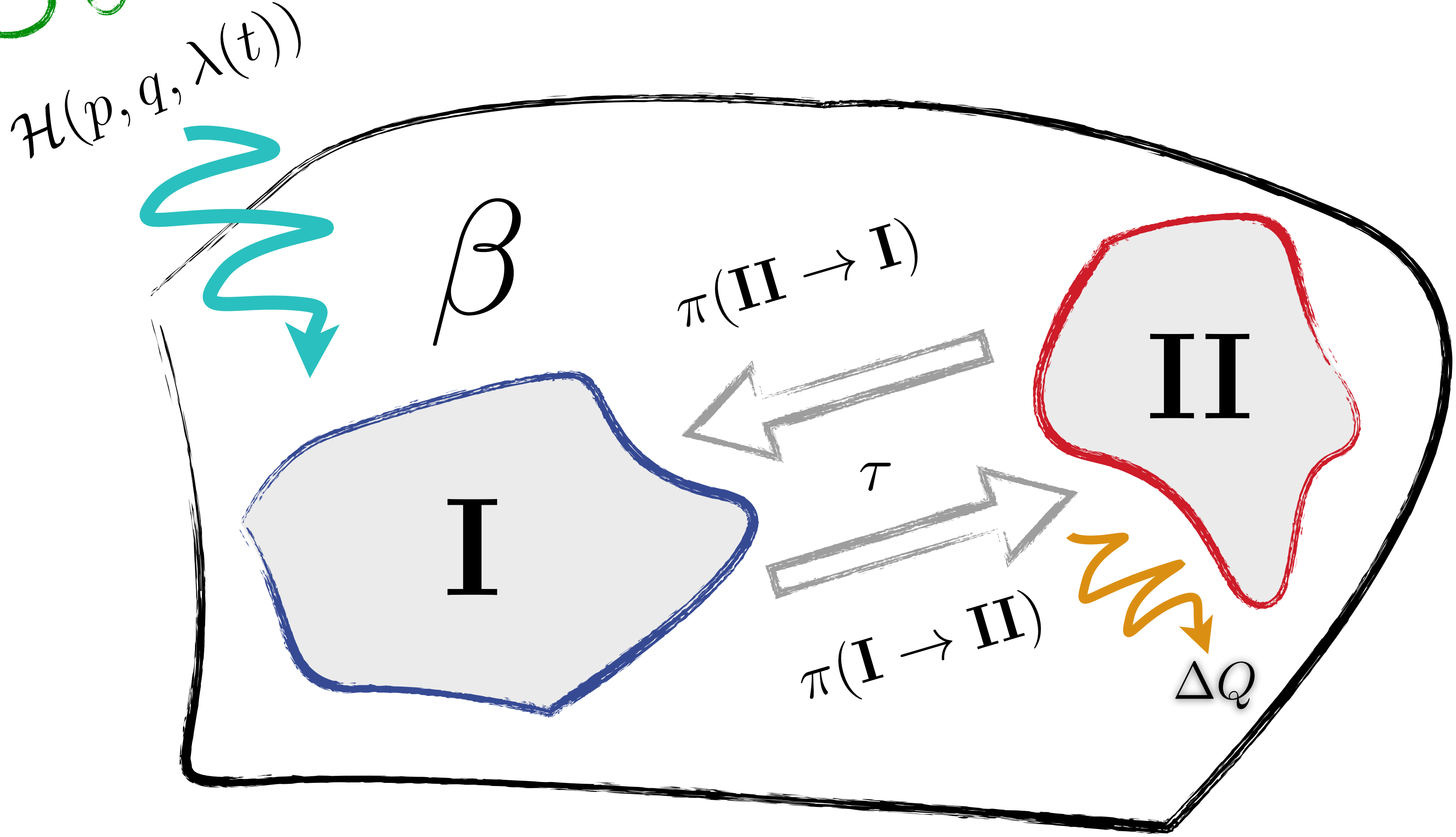
Crooks, 1999

Classification of States



$$\mathbf{I} : i, i''' \qquad \mathbf{II} : j, j', j''$$

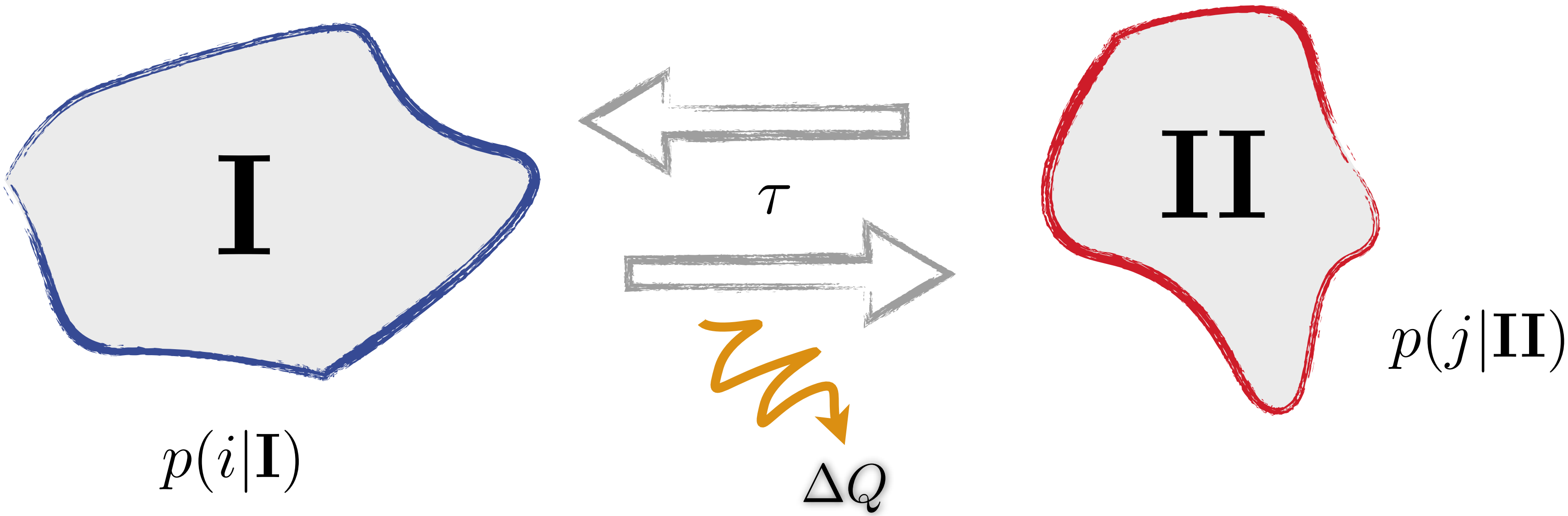
Classification of States



$\mathbf{I} : i, i'''$ $\quad$ $\mathbf{II} : j, j', j''$

$p(i|\mathbf{I})$ $\quad$ $p(j|\mathbf{II})$

The Second Law

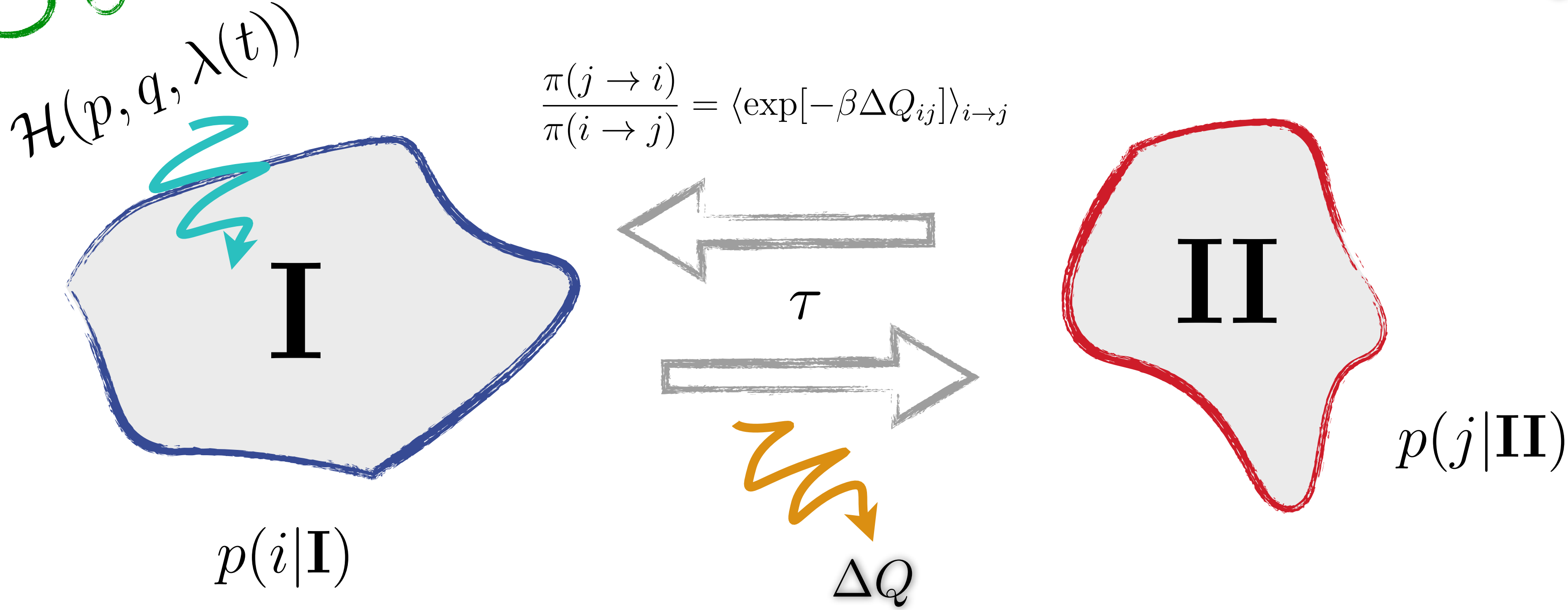


$$\Delta S_{int} = \sum_i p(i|\mathbf{I}) \ln p(i|\mathbf{I}) - \sum_j p(j|\mathbf{II}) \ln p(j|\mathbf{II})$$

$$\Delta S_{tot} = \beta \langle \Delta Q \rangle + \Delta S_{int} \geq 0$$

Irreversibility and entropy

$$\frac{\pi(j \to i)}{\pi(i \to j)} = \langle \exp[-\beta \Delta Q_{ij}] \rangle_{i \to j}$$



England, 2013

$$\frac{\pi(\mathbf{II} \to \mathbf{I})}{\pi(\mathbf{I} \to \mathbf{II})} = \left\langle e^{\ln\left[\frac{p(j|\mathbf{II})}{p(i|\mathbf{I})}\right]} \langle e^{-\beta \Delta Q_{i \to j}} \rangle_{i \to j} \right\rangle_{\mathbf{I} \to \mathbf{II}}$$

$$\Delta S_{tot} = \beta \langle \Delta Q \rangle + \Delta S_{int} \geq \ln \left[\frac{\pi(\mathbf{I} \to \mathbf{II})}{\pi(\mathbf{II} \to \mathbf{I})} \right] \geq 0$$

Irreversibility and entropy

$$\Delta S_{tot} = \beta\langle \Delta Q \rangle + \Delta S_{int} \geq \ln\left[\frac{\pi(\mathbf{I} \rightarrow \mathbf{II})}{\pi(\mathbf{II} \rightarrow \mathbf{I})}\right] \geq 0$$

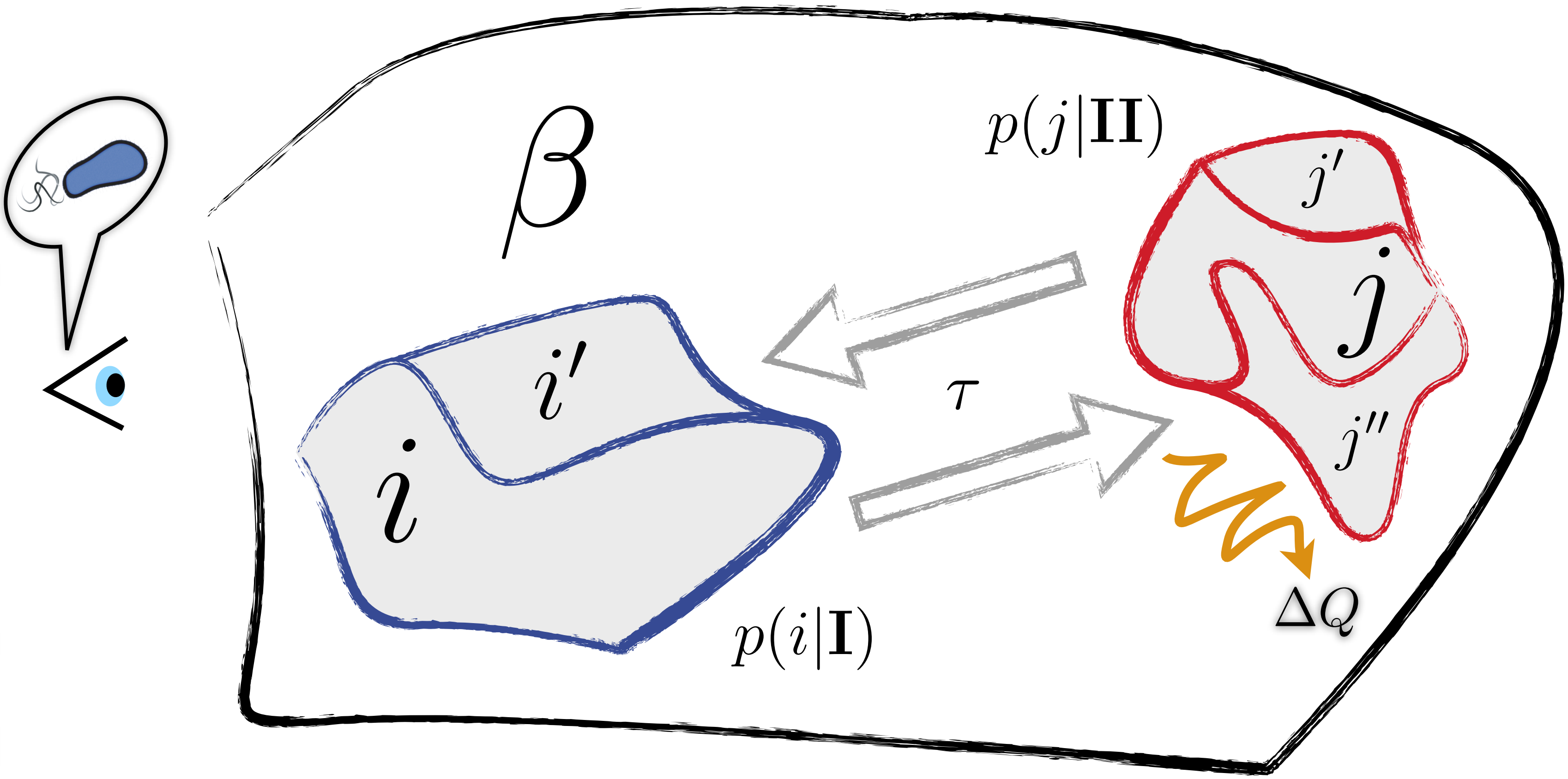
Entropy production tracks with irreversibility at a macroscopic level, even when driven far from equlibrium!

This is true for arbitrary coarse-grainings, including

- **bit erasure/computing** (Laundauer)
- **Markov processes** (Blythe)
- **chemical reactions** (Prigogine & DeDonder) . . .

. . . and for **self-replication**

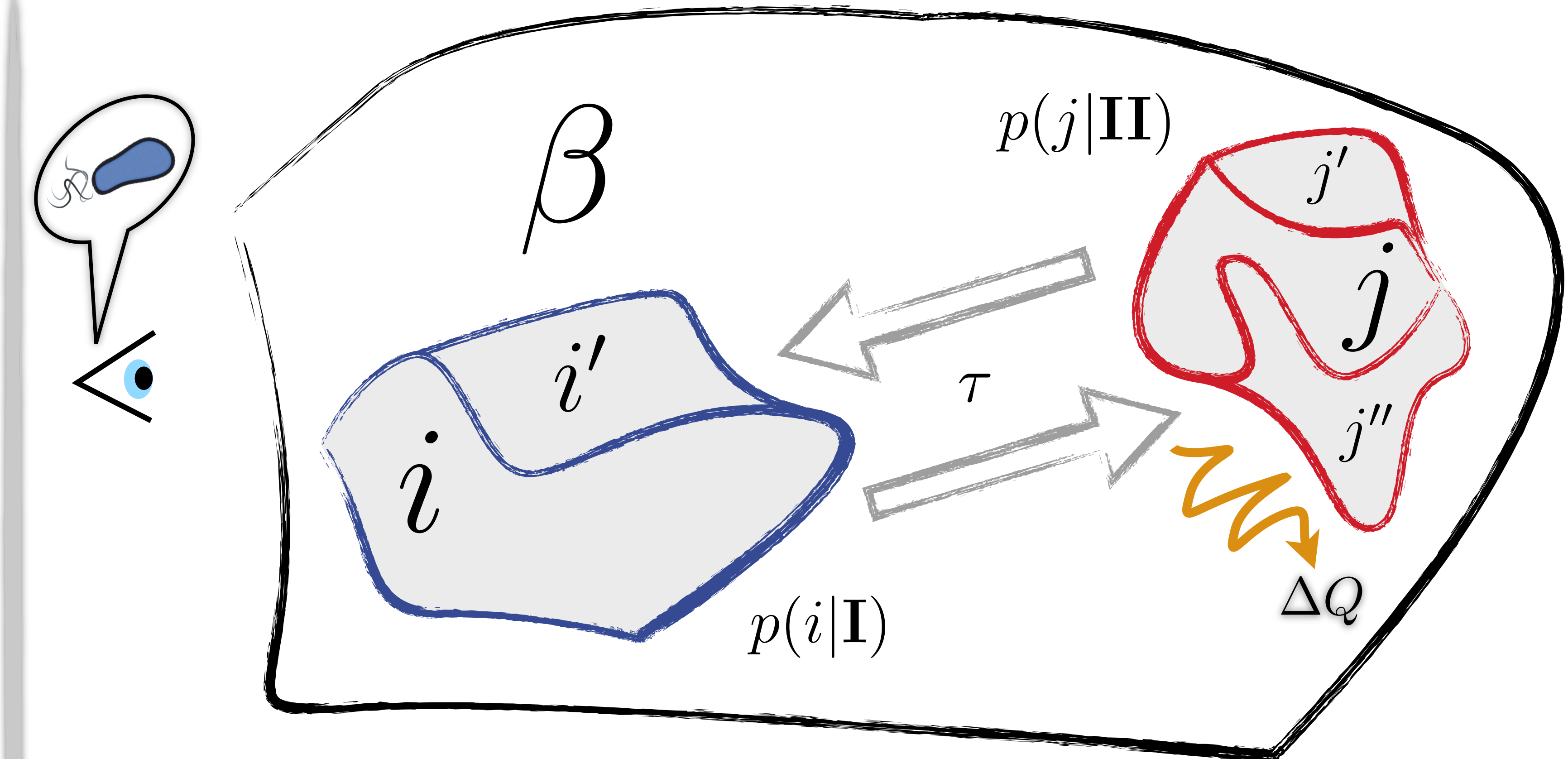
Get a hold of your "self"



"Die Grenzen meiner Sprache
bedeuten die Grenzen meiner Welt."

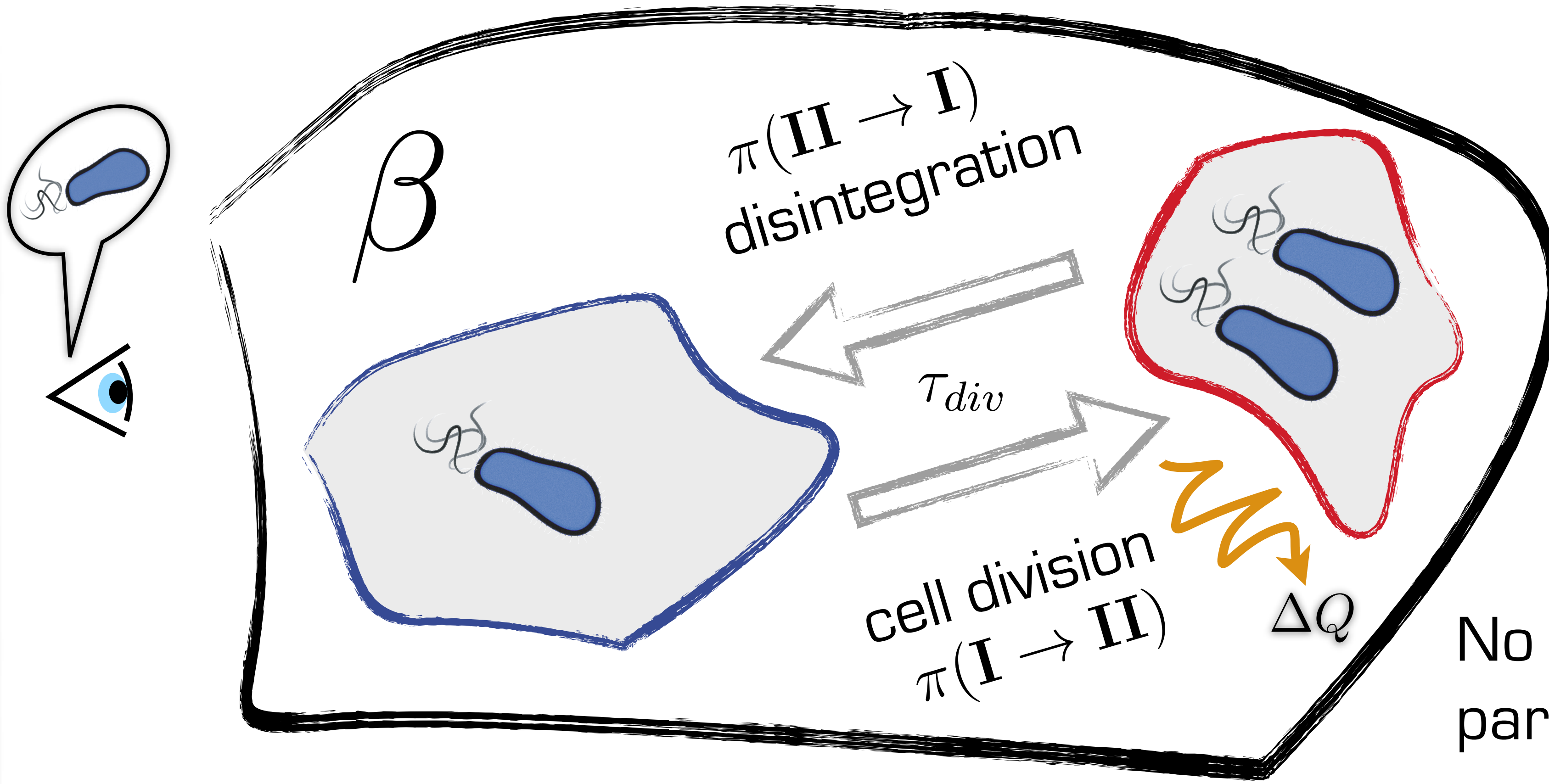
Wittgenstein, 1922

Get a hold of your “self”



The observer has to label the states

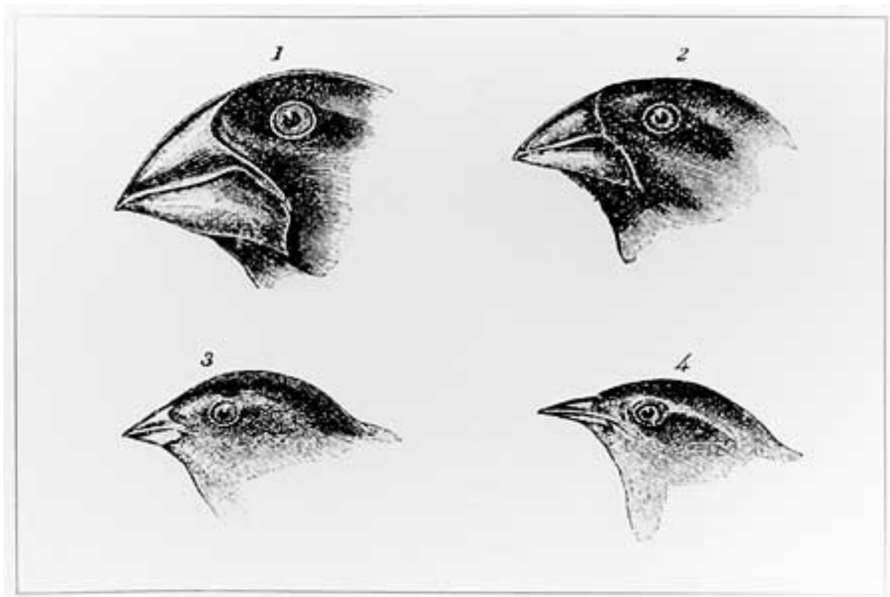
Get a hold of your “self”



No order parameter!

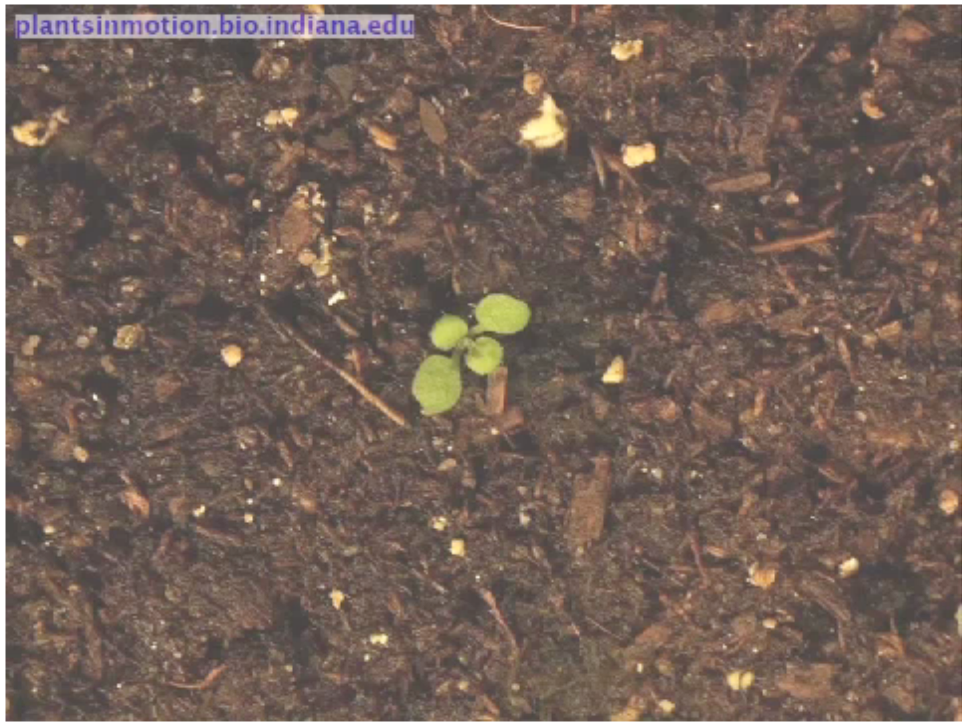
$$\Delta S_{tot} = \beta\langle\Delta Q\rangle + \Delta S_{int} \geq \ln\left[\frac{\pi(\mathbf{I}\to\mathbf{II})}{\pi(\mathbf{II}\to\mathbf{I})}\right] \geq 0$$

Fit Finch



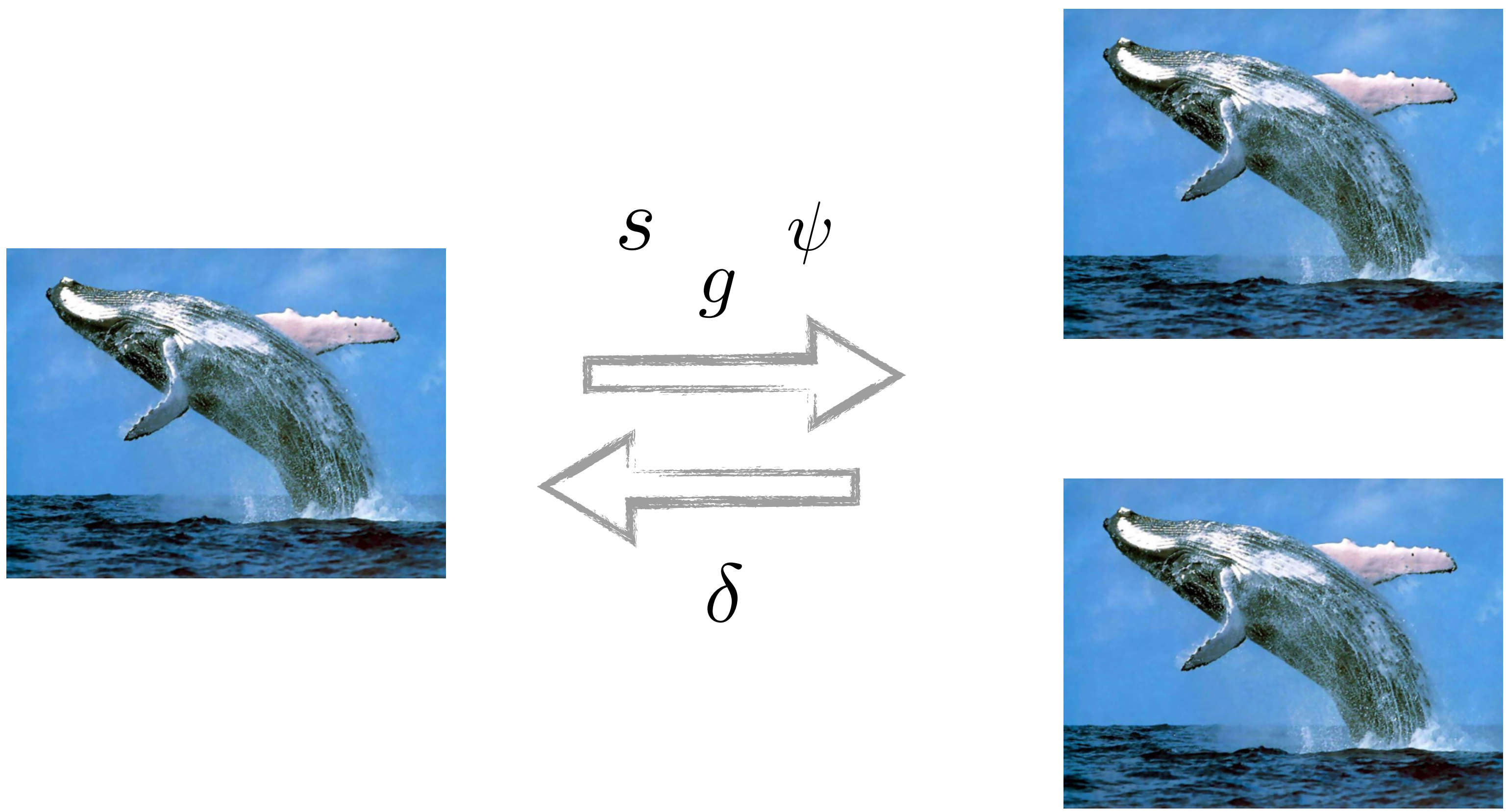
"Fitness" is easiest to define when we are comparing replicators that are very similar

Growth and dissipation



Biological growth is never observed to run itself backwards. **Why not?**

Growth and dissipation



Growth is accompanied by internal entropy change and dissipation

Growth and dissipation

g exponential growth rate

δ spontaneous reversal rate

s system entropy change

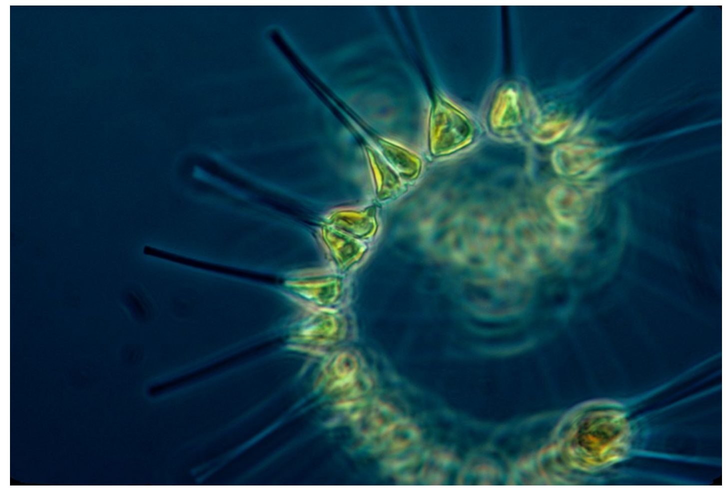
ψ dissipation in reservoir

Doubling time will be roughly proportional to $1/(g-\delta)$

$\psi \geq \ln[g/\delta] - s$ is generally going to be positive

So, winning Darwin's game happens to be about dissipating more than your competitor

Fit Finch?



What really makes evolution interesting is **adaptation**

Boltzmann in Hiding

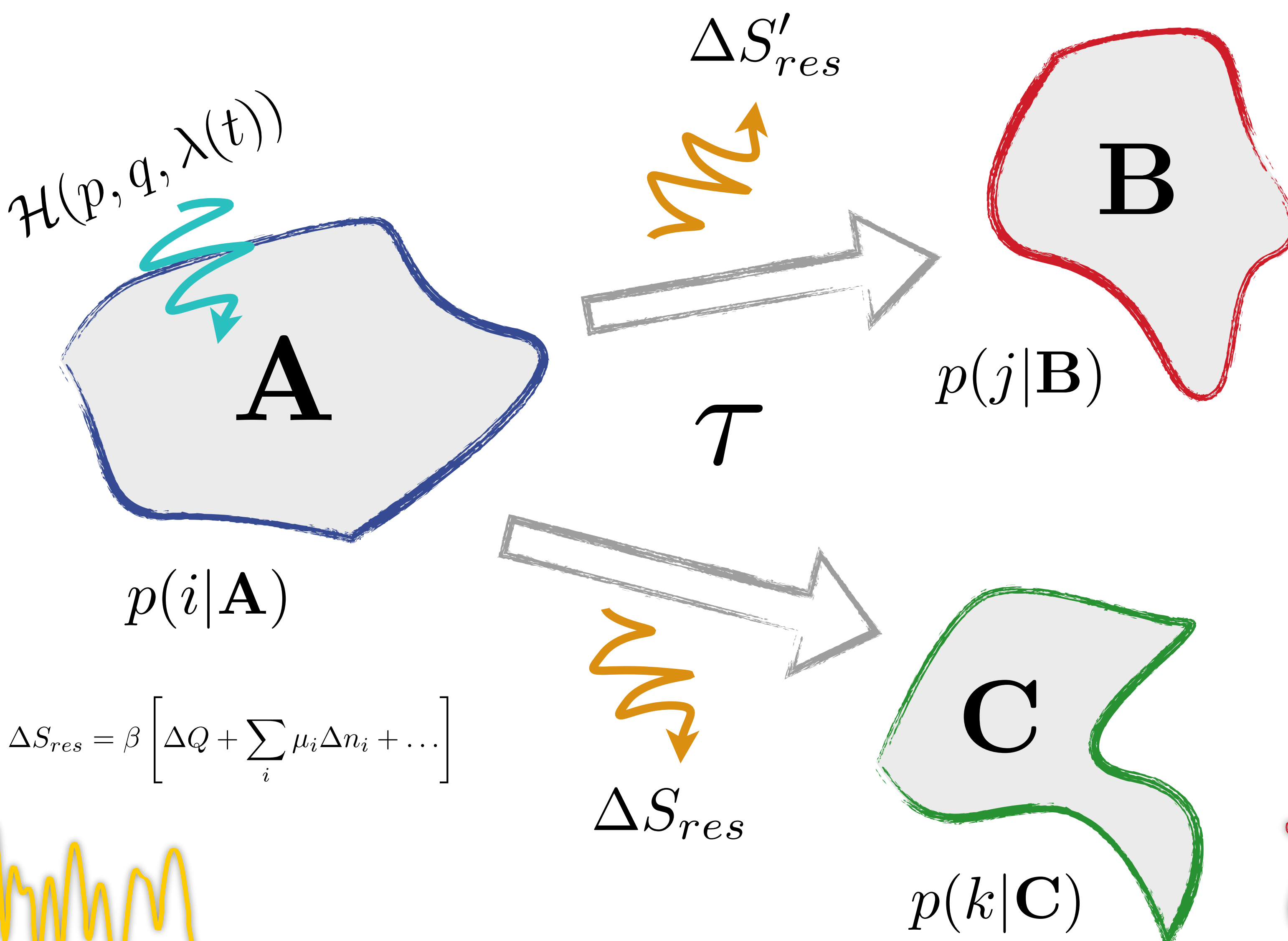
$$\frac{\pi(\mathbf{II} \to \mathbf{I})}{\pi(\mathbf{I} \to \mathbf{II})} = \left\langle e^{\ln\left[\frac{p(j|\mathbf{II})}{p(i|\mathbf{I})}\right]} \left\langle e^{-\beta \Delta Q_{i\to j}} \right\rangle_{i \to j} \right\rangle_{\mathbf{I}\to\mathbf{II}}$$

Energy is actually about **time**

The Boltzmann distribution in a way is a misleading special case because it makes us think about where we **are . . .**

. . . but we should be thinking about where we are going!

Driven Stochastic Evolution



$$\Delta S_{res} = \beta \left[\Delta Q + \sum_i \mu_i \Delta n_i + \dots \right]$$

Driven Stochastic Evolution

$$\ln\left[\frac{\pi(\mathbf{A}\to\mathbf{B})}{\pi(\mathbf{A}\to\mathbf{C})}\right] \simeq \Delta\ln\Omega_{\mathbf{BC}} + \ln\left[\frac{\pi(\mathbf{B}\to\mathbf{A})}{\pi(\mathbf{C}\to\mathbf{A})}\right] - \ln\left[\frac{\langle\exp[-\Delta S_{res}\rangle_{\mathbf{A}\to\mathbf{B}}}{\langle\exp[-\Delta S_{res}\rangle_{\mathbf{A}\to\mathbf{C}}}\right]$$

Reduces to Boltzmann distribution

in the absence of drives

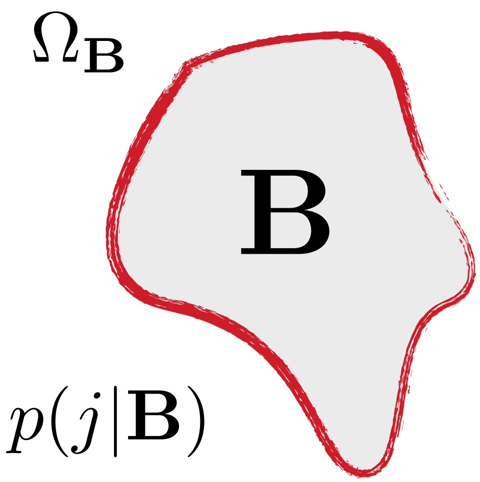
and

after an infinite amount of time

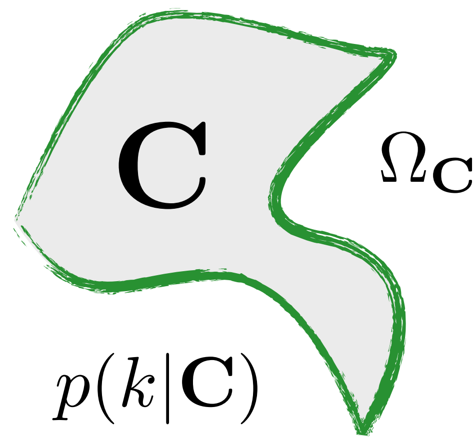
$$-\beta\Delta F_{\mathbf{BC}} = \Delta\ln\Omega_{\mathbf{BC}} - \beta\Delta E_{\mathbf{BC}}$$

Helmholtz free energy

Coming to terms



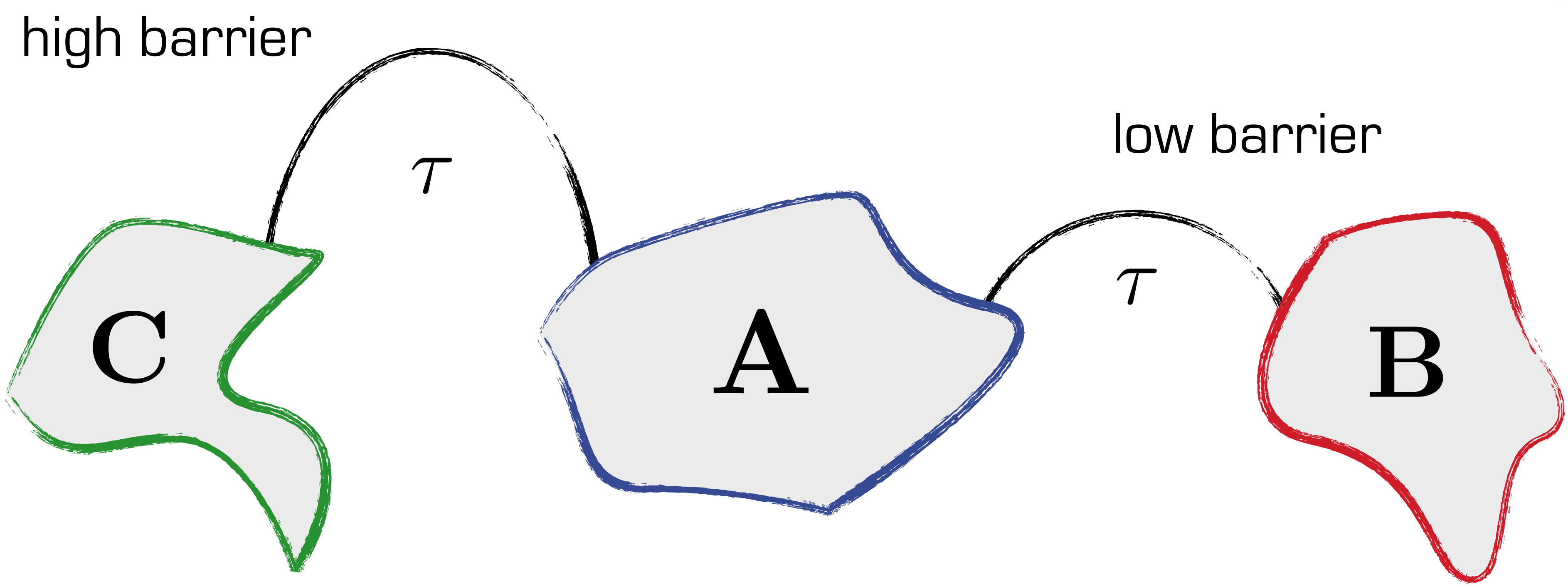
Compare phase space volumes of the two macrostates



$$\Delta \ln \Omega_{\mathbf{BC}} \simeq -\sum_k p(j|\mathbf{B}) \ln p(j|\mathbf{B}) + \sum_k p(k|\mathbf{C}) \ln p(k|\mathbf{C})$$

Systems coupled to reservoirs tend to get more disordered because of fluctuations

Coming to terms



$$\ln\left[\frac{\pi(\mathbf{A}\to\mathbf{B})}{\pi(\mathbf{A}\to\mathbf{C})}\right] = \ldots + \ln\left[\frac{\pi(\mathbf{B}\to\mathbf{A})}{\pi(\mathbf{C}\to\mathbf{A})}\right] + \ldots$$

Higher barriers make kinetics slower in both directions

Coming to terms

$$-\ln\langle\exp[-\Delta S]\rangle = \langle\Delta S\rangle - \frac{\sigma^2_{\Delta S}}{2} + \ldots$$

$$-\ln\langle\exp[-\Delta S]\rangle \equiv \Psi - \Phi$$

Cumulant generating function breaks into two pieces: the **mean dissipation**, and the **fluctuations** about the mean

(**Warning:** Fluctuations can dominate!)

To make this quantity very positive, you need **reliably** high dissipation

Driven Stochastic Evolution

$$\ln\left[\frac{\pi(\mathbf{A}\to\mathbf{B})}{\pi(\mathbf{A}\to\mathbf{C})}\right] \simeq \Delta\ln\Omega_{\mathbf{BC}} + \ln\left[\frac{\pi(\mathbf{B}\to\mathbf{A})}{\pi(\mathbf{C}\to\mathbf{A})}\right] - \ln\left[\frac{\langle\exp[-\Delta S_{res}\rangle_{\mathbf{A}\to\mathbf{B}}}{\langle\exp[-\Delta S_{res}\rangle_{\mathbf{A}\to\mathbf{C}}}\right]$$

order **durability** **fluctuation and dissipation**

Can constrain paths to likely forward trajectories so last term is not dominated by freak events

What does evolution give you?

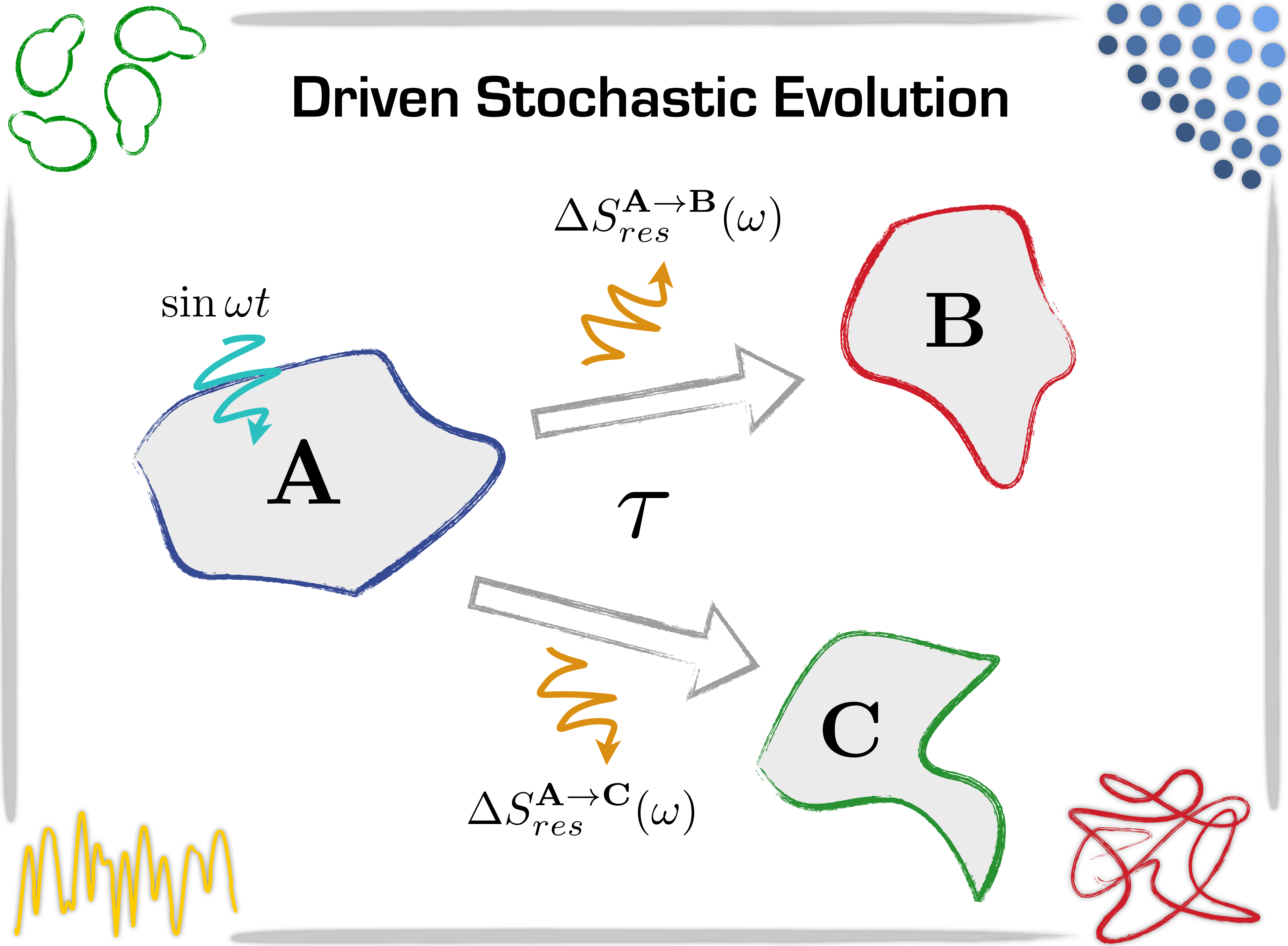
$$\ln \pi(\mathbf{0} \to \mathbf{A}) = \ln \Omega_{\mathbf{A}} + \ln \pi(\mathbf{A} \to \mathbf{0}) + \Psi_{\mathbf{0}\to\mathbf{A}} - \Phi_{\mathbf{0}\to\mathbf{A}}$$

On the one hand, outcomes more likely if disorganized and very kinetically accessible (activation barriers)

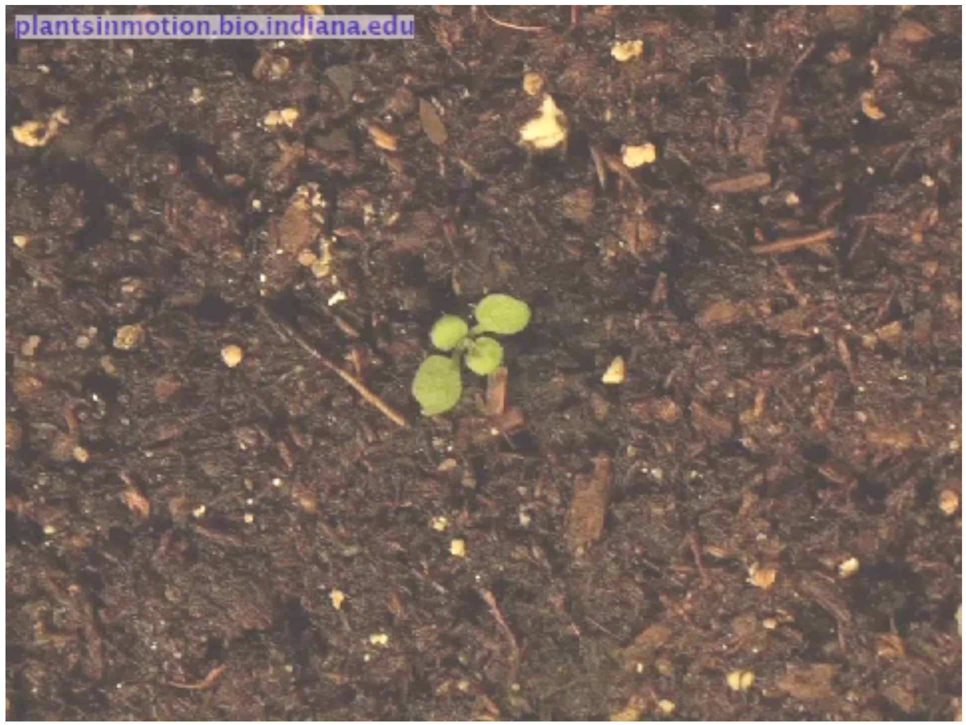
On the other hand, increasing dissipation and cutting down on fluctuation are options too . . . and they presumably have to be achieved through **order and durability**

No natural selection assumed here!

Driven Stochastic Evolution



Not your typical macrostate



Living things are good at getting applied fields to do work on them so they can dissipate the energy

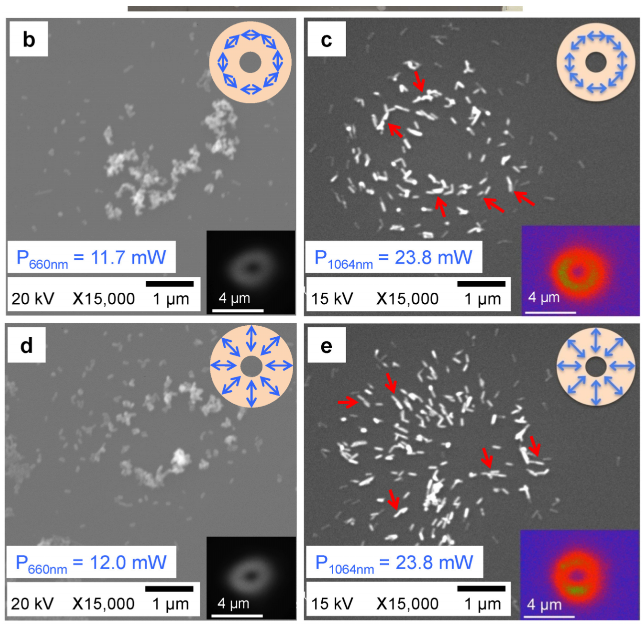
Looking for Darwin

$$\ln \pi(\mathbf{0} \to \mathbf{A}) = \ln \Omega_{\mathbf{A}} + \ln \pi(\mathbf{A} \to \mathbf{0}) + \Psi_{\mathbf{0}\to\mathbf{A}} - \Phi_{\mathbf{0}\to\mathbf{A}}$$

No doubt, self-replication is a way to make this work because discrete exponential growth reliably causes lots of dissipation

But it seems like we expect to see **organization that is ‘adapted’** from an energetic standpoint emerge on its own, even **without heredity and selection**, and just from underlying Newtonian/Hamiltonian mechanics

Resonant adaptation

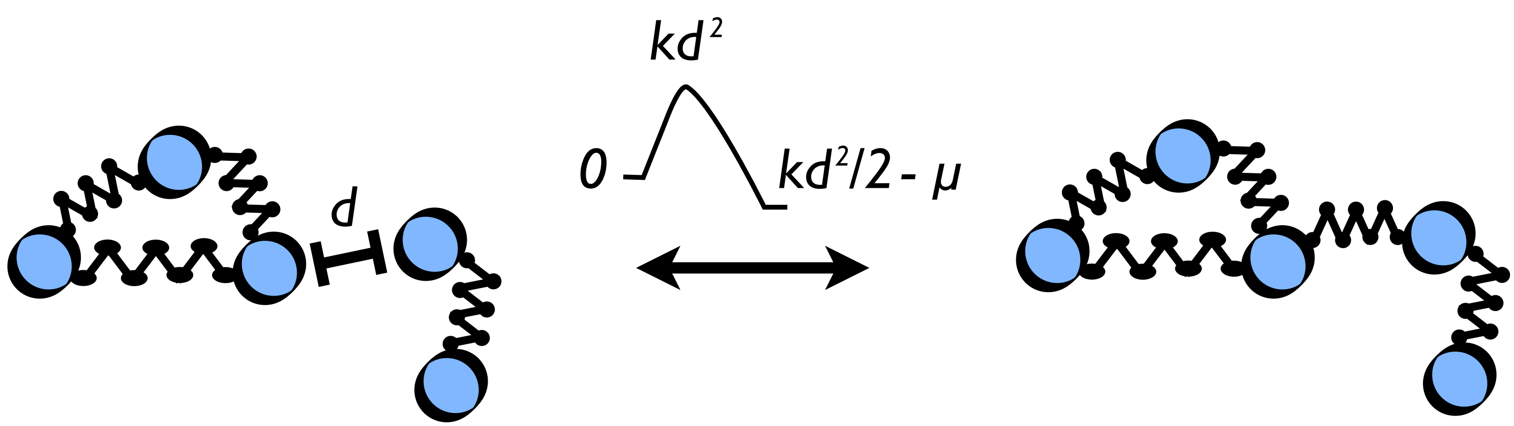


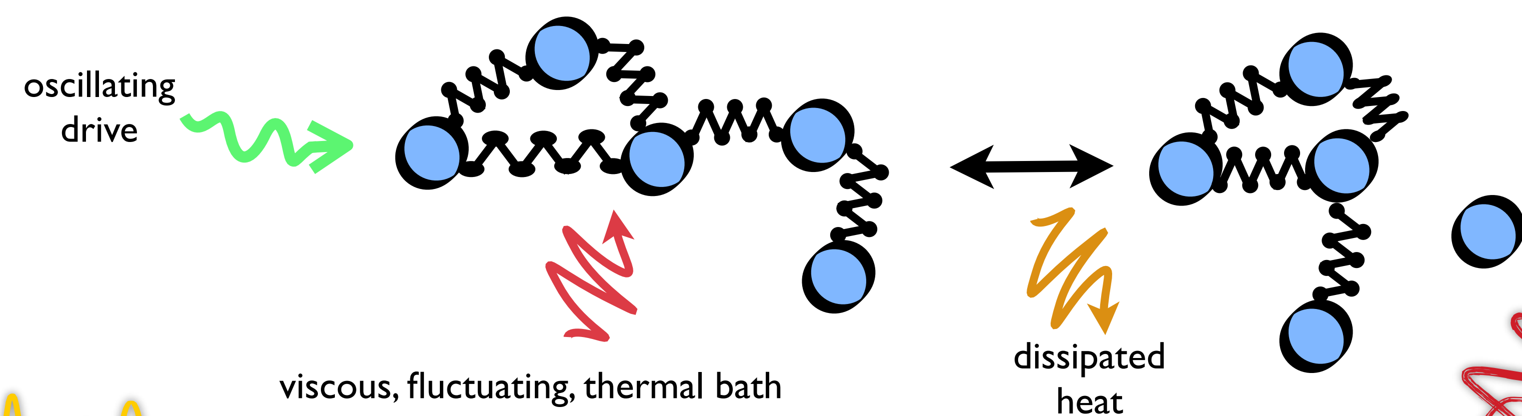
Ito et al., Scientific Reports, 2013

Silver nanorods self-assemble into structures that match surface plasmon resonance to wavelength of driving light field

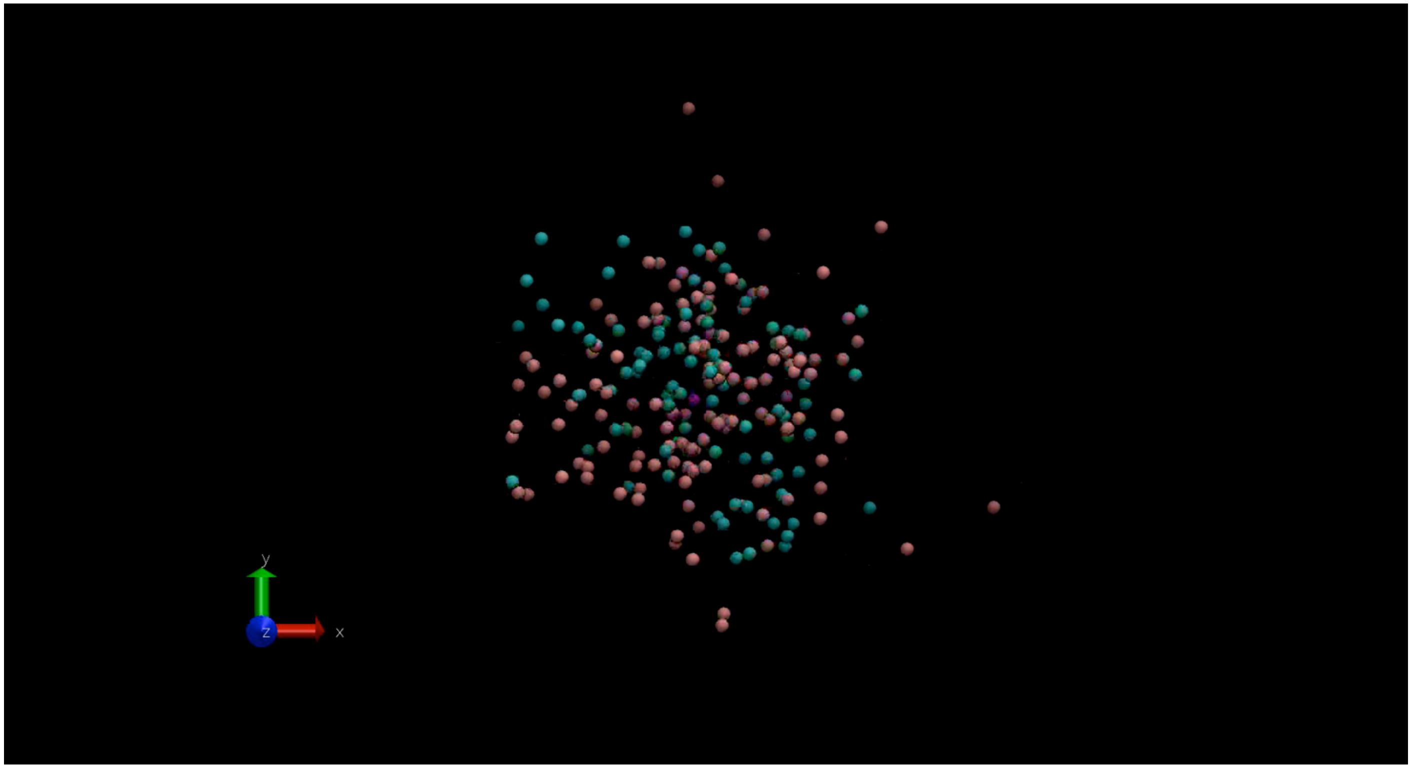
No need to talk about anything in the system making a copy of itself . . .

Spontaneous Rewiring



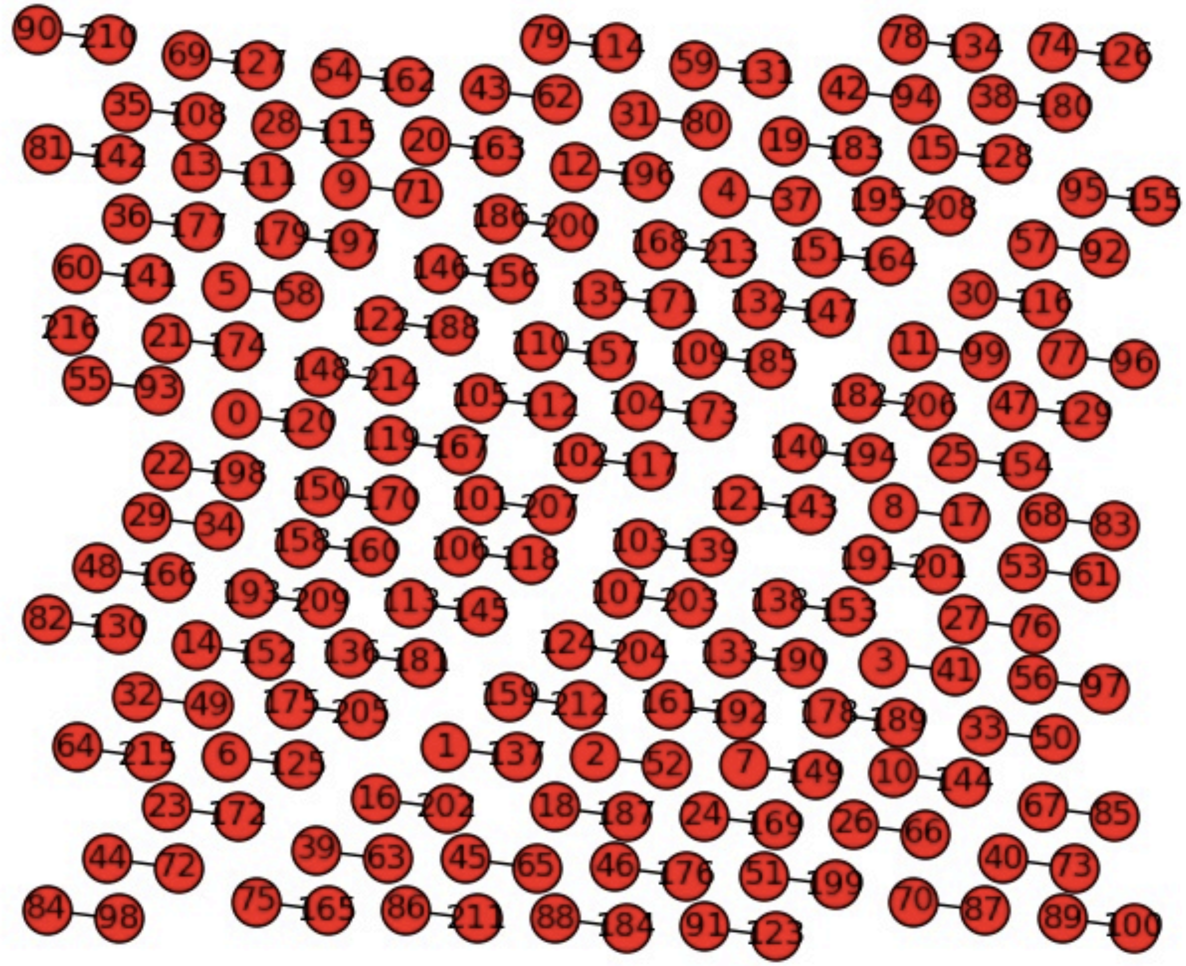


Oscillatory driving

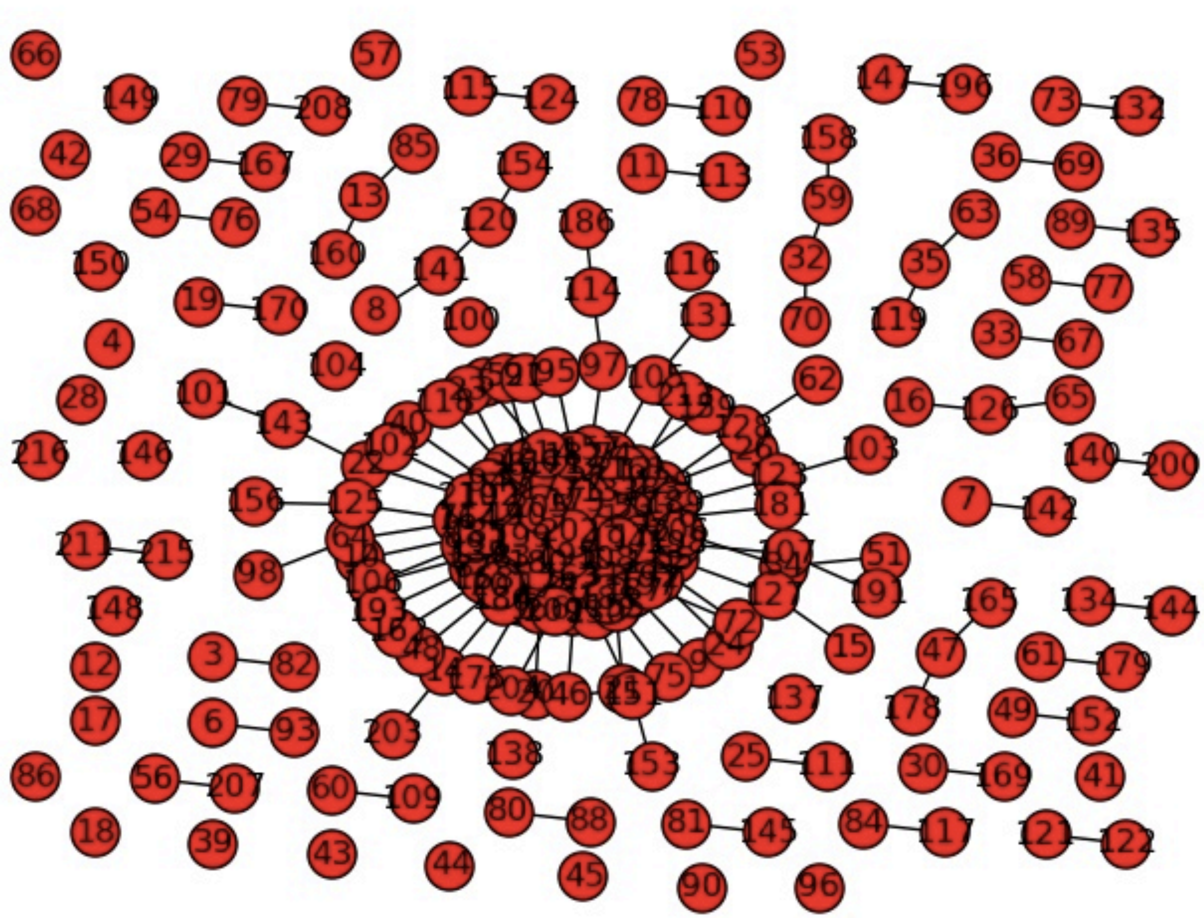


As external force oscillates,
bond network reconfigures

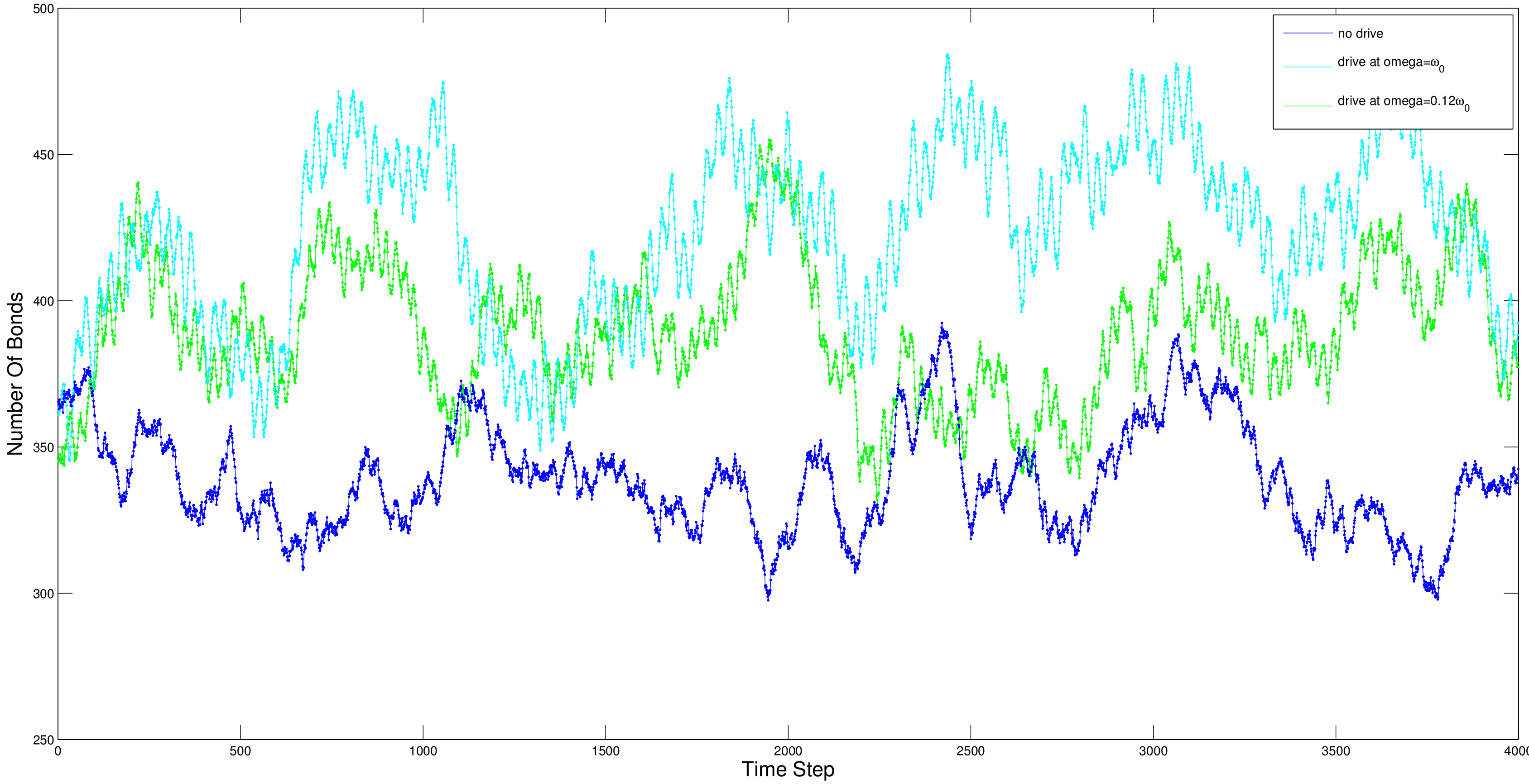
High amplitude, high frequency



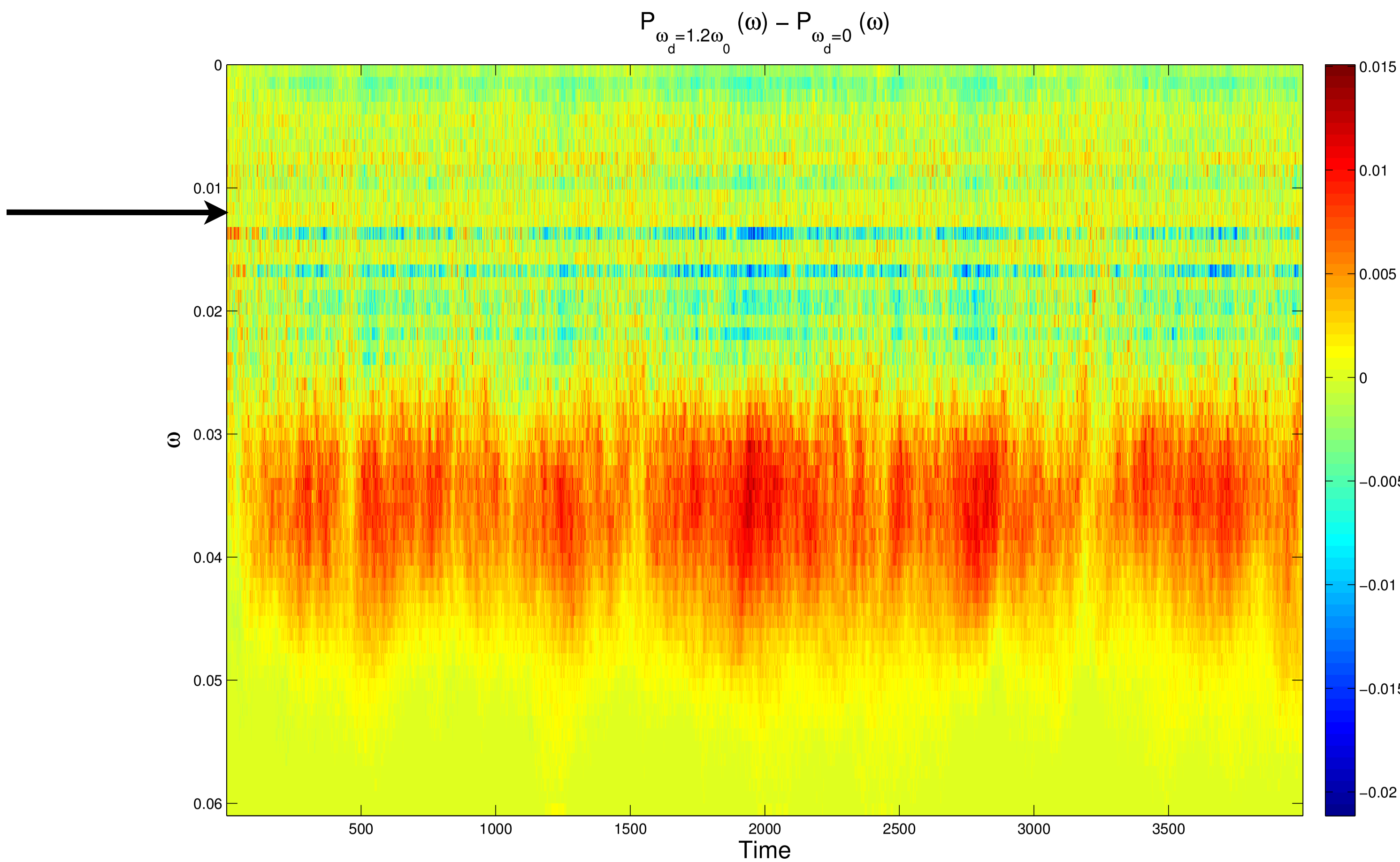
High amplitude, low frequency



Bond dynamics



Spectrum dynamics



Summing up

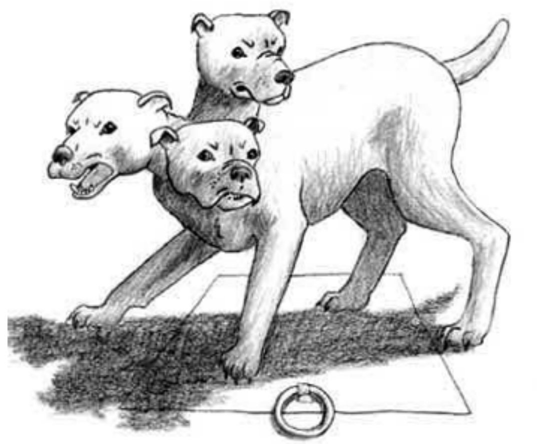
Time-reversibility guarantees an exact, quantitative relationship between irreversibility and entropy production

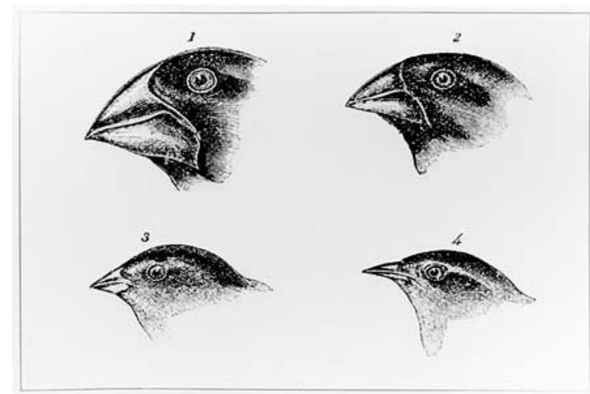
This implies a link between probability and dissipation

As a consequence, one expects driven, reservoir-coupled systems to become better ‘adapted’ to absorbing energy from their drives over time. **And we don’t have to explain this by making reference to Darwinian selection.**

In this light, we can view adaptive evolution as a requirement of general physical laws

Thanks!





Robert Marsland
MIT

Tal Kachman
Technion

Living within the law

$$\Delta S_{tot} = \beta \langle \Delta Q \rangle + \Delta S_{int} \geq -\ln p_{dis} \gg 0$$

Bacteria generate heat as they grow, that is, they increase the entropy of the surrounding heat bath

They also organize their surroundings into new copies of themselves, that is, they catalyze change in internal entropy

They also are made of a particular combination of materials with a particular degree of durability

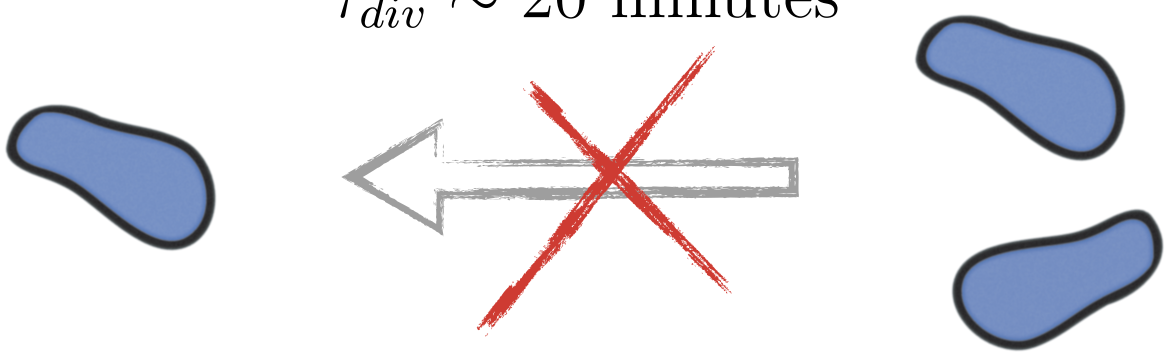
How must these properties be related?

Quantifying the impossible

Bacteria never “un-eat” and “de-respirate” themselves

They’re not going to, even if we wait very patiently

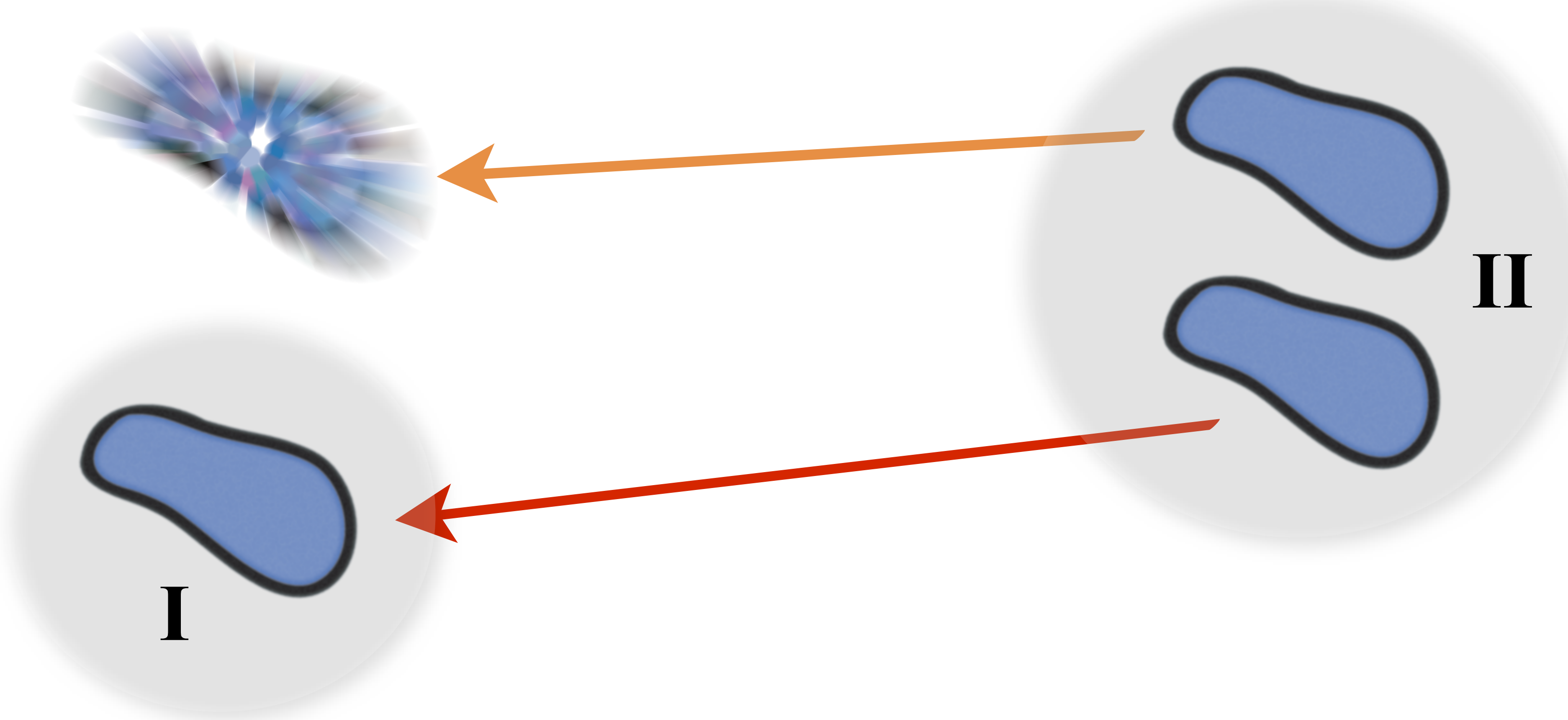
$\tau_{div} \sim 20$ minutes



Can we bound the irreversibility from below?

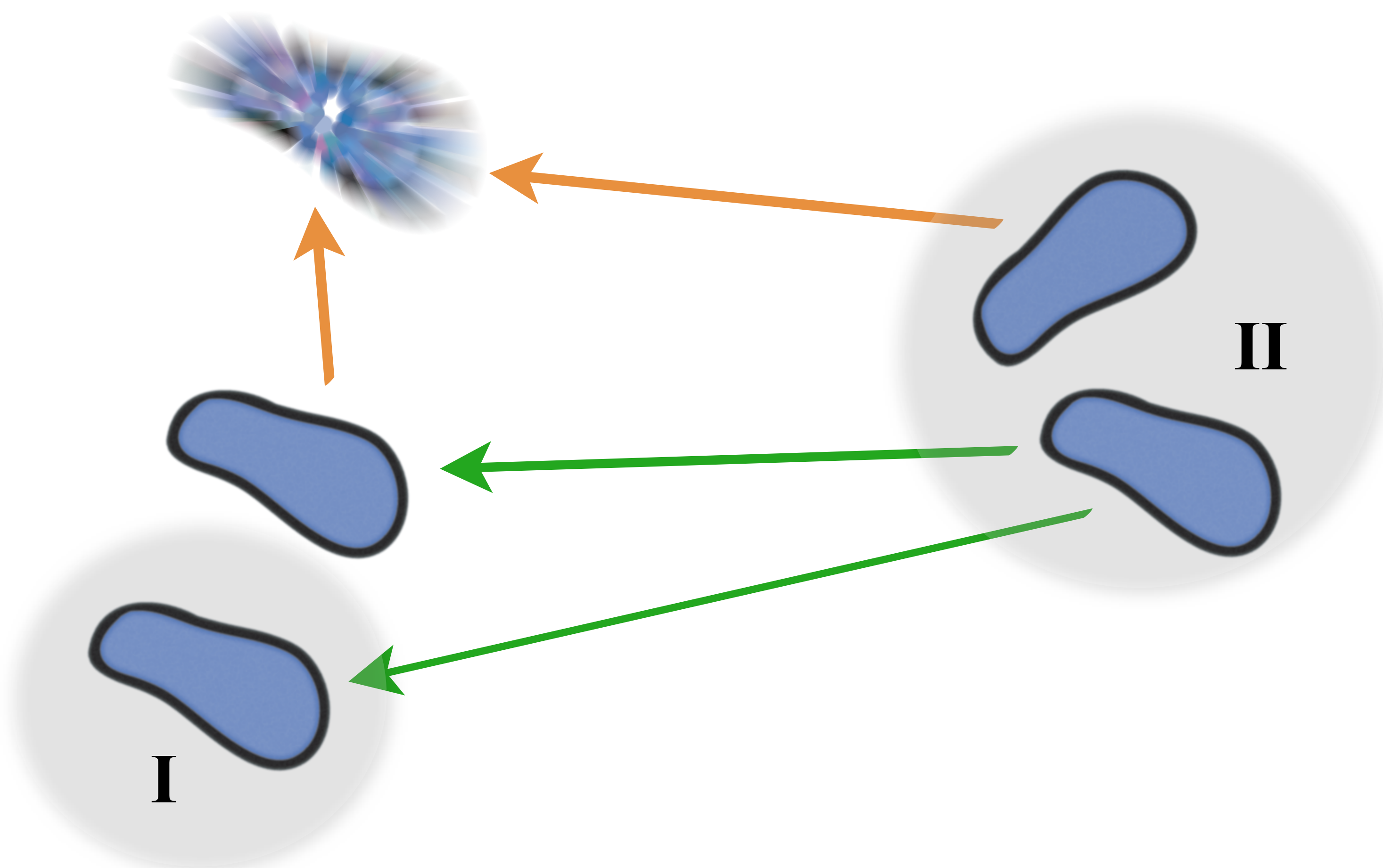
$$-\ln p_{dis} > \ ?$$

In search of a mechanism



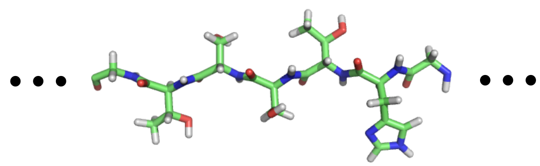
How do you pause processive growth?

In search of a mechanism



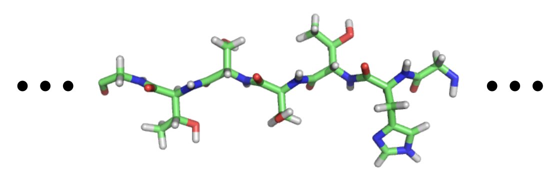
A biological shortcut?

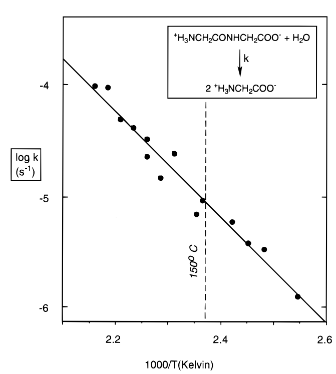
Lowering the bar



Cells are over 60% protein (dry weight)

Peptide bonds spontaneously break

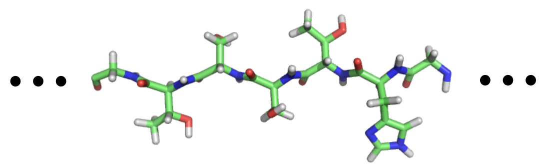




Radzicka & Wolfenden, 1996

One bond takes roughly 600 years

Lowering the bar



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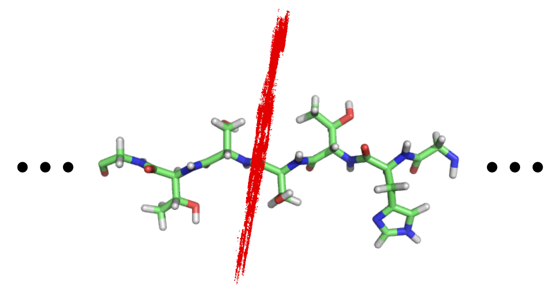
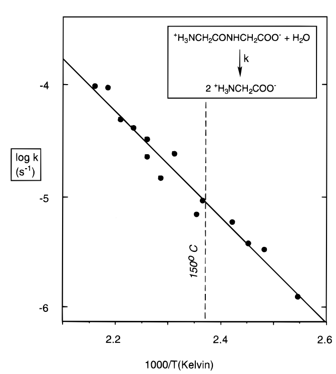


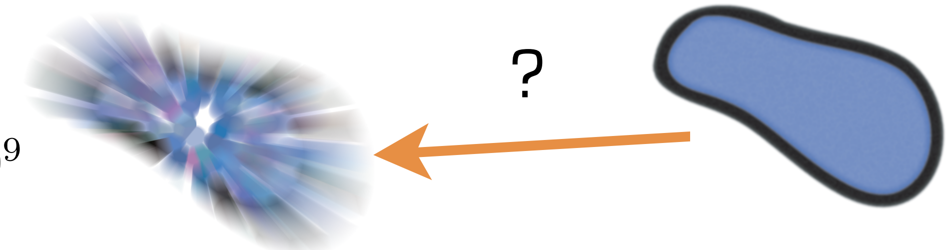


Radzicka & Wolfenden, 1996

One bond takes roughly 600 years

Pep rally!

$$n_{pep} \sim 1.6 \times 10^9$$



$$r = n_{pep}/\tau_{div}$$

$$\ln p_{hyd} \simeq (n_{pep} + rt)\ln[t/\tau_{hyd}]$$

Over some time t, assume all bonds independently break

$$|\ln p_{hyd}| \simeq |n_{pep} \ln[t_{max}/\tau_{hyd}]| = n_{pep}(\tau_{div}/t_{max} + 1)$$

$$t_{max} \sim 1 \text{ minute} \qquad 2n_{pep}(\tau_{div}/t_{max} + 1) = 6.7 \times 10^{10} \simeq 42 n_{pep}$$

$$-\ln p_{dis} \geq 2n_{pep}(\tau_{div}/t_{max} + 1)$$

By heats and bounds

$$\beta\langle Q\rangle \geq 2n_{pep}(\tau_{div}/t_{max}+1) - \Delta S_{int}$$

ΔS_{int} Internal entropy contribution turns out to be small for aerobic growth

$\beta\langle Q\rangle = 220 n_{pep}$ Exponential growth, rich media: Rothbaum & Stone, 1961

$$2n_{pep}(\tau_{div}/t_{max}+1) = 6.7\times 10^{10} \simeq 42 n_{pep}$$

$$\langle Q\rangle < 6\langle Q\rangle_{min}$$

A few comments

We estimated a very conservative lower bound: e.g. ignored reversal of gas exchange

We don't expect selective pressure to lead to maximal efficiency: living is not just growing and computations also generate heat, whereas adaptations cost efficiency

A synthetic bacterium might be able to grow much faster!

Quasi-steady-states raise bound

Please read line 3

$$\pi(\mathbf{I} \to \mathbf{II}) = \int_{\mathbf{II}} dj \int_{\mathbf{I}} di \; p(i|\mathbf{I})\pi(i \to j)$$

$$\pi(\mathbf{II} \to \mathbf{I}) = \int_{\mathbf{I}} di \int_{\mathbf{II}} dj \; p(j|\mathbf{II})\pi(j \to i)$$

$$\frac{\pi(\mathbf{II} \to \mathbf{I})}{\pi(\mathbf{I} \to \mathbf{II})} = \frac{\int_{\mathbf{I}} di \int_{\mathbf{II}} dj \; \left(\frac{p(j|\mathbf{II})}{p(i|\mathbf{I})}\right) p(i|\mathbf{I})\pi(j \to i)}{\int_{\mathbf{I}} di \int_{\mathbf{II}} dj \; p(i|\mathbf{I})\pi(i \to j)} = \frac{\int_{\mathbf{I}} di \int_{\mathbf{II}} dj \; p(i|\mathbf{I})\pi(i \to j) \frac{\langle e^{-\beta \Delta Q_{ij}} \rangle_{i \to j}}{e^{\ln\left[\frac{p(i|\mathbf{I})}{p(j|\mathbf{II})}\right]}}}{\int_{\mathbf{I}} di \int_{\mathbf{II}} dj \; p(i|\mathbf{I})\pi(i \to j)} = \left\langle \frac{\langle e^{-\beta \Delta Q_{ij}} \rangle_{i \to j}}{e^{\ln\left[\frac{p(i|\mathbf{I})}{p(j|\mathbf{II})}\right]}} \right\rangle_{\mathbf{I} \to \mathbf{II}}$$