There and Back Again:
The statistical dynamics of trajectories

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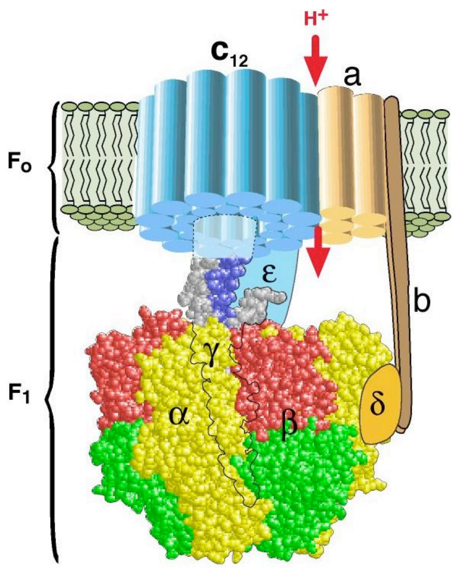
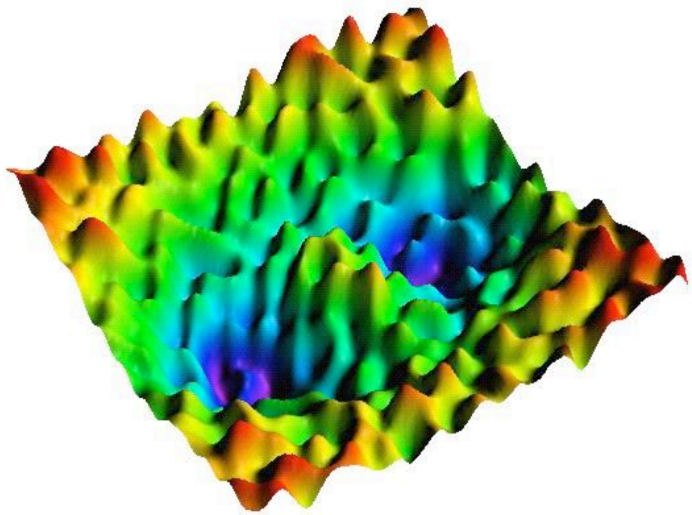
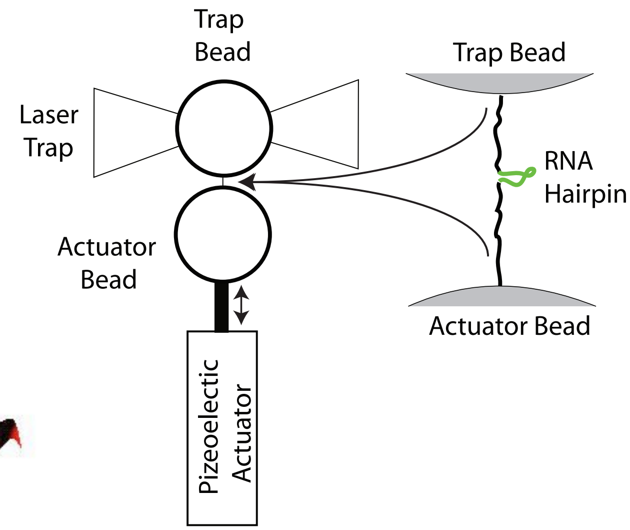
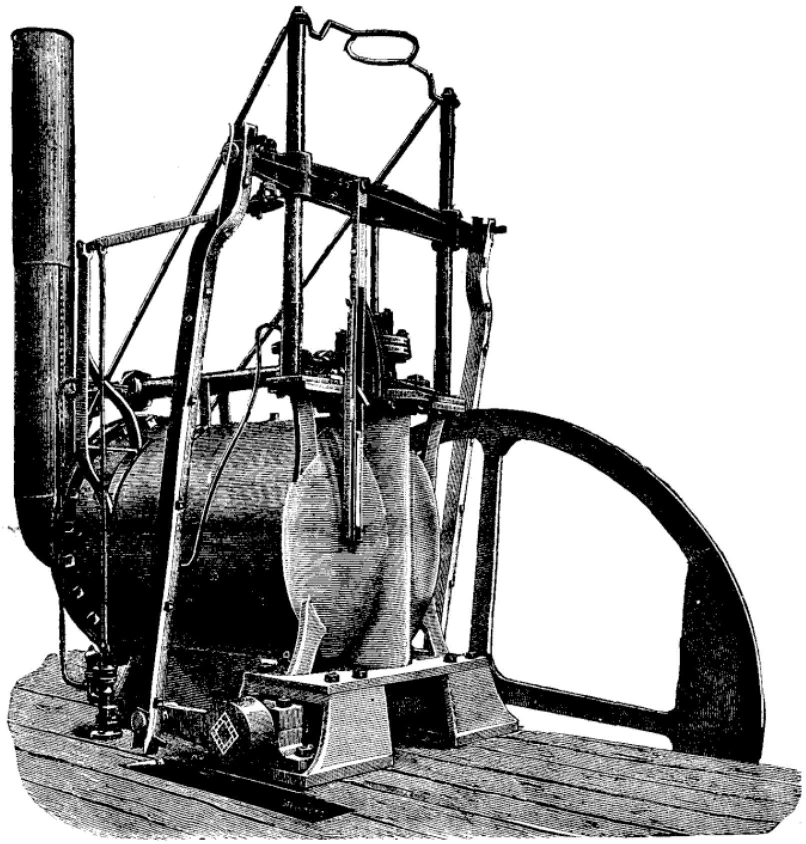






Steam Engines

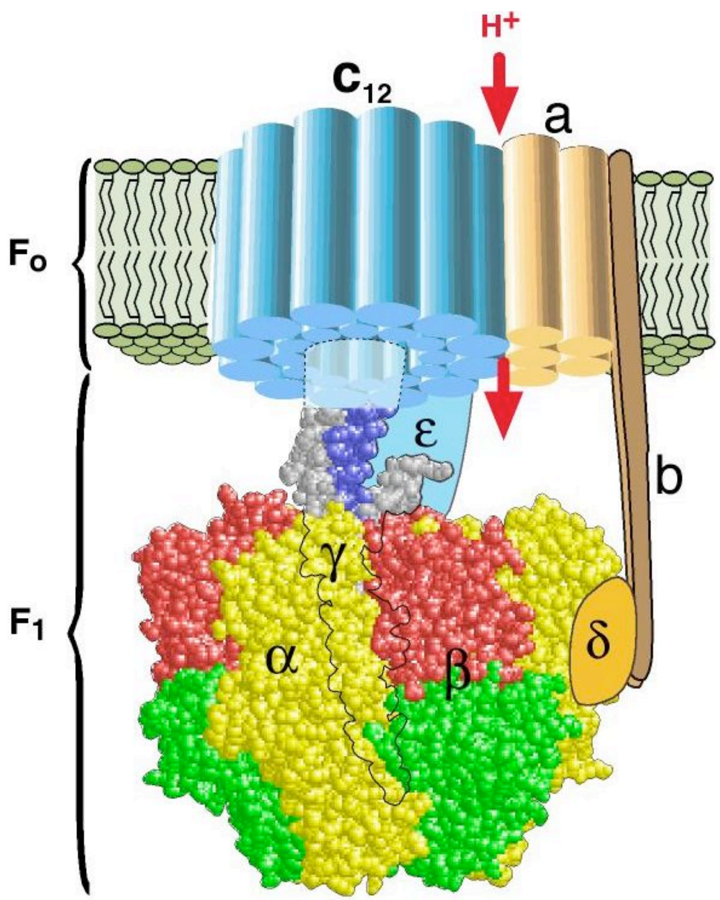
19th Century Thermodynamics



meters
kilojoules/cycle

21th Century Thermodynamics

Molecular Engines



ATP Synthase

Nanometers
Out-of-equilibrium
Large fluctuations
Dissipation~kT per cycle

Equilibrium Statistical Mechanics

Probability of state *i*

Temperature

$\beta = 1/kT$

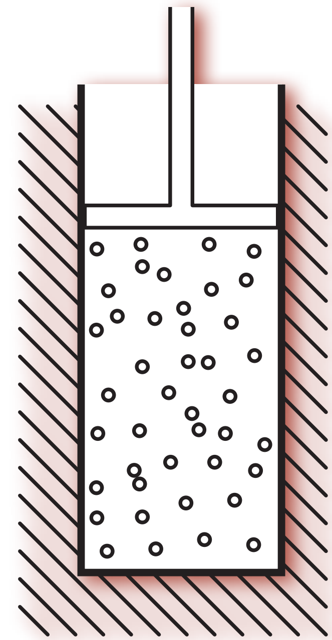
$$\rho_i = \frac{1}{Z} e^{-E_i/k_{\mathrm{B}}T} = e^{\beta F - \beta E_i}$$

Partition Function

Boltzmann's Constant

Free Energy

Energy of state *i*



This fundamental law is the summit of statistical mechanics, and the entire subject is either the slide-down from this summit, as the principle is applied to various cases, or the climb-up to where the fundamental law is derived. . . — Feynman

Out-of-Equilibrium

Probability of state *i*

Temperature

β=1/*kT*

$$\rho_i \neq \frac{1}{Z} e^{-E_i/k_{\mathrm{B}}T} = e^{\beta F - \beta E_i}$$

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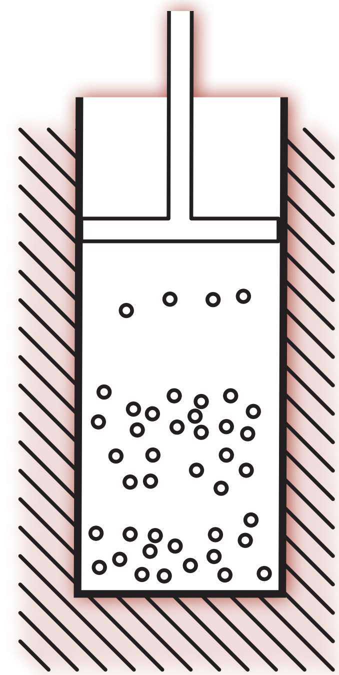


Dynamics around equilibrium is always more interesting than equilibrium itself

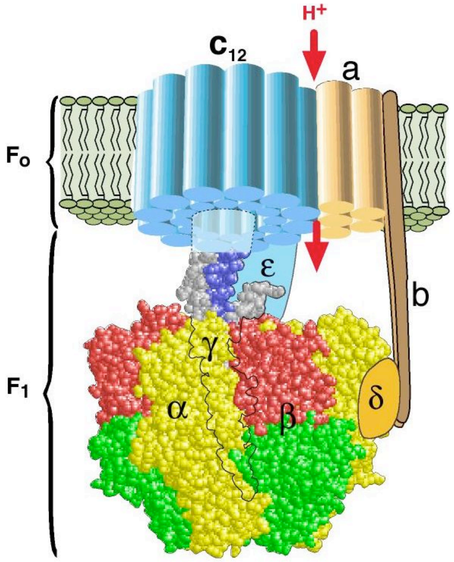
- John Doyle 2007

Information is physical — Rolf Landauer

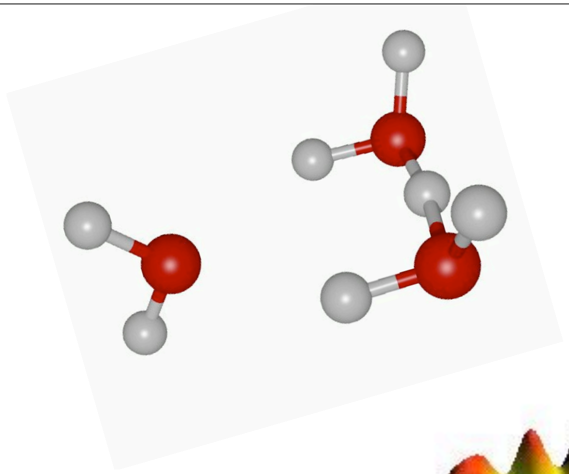
Information is bits

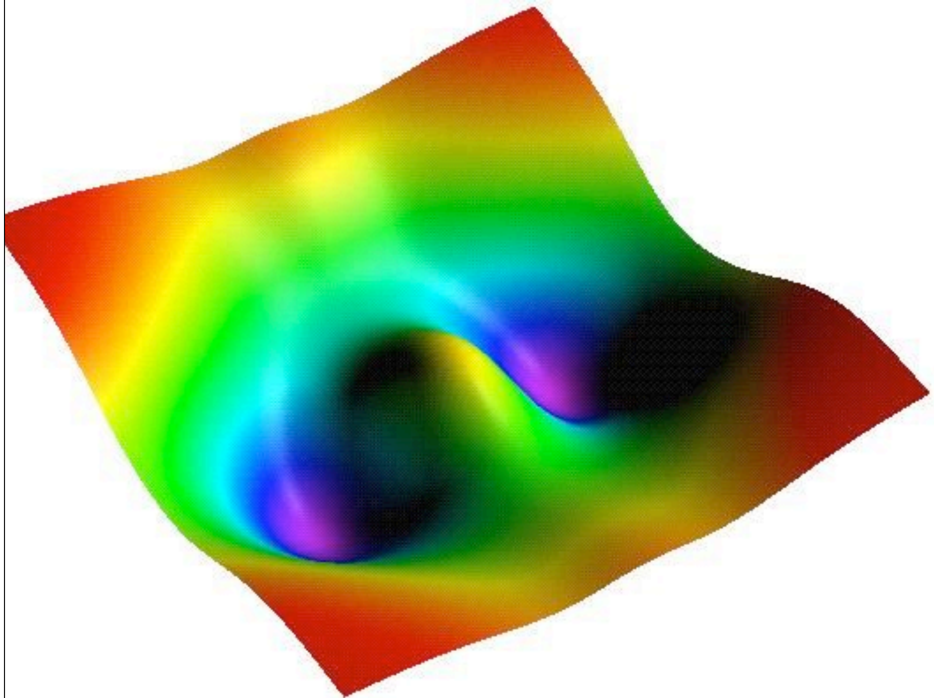
$$\Delta S_{\mathrm{Melting}} = 22\ \mathrm{J} / (\mathrm{mol\ K})$$
$$\sim 2.5\ \text{nats / molecule}$$
$$\sim 4\ \text{bits / molecule}$$

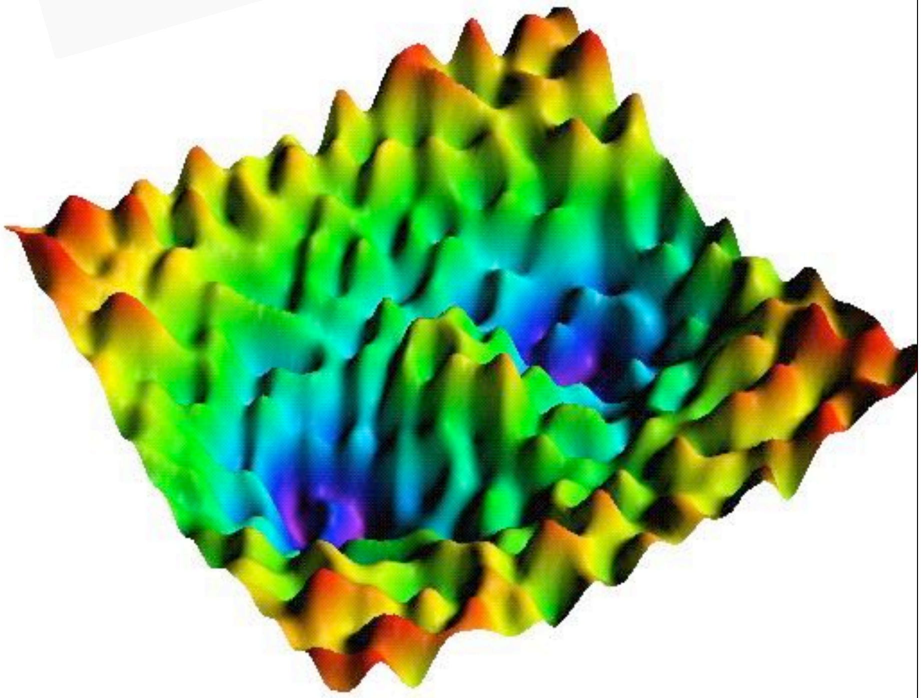
$$\Delta F_{\mathrm{ATP\ Hydro.}} = 20\ \mathrm{kJ} / \mathrm{mol}$$
$$\beta \Delta F_{\mathrm{ATP\ Hydro.}} \sim 8\ \text{nats / molecule}$$
$$\sim 12\ \text{bits / molecule}$$



Transition Path Sampling







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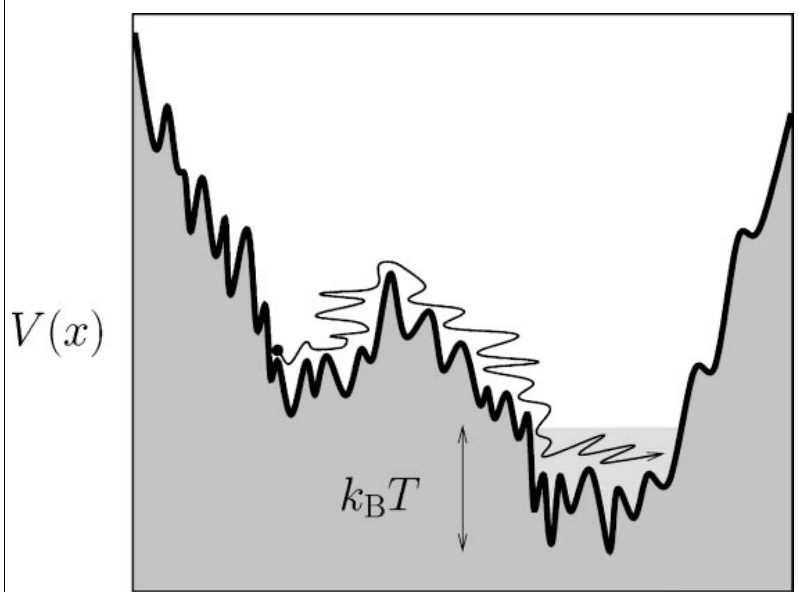
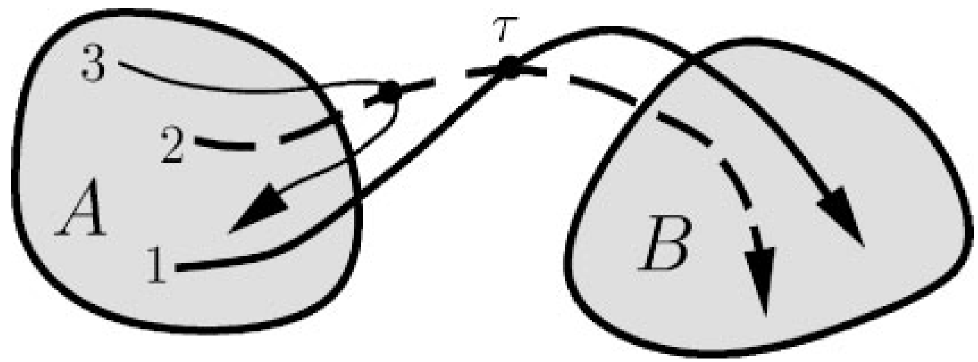
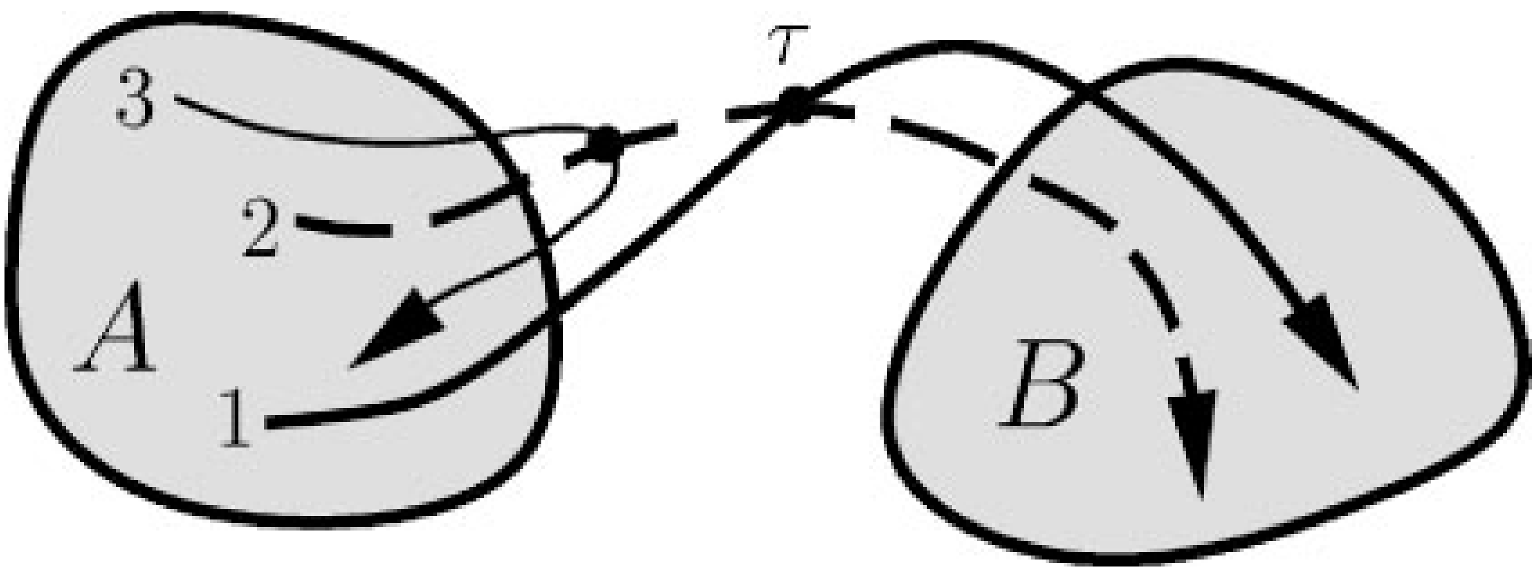


Configurational
Monte Carlo

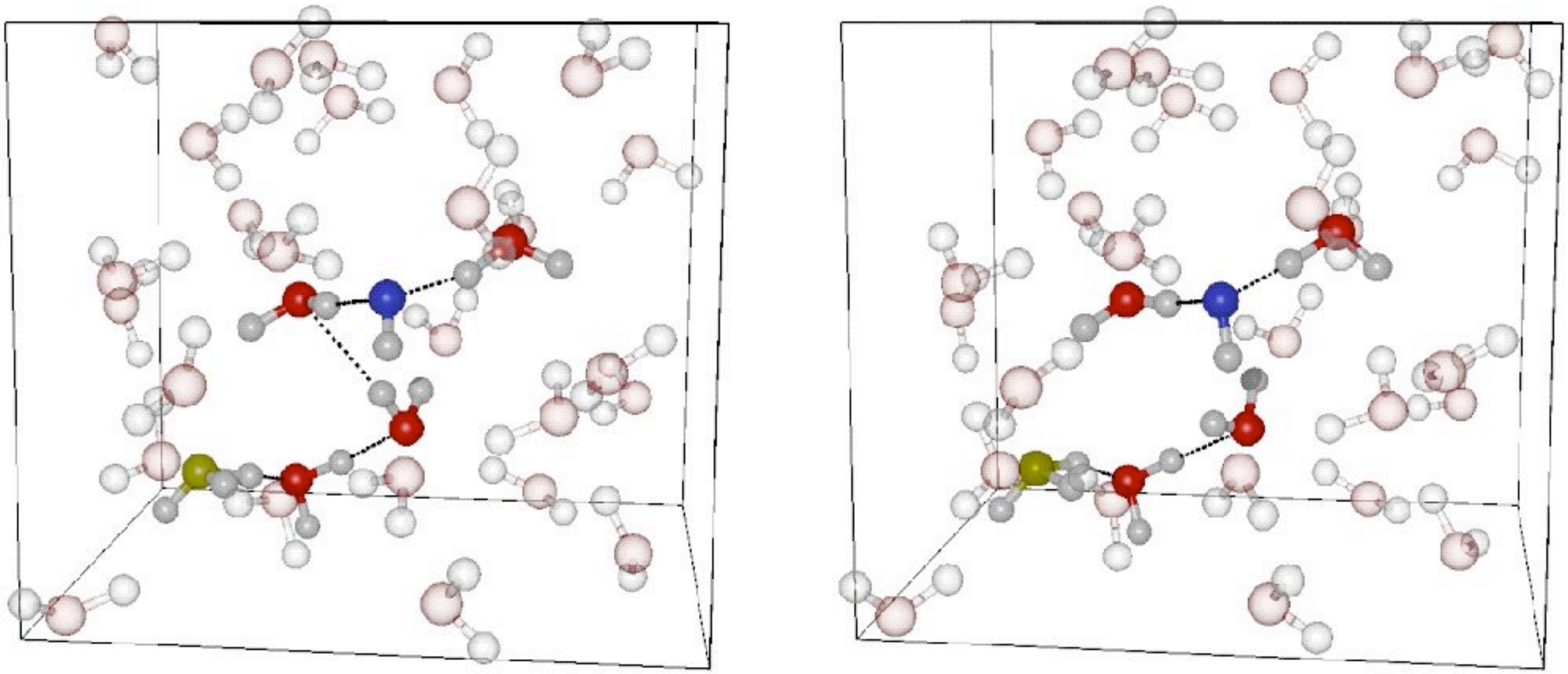


Transition Path
Monte Carlo

Transition Path Sampling



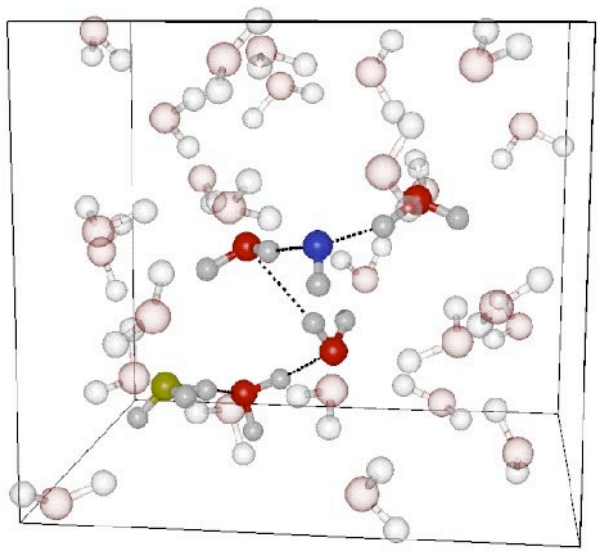
Water Autoionization

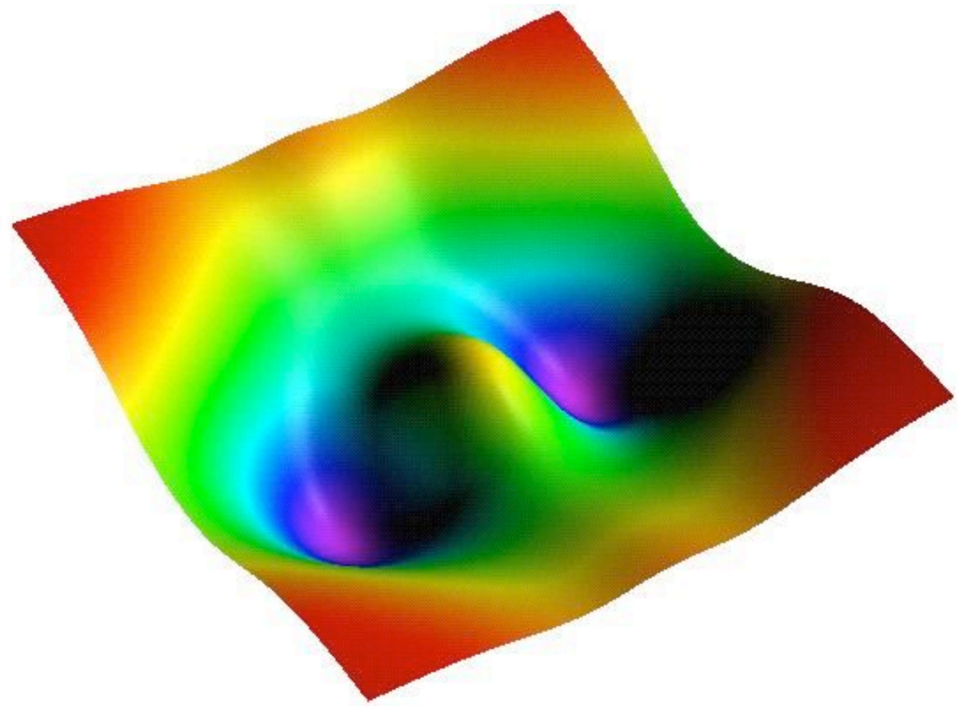


Geissler et al 2000

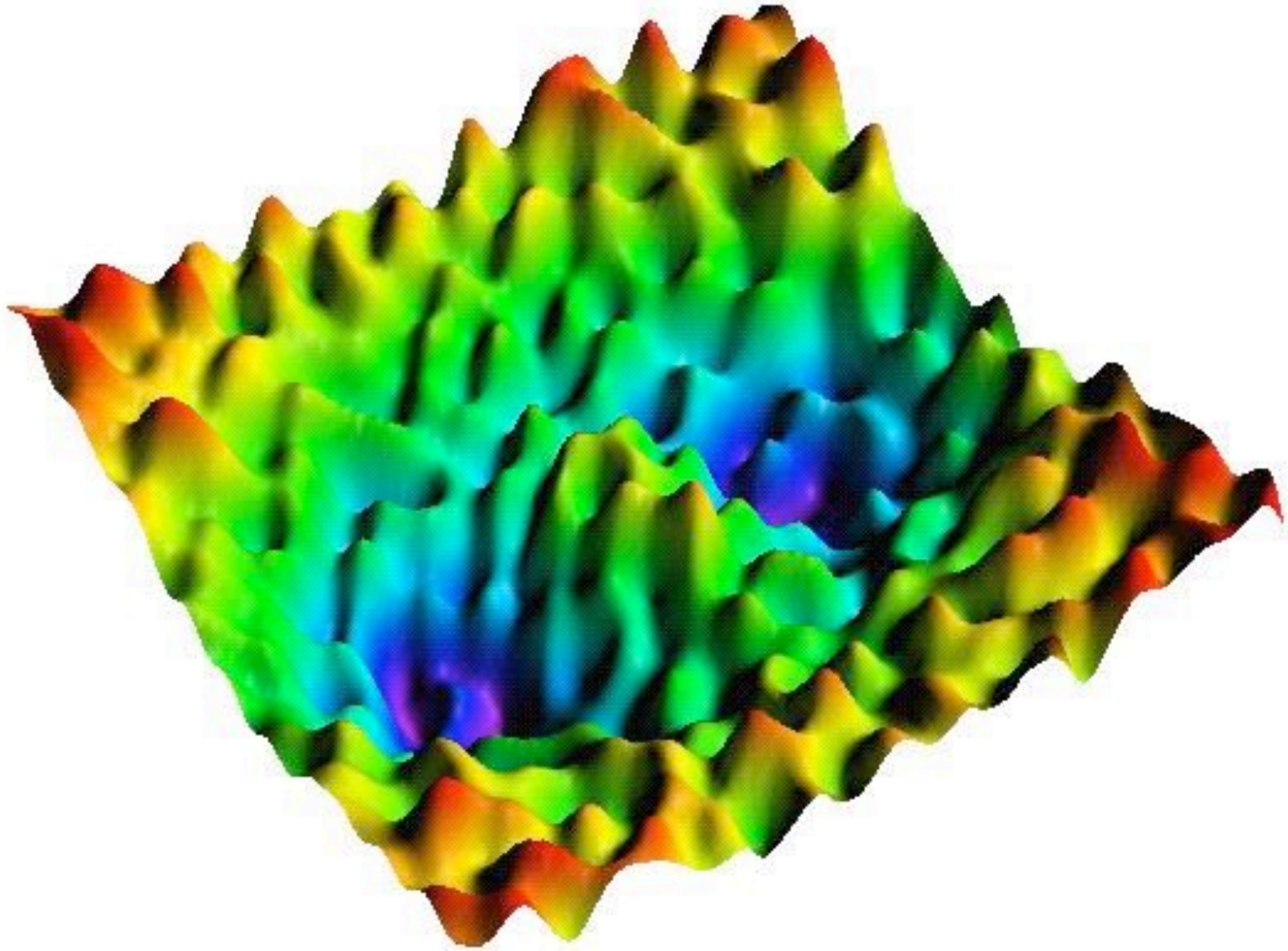
Open Problem:

Assume we obtained a transition path ensemble between two conformations of a protein, how do we write a paper describing what happens? -Peter Bolhuis





Open Problem : Intermediate Metastable states



Protein Evolution

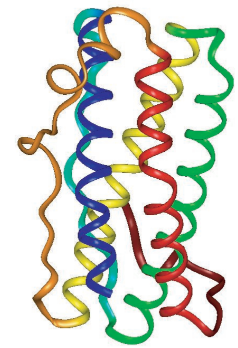
Sequence

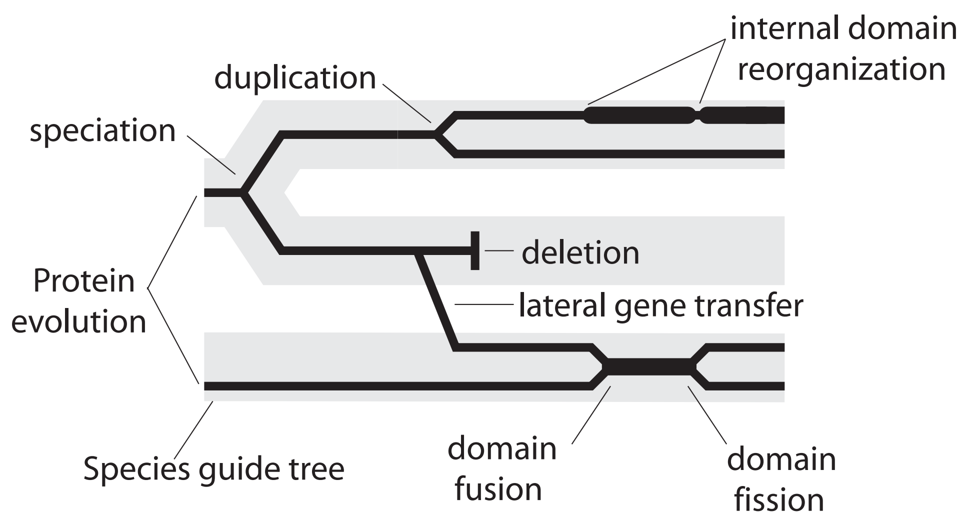
Structure and Function

...SLFAKLGGREA
VEAAVDKFYNKIVA
DPTVSTYFSN...

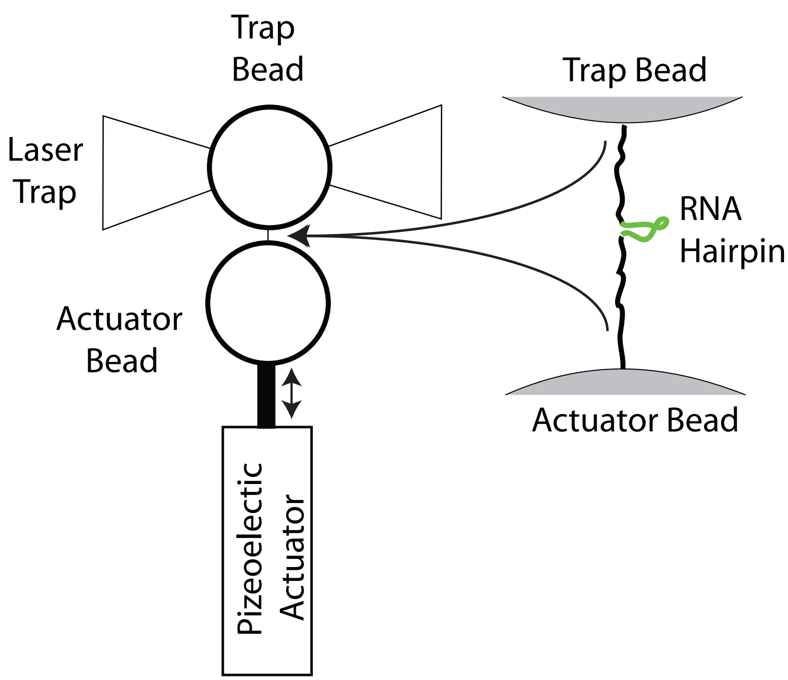
Folding

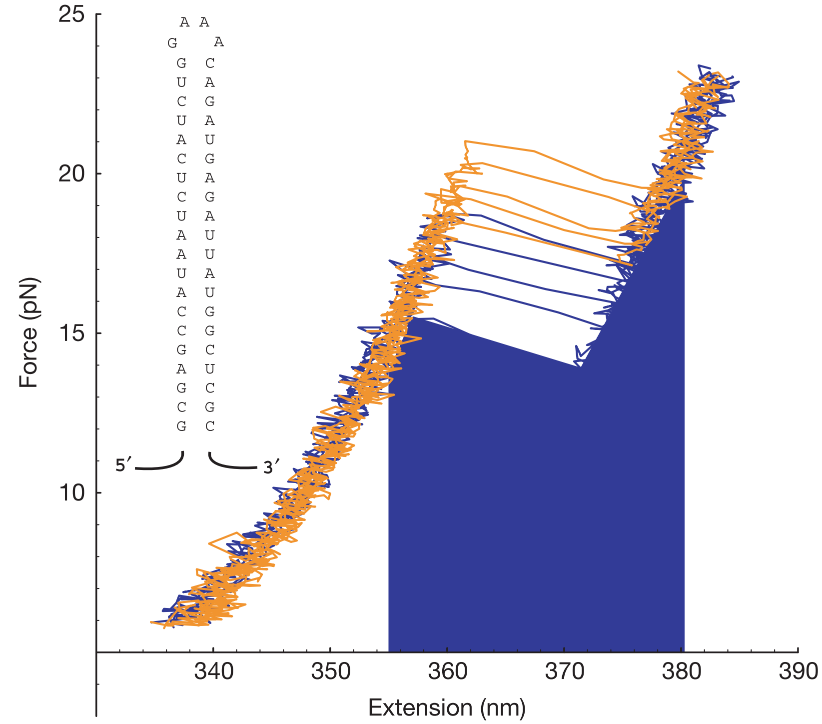
Evolution





RNA hairpin unfolding (& refolding)





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D. Collin, F. Ritort, C. Jarzynski, S.B. Smith, I. Tinoco, C. Bustamante (2005)

Clausius Inequality

(1865)

$$dS \geq \frac{1}{T} dQ$$

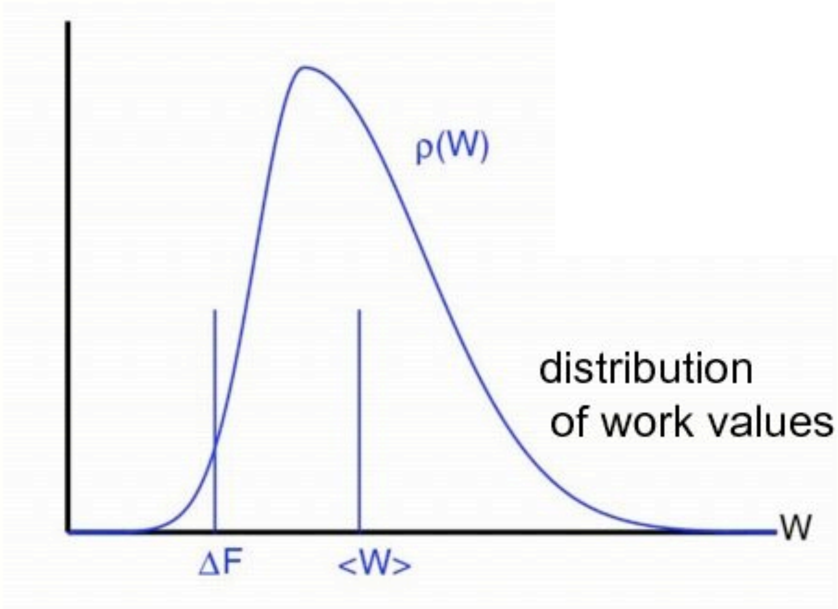
$$\Delta F \leq \langle W \rangle$$

Free Energy — Work

Jarzynski Equality

(1997)

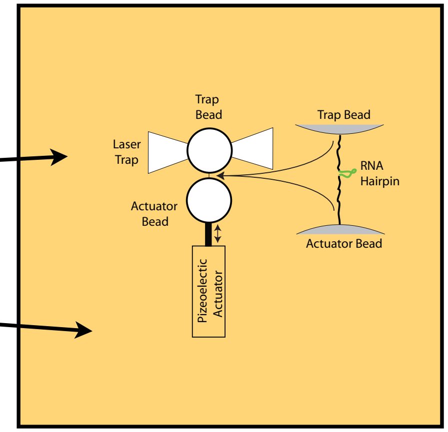
$$\langle e^{-\beta W} \rangle = e^{-\beta \Delta F}$$



Heat & Work

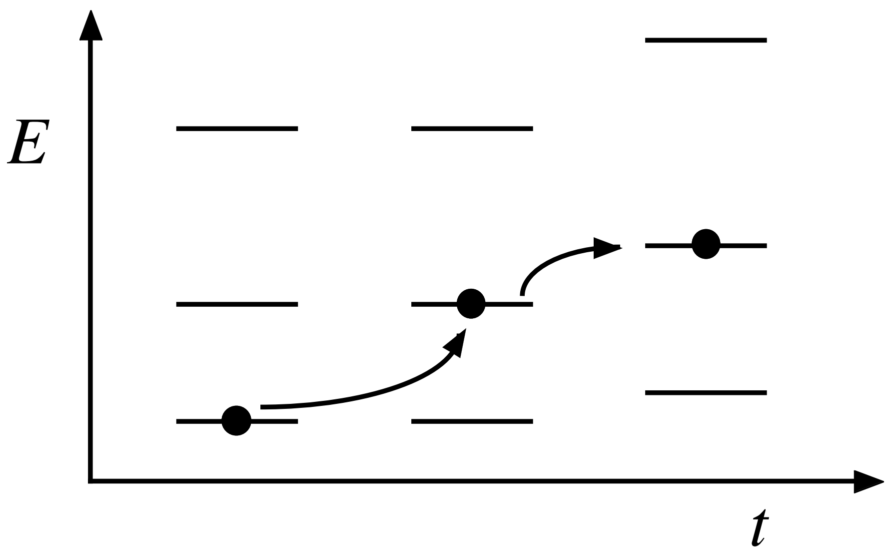
System of Interest

Thermal Environment



$$\Delta E = Q + W$$

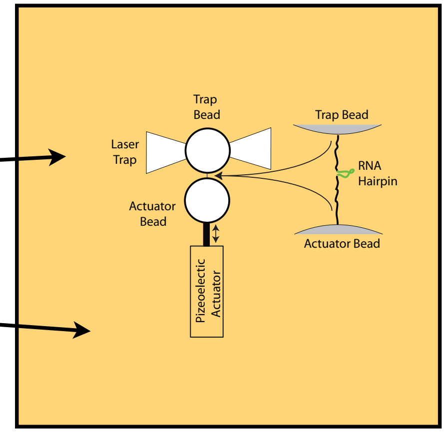
Internal Energy — Heat — Work



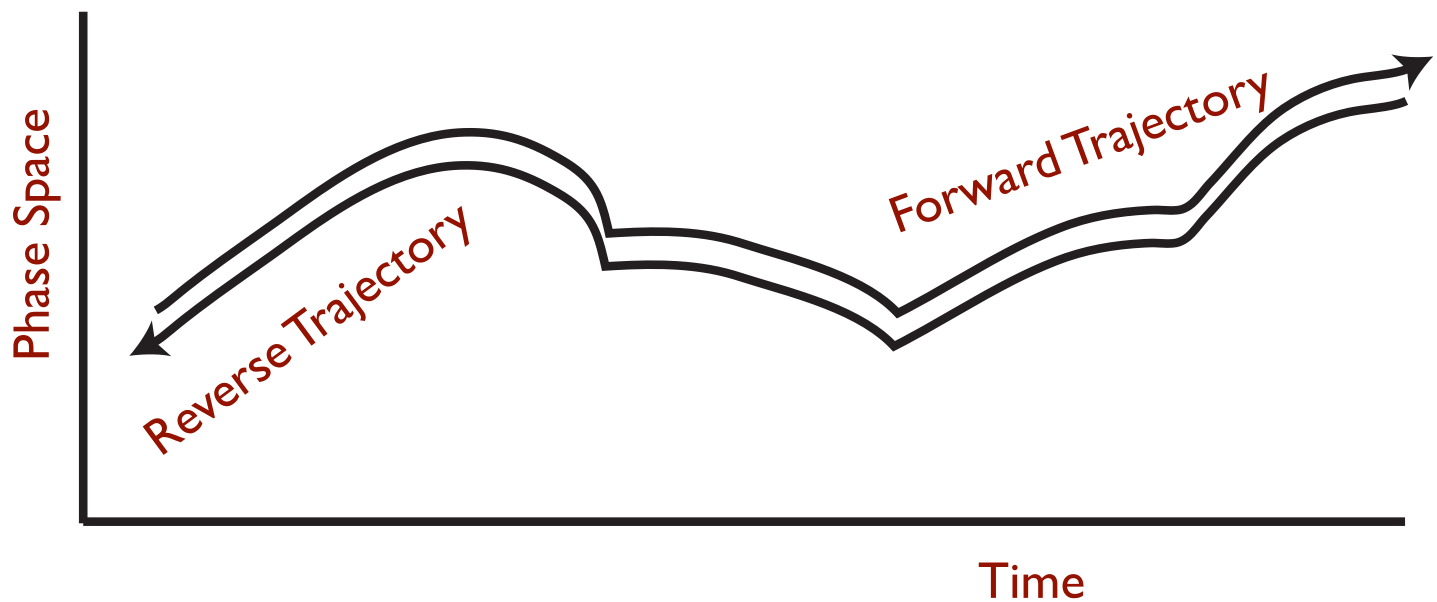
Time Reversibility

System of Interest

Thermal Environment



$$\frac{P(\text{Forward})}{P(\text{Reverse})} = e^{+\beta Q}$$ Heat



Work Fluctuation Theorem

Assumptions:

1) Equilibrium boundaries
2) Time-reversal symmetry

Forward protocol (e.g. compression, unfolding)

Work probability distribution

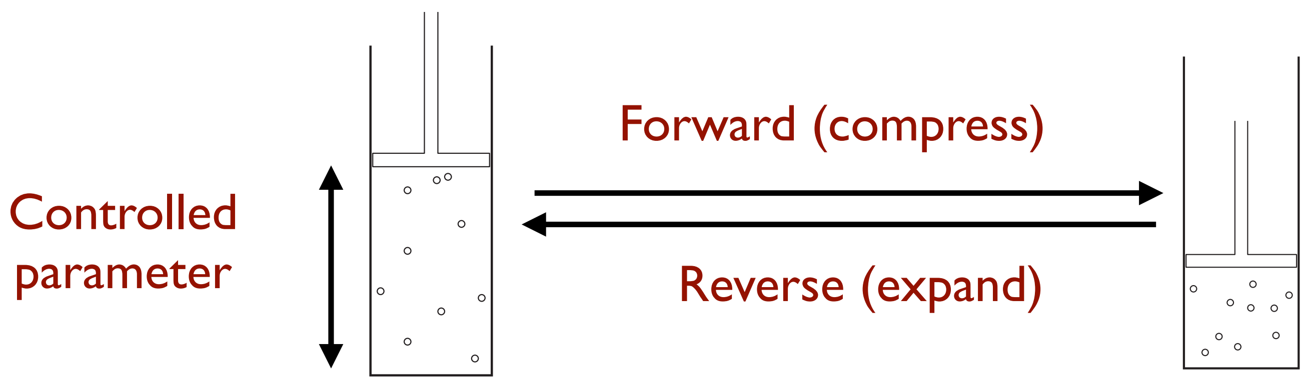
$$\frac{\rho_{\mathrm{F}}(+W)}{\rho_{\mathrm{R}}(-W)} = e^{\beta(W-\Delta F)}$$

Work

Free Energy Change

Conjugate reverse protocol (e.g., expansion, refolding)

Inverse Temperature



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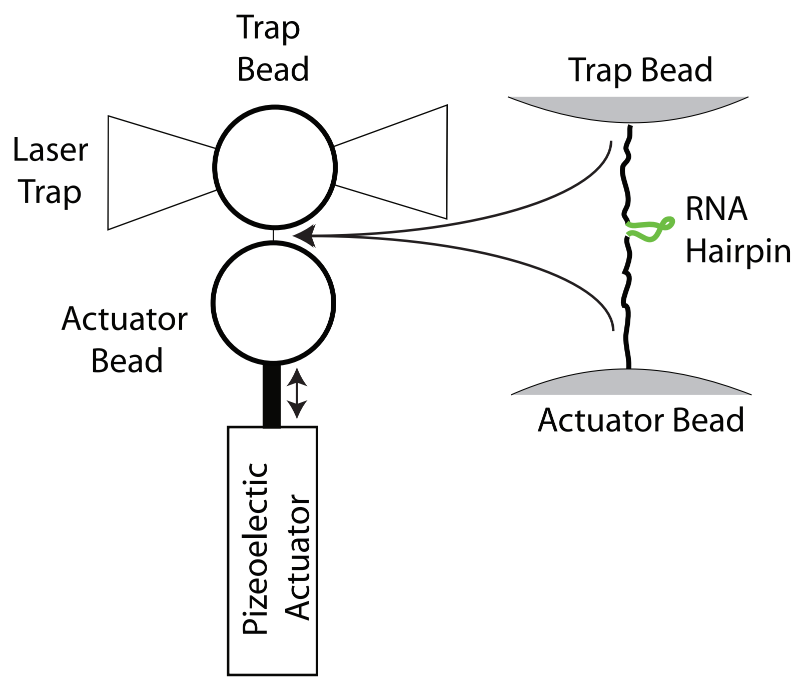

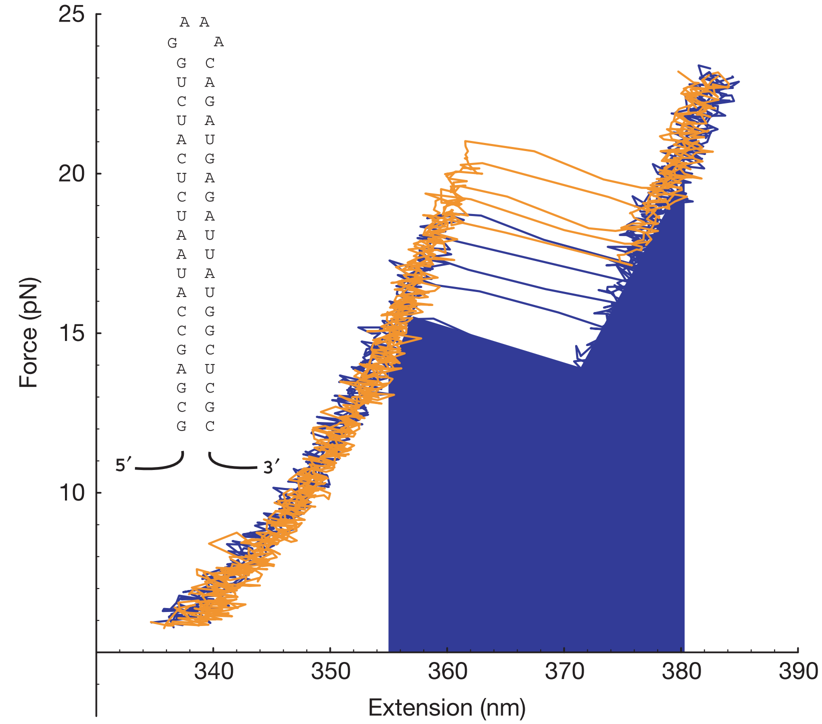

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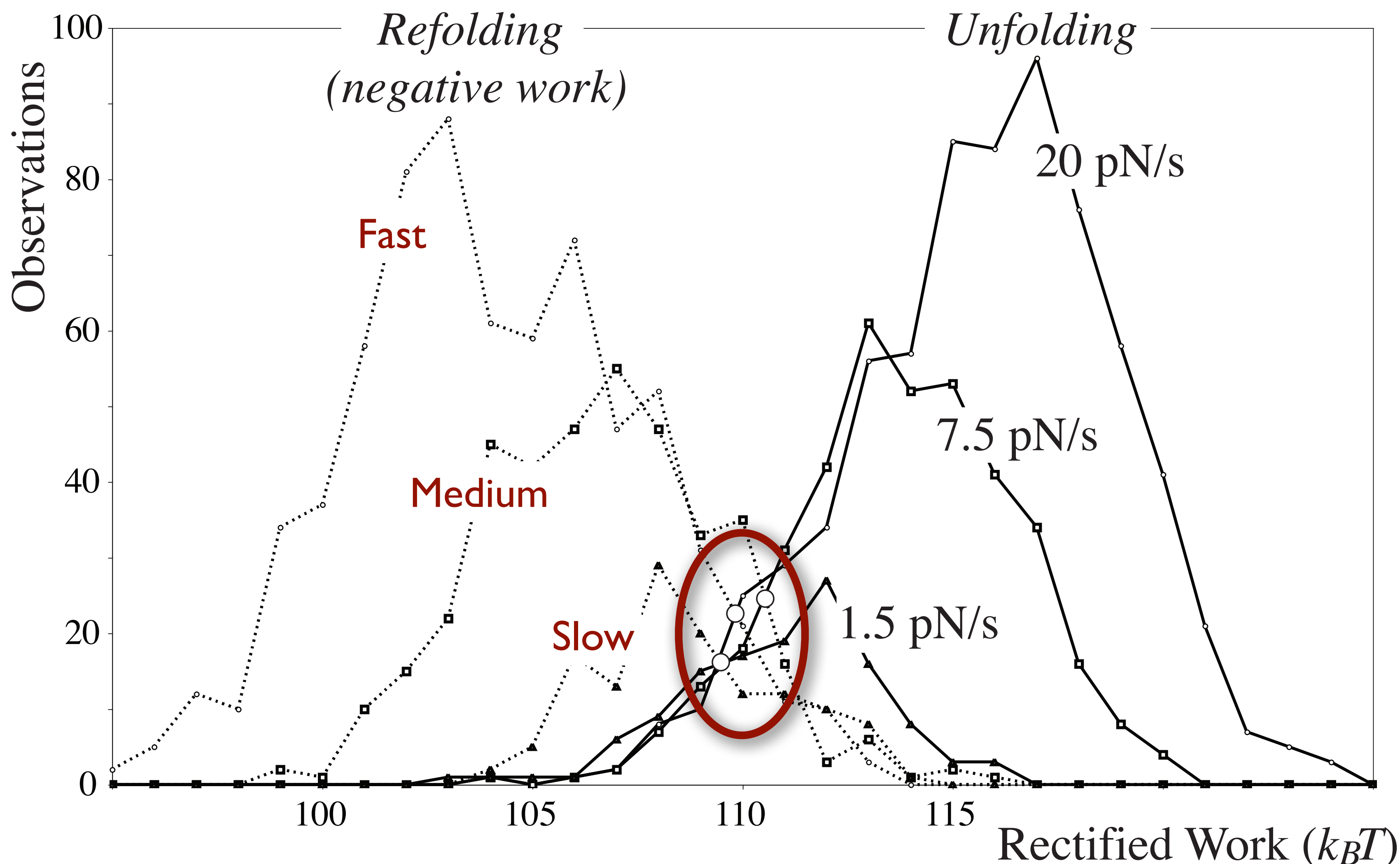
Work of Unfolding

$$\frac{\rho_{\rm F}(+W)}{\rho_{\rm R}(-W)} = e^{\beta(W-\Delta F)}$$



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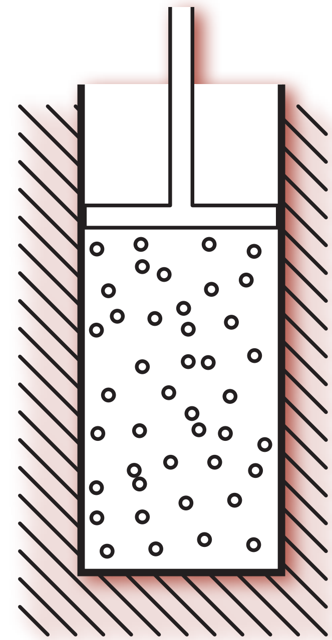
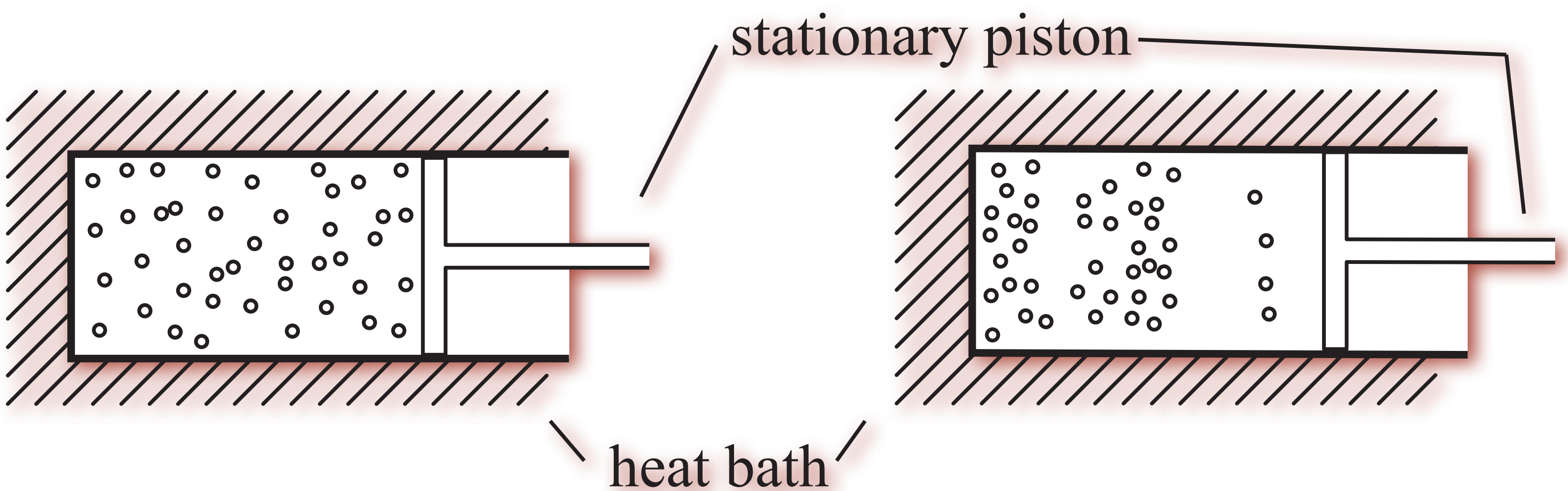


Non-Equilibrium Statistical Ensembles

What is the best description that we can construct of a thermodynamic system that is not in equilibrium, given only one (or a few) extra parameters over and above those needed for a description of the same system at equilibrium?



Non-Equilibrium Statistical Mechanics

What is the best description that we can construct of a thermodynamic system that is not in equilibrium, given only one (or a few) extra parameters over and above those needed for a description of the same system at equilibrium?

- Tsallis Statistics (Tsallis 1988)
  Maximize generalized q-entropy

$$S_q(\rho) = \frac{1}{q-1}(1 - \sum_i \rho_i^q)$$

- Superstatistics (Beck & Cohen 2002)

Canonical Hyperensemble

Entropic distribution

$$P(\theta) \propto \exp\left(-\lambda \sum_i \theta_i \log \frac{\theta_i}{\rho_i}\right)$$

Ensemble of ensembles

Relative entropy

$$D(\theta \| \rho) \geq 0$$

Reference distribution

$$\rho_i = \frac{1}{Q(\beta)} \exp(-\beta E_i)$$

Dispersion

$$\lambda \to \infty \quad \theta \to \rho$$

Effective Inverse Temperature

Open Problems

- Design principles of molecular machines.
- Transition path sampling with meta-stable intermediate states.
- Extracting meaningful reaction coordinates.
- Statistical ensembles out-of-equilibrium.
- Measuring non-equilibrium entropy.