Stochastic thermodynamics for the study of life

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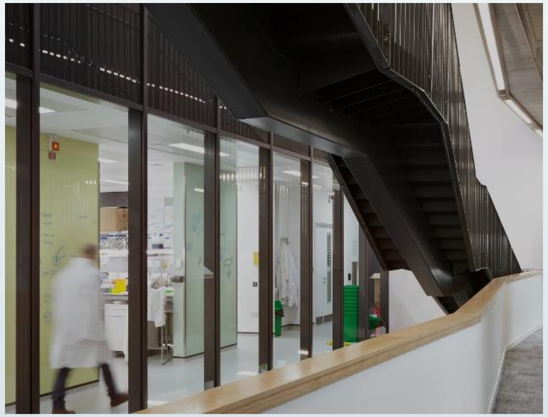
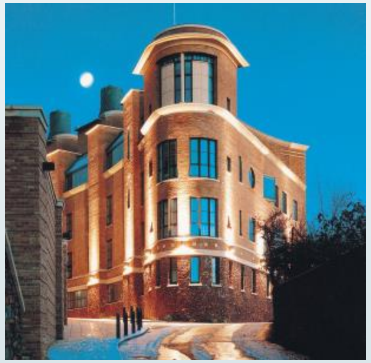


Living Systems Institute (Exeter)



University of Bristol

LSI seminar

2021, 27th January

An interdisciplinary approach to the physics of life


Jesús Rubio   Janet Anders

(quantum & stochastic thermo. + quantum info. & estimation)


Frank Vollmer   Jennifer Littlechild

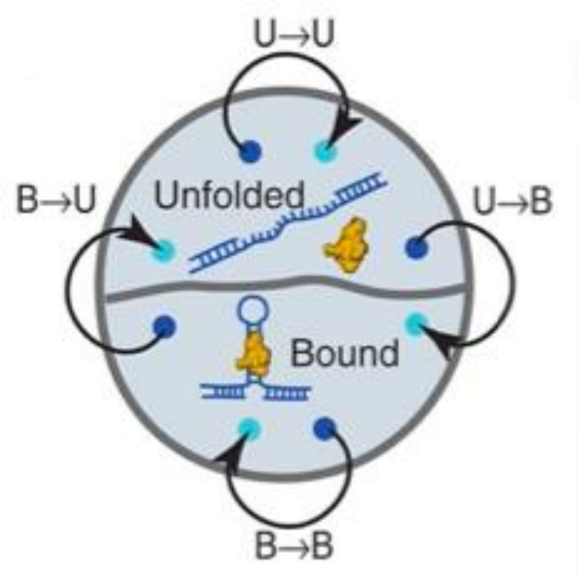
(nano & quantum biosensing + biochemistry)


Sofia Oliveira   Adrian Mulholland

(molecular dynamics simulations in chemistry)

- Interdisciplinary team with more than 20 scientists
- https://www.exeter.ac.uk/livingsystems/research/mmi/

Contents



Picture source: Camunas-Soler et al., Science 355, 412–415 (2017)

Life and the thermodynamics of small systems

Searching for the mechanisms of life in **molecular terms**

- Molecules associated with living organisms are at different energy levels than their surroundings -> **nonequilibrium**
- The direction of physical processes matters -> **irreversibility**, **second law**

transfers of energy

Thermodynamics

- Manipulation of **single molecules** to extract more detailed information (basic building blocks)
- Bulk averages of relevant quantities are no longer sufficient; *laws for their* ***fluctuations*** are also needed

Stochastic thermodynamics

U. Seifert 2012 Rep. Prog. Phys. 75 126001

Stochastic thermodynamics and the second law

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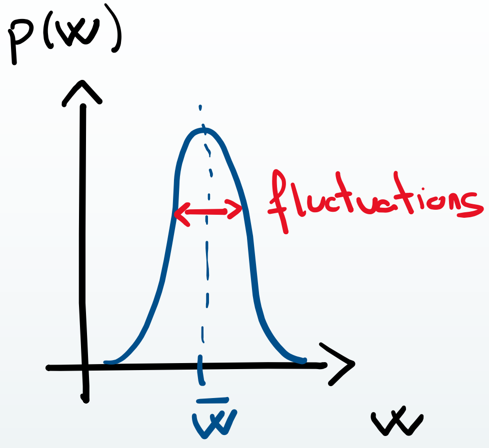
2nd LAW:

$$\underbrace{\overline{W}}_{\text{work on system}} \geq \overbrace{\Delta F}^{\text{free energy diff.}} \xrightarrow[\text{stochastic thermodynamics}]{} \langle W \rangle \geq \Delta F$$



THE POWER OF STOCHASTIC THERMODYNAMICS:

$$\underbrace{\frac{p(W \mid \Delta F, \Lambda)}{p(-W \mid \Delta F, \tilde{\Lambda})} = e^{\beta(W-\Delta F)}}_{\boxed{1}\ \text{Crooks relation}} \longrightarrow \underbrace{\langle e^{-\beta W} \rangle = e^{-\beta \Delta F}}_{\boxed{2}\ \text{Jarzynski equality}} \longrightarrow \underbrace{\langle W \rangle \geq \Delta F}_{\boxed{3}\ \text{Clausius statement}}$$

$\Rightarrow$ 2nd law refinement

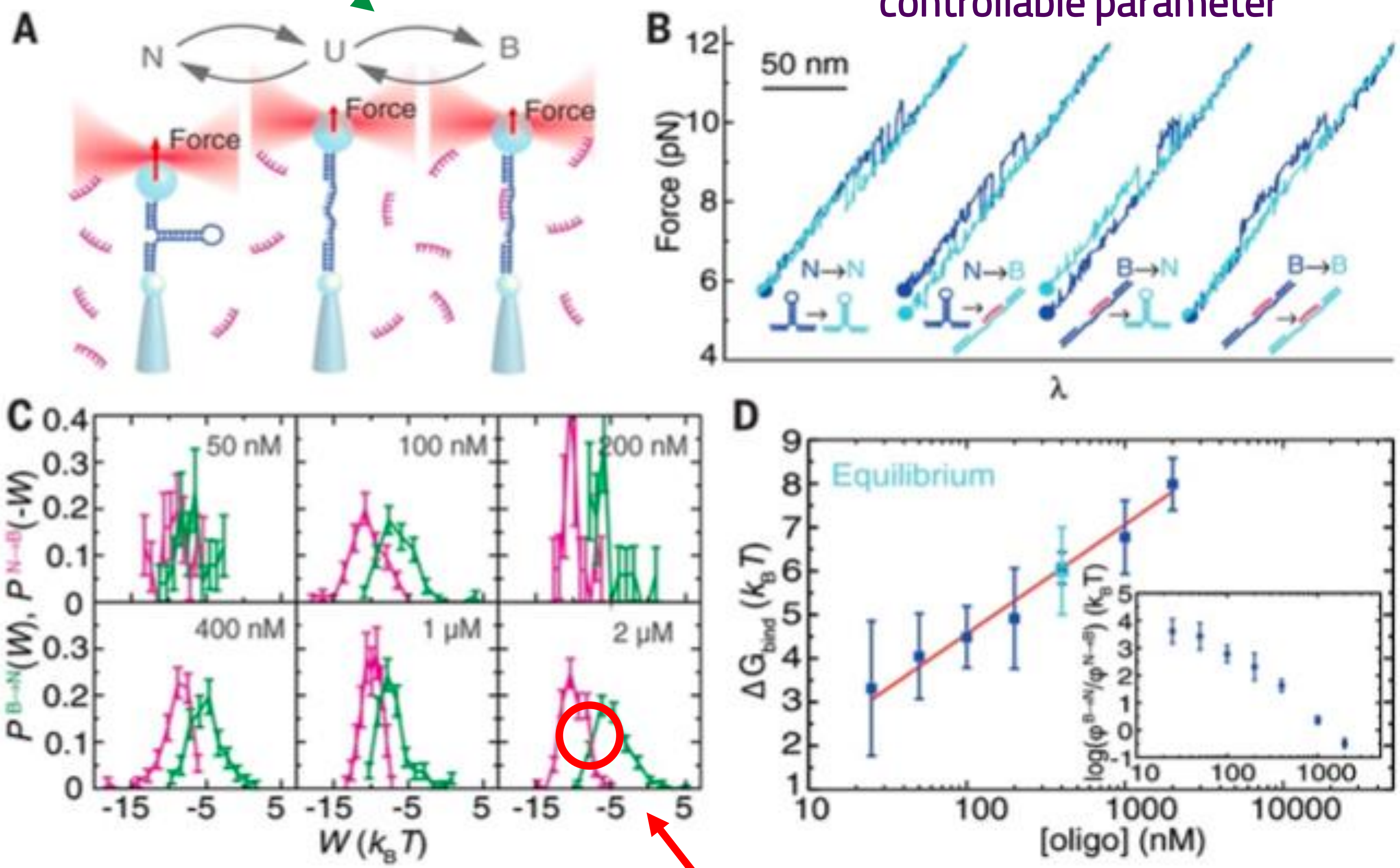
S. Vinjanampathy and J. Anders 2016 Contemporary Physics, 57, 545

U. Seifert 2012 Rep. Prog. Phys. 75 126001

Forwards and backwards protocol

Extension λ as the controllable parameter

Fig. 2. Oligonucleotide binding to DNA. (**A**) Scheme of N, U, and B states. (**B**) Cyclic pulling curves that start and end at low forces (~6 pN) classified according to their initial (blue dot) and final (cyan dot) state. (**C**) Partial work distributions of B → N (green) and N → B (magenta) transitions. (**D**) Binding energy of the 10-base oligonucleotide (blue) and fit to the law of mass action (red line). The value obtained from hopping equilibrium experiments at [oligonucleotide] = 400 nM is shown in cyan (see section S1.7 of the supplementary materials and methods). (D, inset) Contribution of the ratio $\phi^{N\to B}/\phi^{B\to N}$ to the binding energy. Error bars were obtained from bootstrap as described in Fig. 1.



Forwards and backwards histograms

Example of Crooks relation crossing point

Crooks relation + Bayes theorem: a finite-information approach to the estimation of free energy differences

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* We seek:

$$\underbrace{p(\Delta F \mid w, \Lambda)}_{\text{posterior}} \propto \underbrace{p(\Delta F)}_{\text{prior}} \, \underbrace{p(w, \Lambda \mid \Delta F)}_{\text{likelihood}}$$

* Available information:

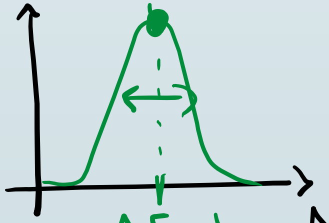
1. $p(\Delta F) \propto 1$
2. Crooks relation
3. $p(w, \Lambda \mid \Delta F) + p(-w, \hat{\Lambda} \mid \Delta F) \propto 1$
4. $\{(w_1, \Lambda_1), (w_2, \Lambda_2), \ldots\}$

$\Rightarrow$

$$p(\Delta F \mid w_1, \Lambda_1, w_2, \Lambda_2, \ldots) \propto \prod_k f\left[\beta\left(w_k - \Delta F_{\Lambda_k}\right)\right]$$

with

$$f(x) = 1/(1 + e^{-x})$$

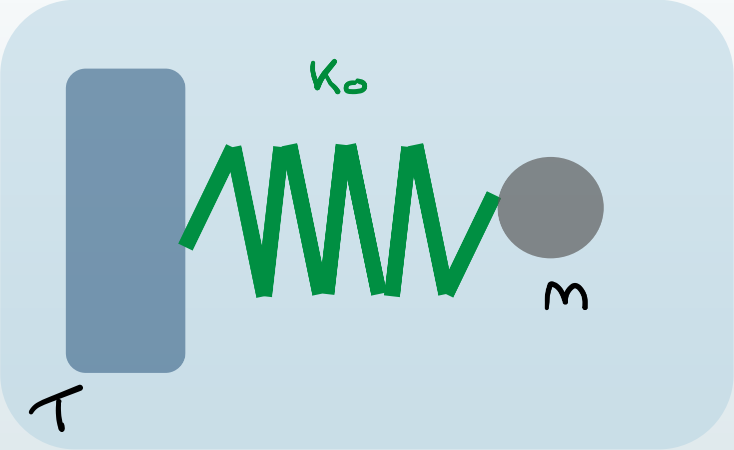


P. Maragakis et al. 2008 J. Chem. Phys. 129, 024102
J. Rubio and J. Dunninham 2019 New J. Phys. 21 043037

Harmonic oscillator protocol

Energy: $H(q, p) = \frac{p^2}{2m} + \frac{m\omega^2 q^2}{2}$, with $\omega = \sqrt{\frac{k}{m}}$

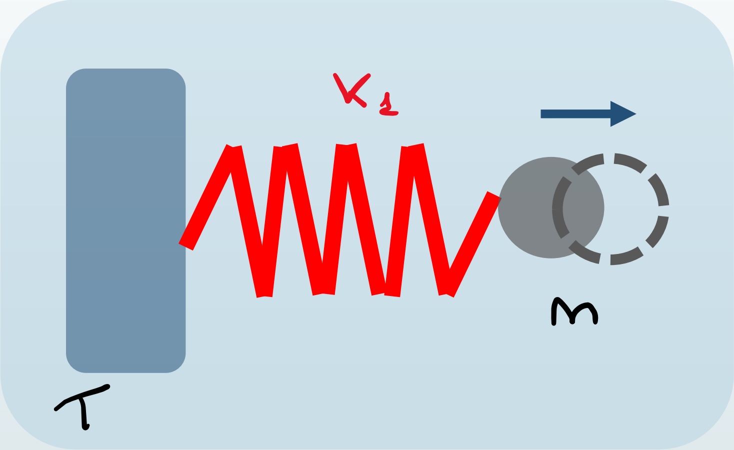
position momentum



equilibrium state

$k_0 \longrightarrow k_1$

$\omega_0 \longrightarrow \omega_1$



non equilibrium state

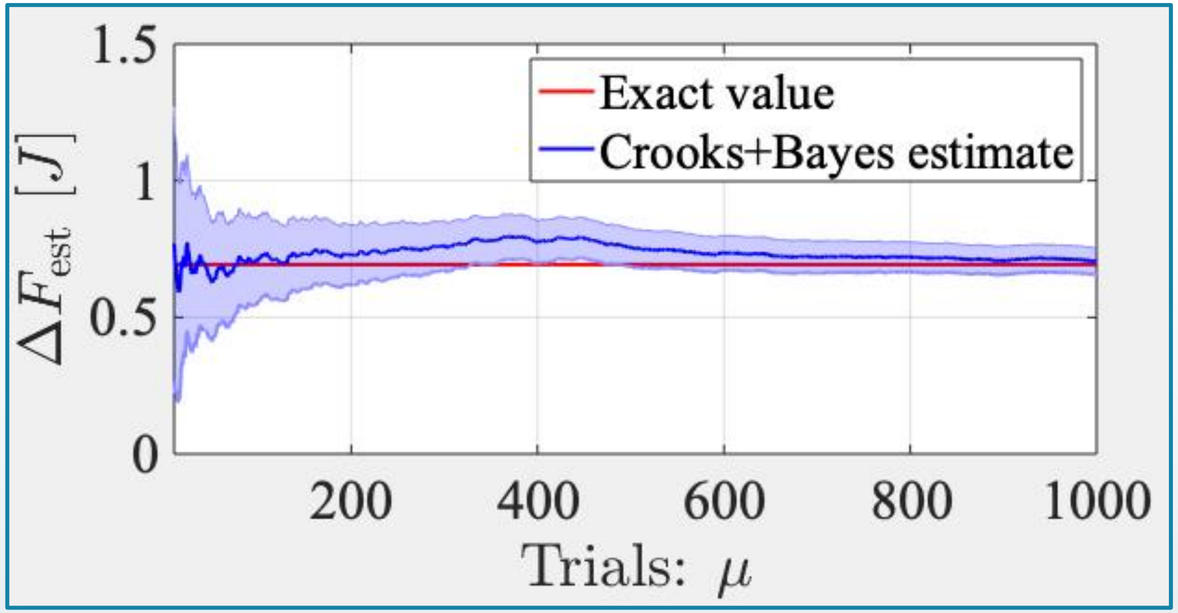
* Work associated with shift of controllable parameter:

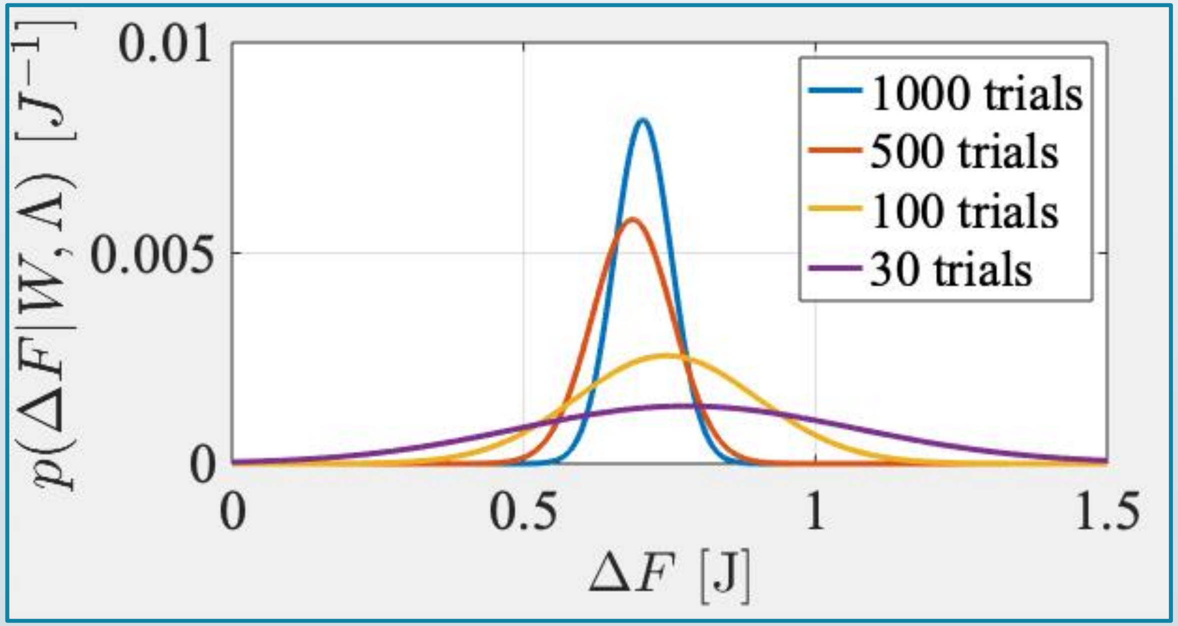
$$\left[W = H(q_1^i, p_1^i) - H(q_0^i, p_0^i) \equiv \Delta H_i \right]$$

instantaneous protocol

initial

Harmonic oscillator protocol: free energy estimates



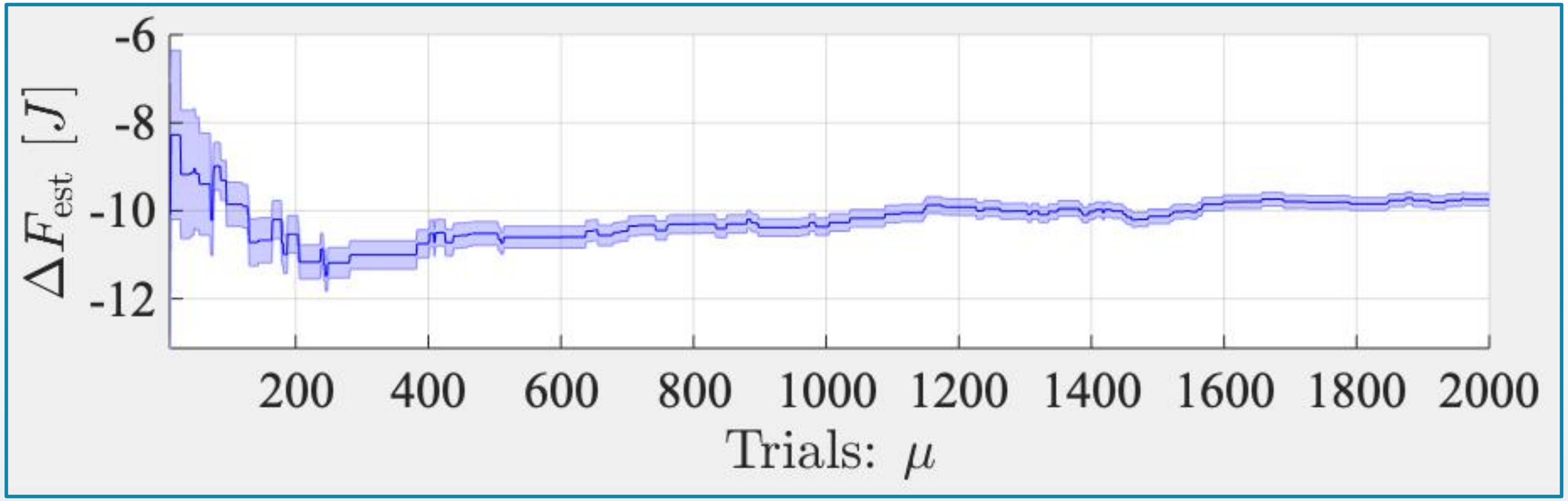


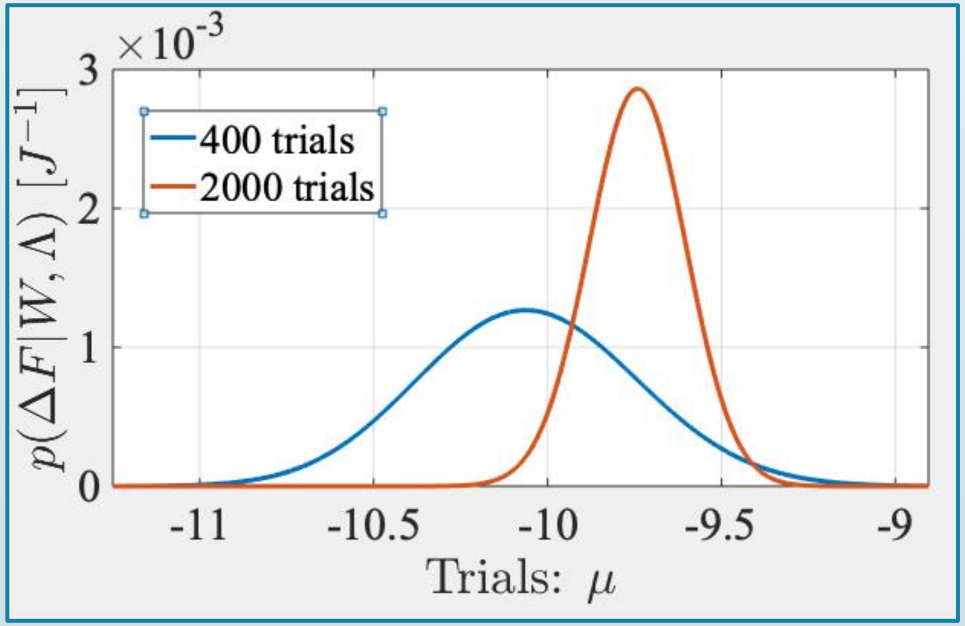
$$\boxed{\Delta F_{\mathrm{exact}} = \log 2\, J \simeq 0.69\, J}$$

Trials	Estimate [J]	Error [J]
30	0.8	0.3
100	0.8	0.2
500	0.69	0.07
1000	**0.70**	**0.05**

✓

Single-molecule redox reaction as a stochastic-thermodynamical protocol





$V_{\mathrm{exp}} = -11$ kJ/mol

Trials	Estimate [kJ/mol]	Error [kJ/mol]
400	-10.1	0.3
2000	-9.7	0.1

Conclusions and outlook

- **Stochastic thermodynamics** studies transfers of energy and their fluctuations in small systems. It thus **enables the study of the nonequilibrium aspects of life**.
- **Fluctuation theorems** enable the measurement of quantities such as binding energies or redox potentials in situations where traditional bulk measurements may be inaccurate or unfeasible.
- The MMI is implementing a **realistic, finite-information** estimation approach to the estimation of free energy differences in biological protocols.

Thank you for your attention!

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