BIRS workshop, Banff, July 2020

From stochastic thermodynamic to thermodynamic inference

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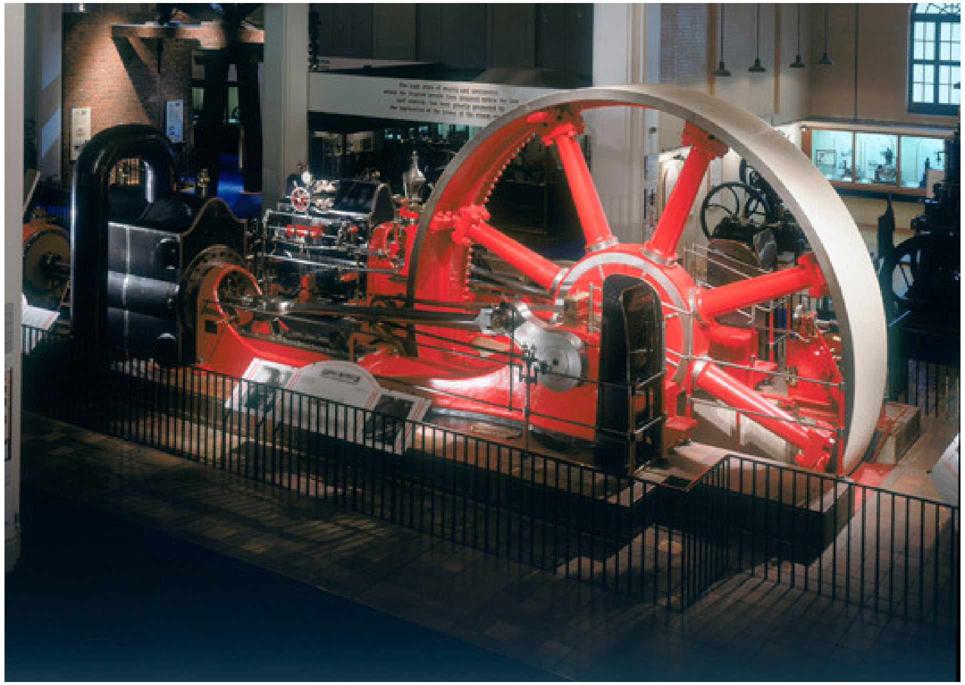
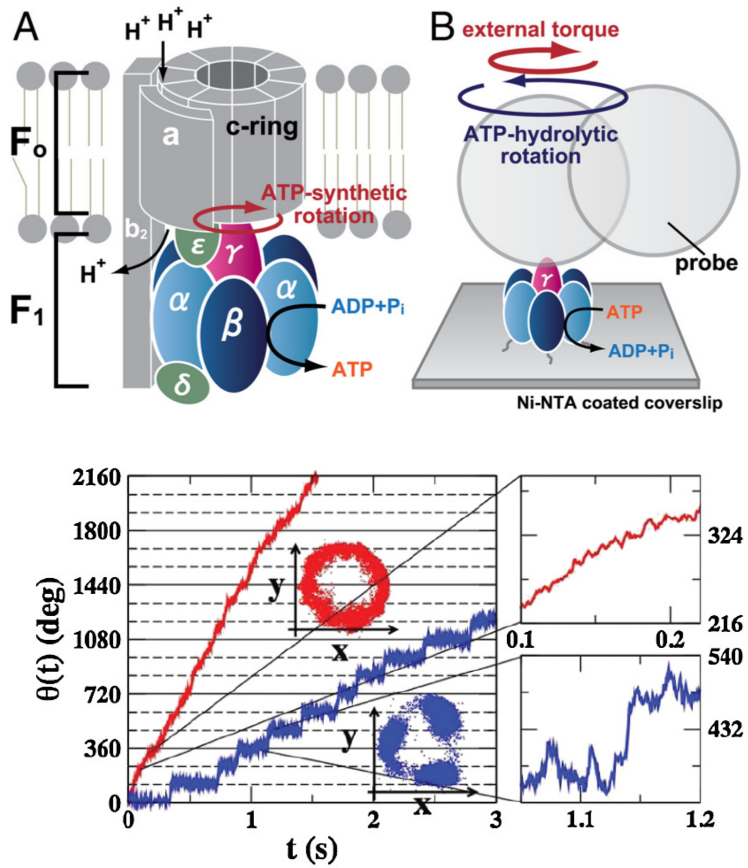
- Principles of stochastic thermodynamics
- Molecular motors as paradigm
- Cost of temporal precision
- (Modelfree) inference from experimental data
- Efficiency of cellular information processing

• From classical th'dynamics to stochastic th'dynamics



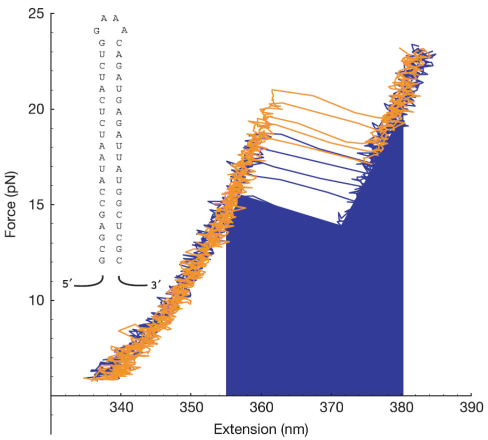


[K. Hayashi, ... H. Noji, PRL 104, 218103 (2010)]

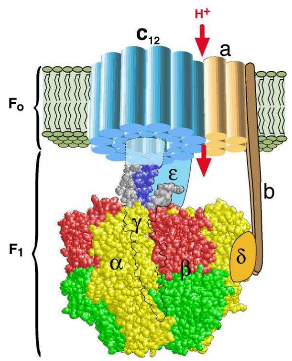
19^{th} century steam engine

21^{st} century nano-engine: F_1ATP-ase

- **Stochastic thermodynamics** applies to systems for which
  - non-equilibrium is caused by mechanical or chemical forces
  - ambient solution provides a thermal bath of well-defined T and μ_i
  - fluctuations are relevant due to small numbers of involved molecules



[Collin et al, Nature 437, 231, 2005]

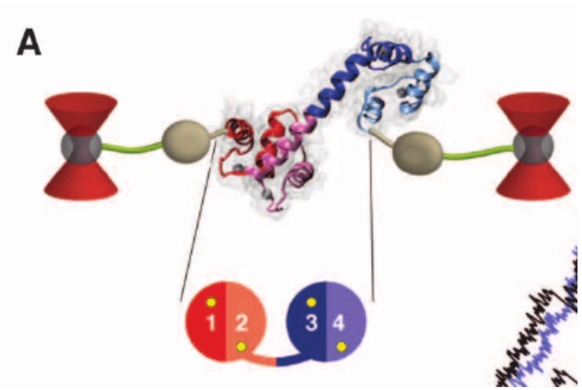


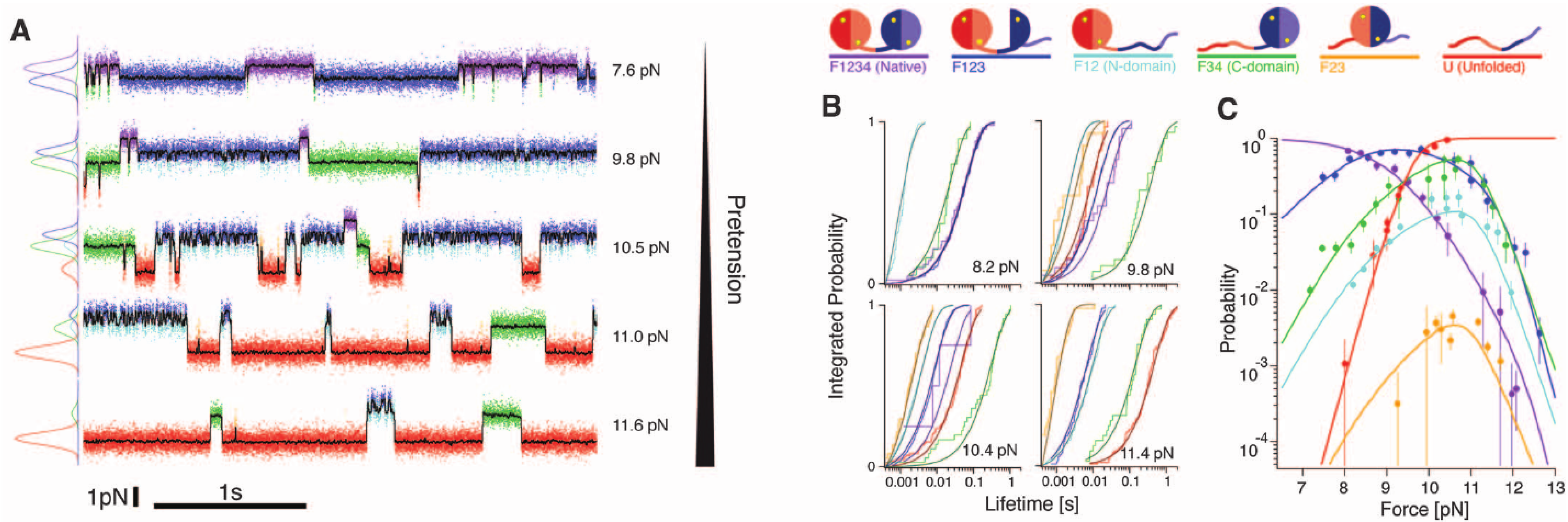
H. Wang and G. Oster (1998). Nature 396:279-282.

- Main idea: Energy conservation (1^{st} law) and entropy production (2^{nd} law) along an individual stochastic trajectory

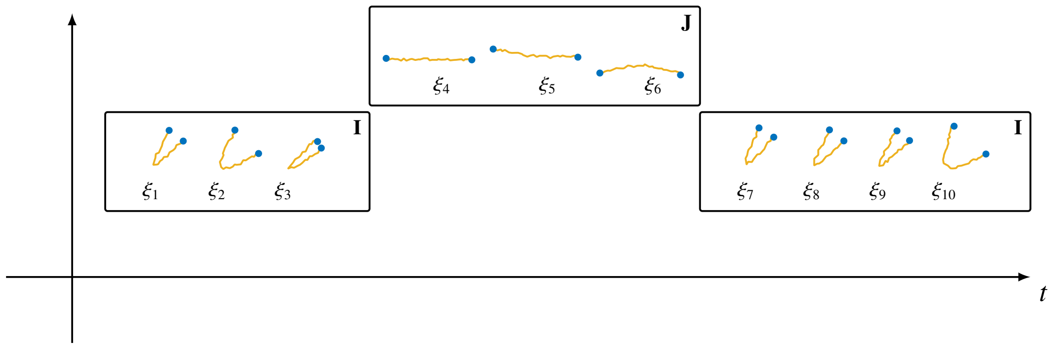
- Review: U.S., Rep. Prog. Phys. **75** 126001, 2012.

• Biomolecules in equilibrium: Meso-states of calmodulin [J. Stigler et al, Science **334** 512 (2011)]





- Thermodynamically consistent markovian dynamics on meso-states



- trajectory $I(t)$
- crucial time-scale separation:
  * transitions between meso-states are slow
  * transitions between the micro-states belonging to one meso-state are fast
- master equation

$$\partial_t P_I(t) = \sum_J [P_J(t) K_{JI} - P_I(t) K_{IJ}].$$

- local detailed balance condition on the rates $\{K_{IJ}\}$

$\Rightarrow$ $K_{IJ}/K_{JI} = P_J^e/P_I^e = \tau_J^e/\tau_I^e = \exp(-\beta \Delta_{IJ} F) = \exp(-\beta \Delta_{IJ} E + \Delta_{IJ} S)$

- th'dyn potentials of meso-states operationally accessible from traj' data

- Thermodynamics along a trajectory $I(t)$ of biochemical/physical meso-states

[T. Schmiedl and U.S., J. Chem. Phys. 126, 044101 (2007)]

  – internal energy $E(t) = E_{I(t)}$ becomes stochastic

  – first law (Sekimoto 1998) $\Delta_{IJ}E \equiv E_J - E_I = -Q_{IJ}$

  – entropy of "system" $S_{\text{sys}}(t) \equiv S_{I(t)} - \ln[P_{I(t)}(t)]$

  – total entropy change in a transition from I to J at time t

$$\Delta_{IJ}S_{\text{tot}}(t) = \beta Q_{IJ} + \Delta_{IJ}S_{\text{sys}}(t) = \ln[P_I(t)K_{IJ}/P_J(t)K_{JI}]$$

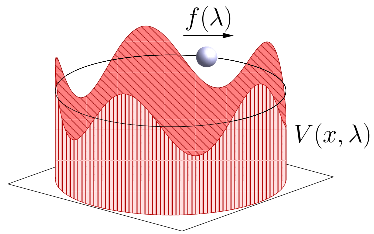
  – integral fluctuation theorem for total entropy production

$$\langle \exp[-\Delta S_{\text{tot}}]\rangle = 1 \quad \Rightarrow \langle \Delta S_{\text{tot}}\rangle \geq 0$$

    * any lengths t, any initial distribution $\{P_I^0\}$ [U.S., PRL 2005]

  – second law on ensemble level (Schnakenberg 1976)

$$\langle \dot{S}_{\text{tot}}(t)\rangle \equiv \sum_{IJ} P_I(t)K_{IJ}\Delta_{IJ}S_{\text{tot}}(t) \geq 0$$



- Stochastic th'dynamics of NESS: Driven colloidal particle as paradigm
  - Langevin dynamics $\dot{x} = \mu[-V'(x) + f] + \zeta$ with $\langle \zeta_1 \zeta_2 \rangle = 2\mu T \delta(t_2 - t_1)$
  - first law [(Sekimoto, 1997)]: $\boxed{dw = du + dq}$
    - applied work: $dw = f\ dx$
    - internal energy : $du = dV$
    - dissipated heat: $dq = dw - du = [-\partial_x V(x) + f]dx = T ds_b$
  - total entropy as quantitive measure of broken time reversal symmetry

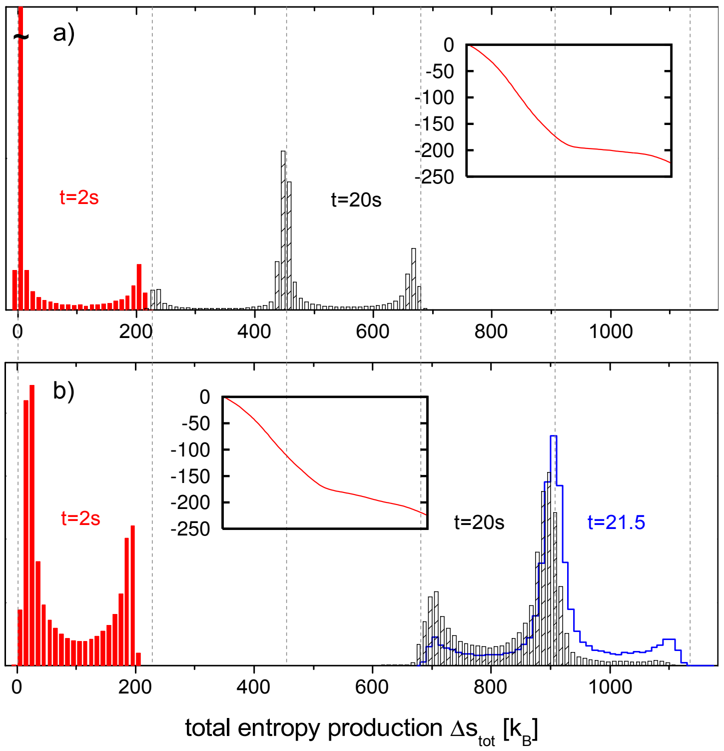
$$x(t) \to \tilde{x}(t) \equiv x(\mathcal{T} - t) \qquad \boxed{\Delta s_{\text{tot}}[x(t)] \equiv \ln[p[x(t)]/p[\tilde{x}(t)]] = \Delta[-\ln p^s(x)] + q/T}$$

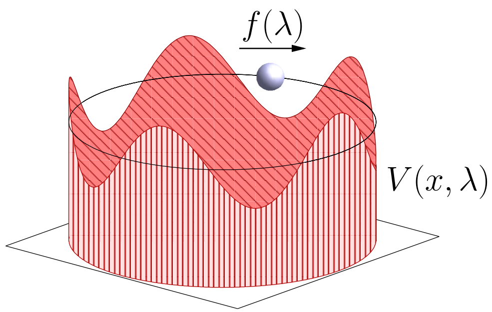
  - IFT for total entropy production $\boxed{\langle \exp[-\Delta s_{\text{tot}}] \rangle = 1 \Rightarrow \langle \Delta s_{\text{tot}} \rangle \geq 0}$ [U.S., PRL 2005]

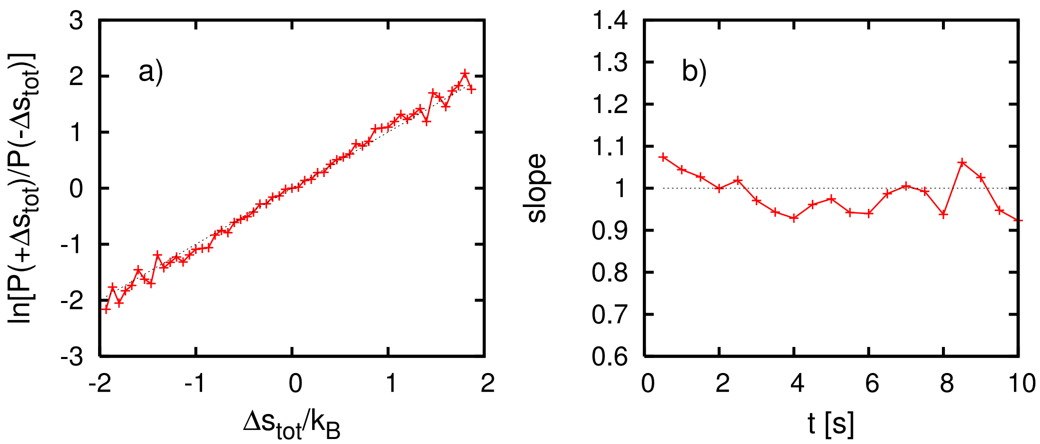
- Fluctuation theorem $\boxed{p(-\Delta s_{\rm tot})/p(\Delta s_{\rm tot}) = \exp(-\Delta s_{\rm tot})}$ in any NESS

  Evans et al (1993), Gallavotti & Cohen (1995), Kurchan (1998), Lebowitz & Spohn (1999), U.S. (2005)

- Experimental data [Speck, Blickle, Bechinger, U.S., EPL **79** 30002 (2007)]

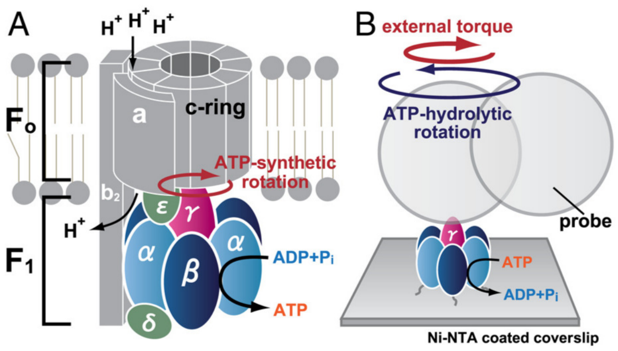


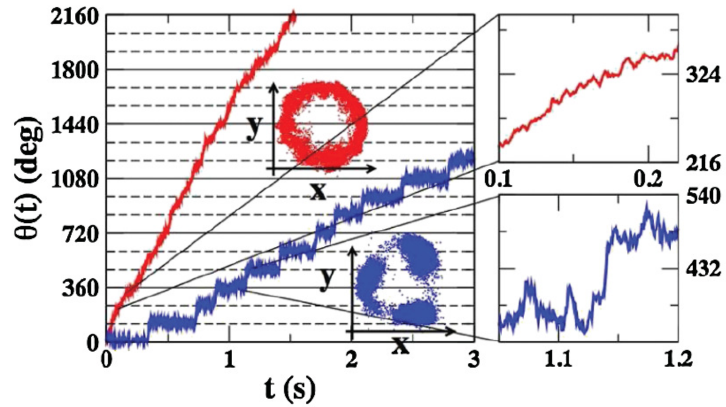


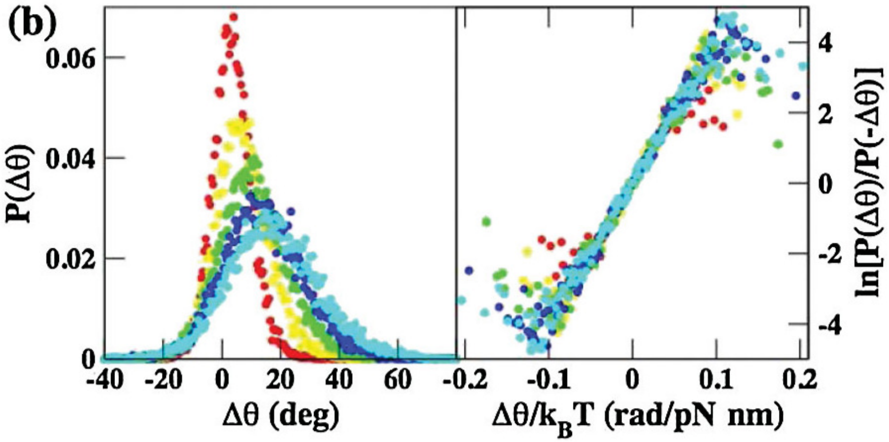


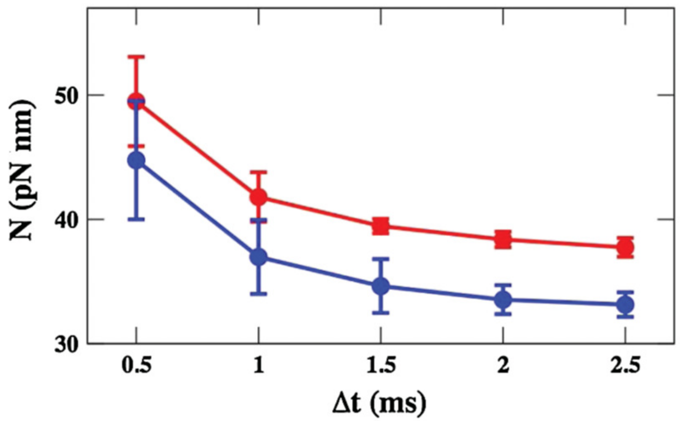
FT-representation

- F1-ATPase and the fluctuation theorem [K. Hayashi et al, PRL 104, 218103 (2010)]









$\Gamma\dot{\theta} = N + \zeta$

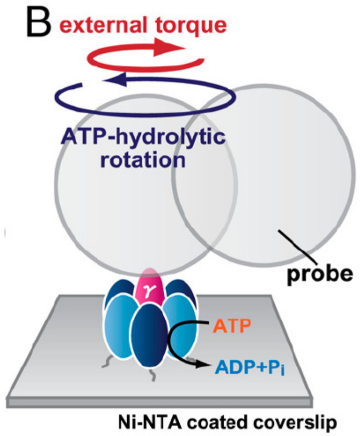
$\Rightarrow \ln[p(\Delta\theta)/p(-\Delta\theta)] = N\Delta\theta/k_B T$

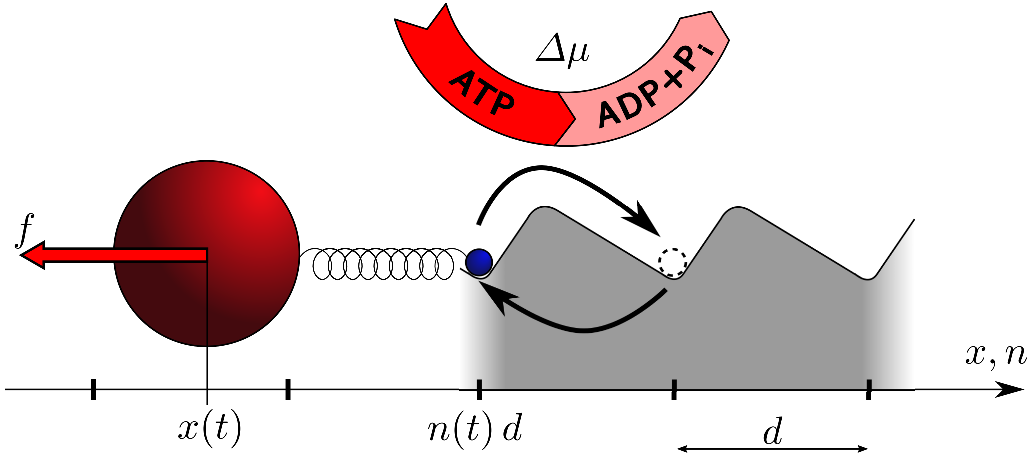
independent of friction coefficient Γ

time-dependence?

torque N from $\Delta t \to \infty$?

- Hybrid model [E. Zimmermann and U.S., New J. Phys. 14, 103023, 2012]





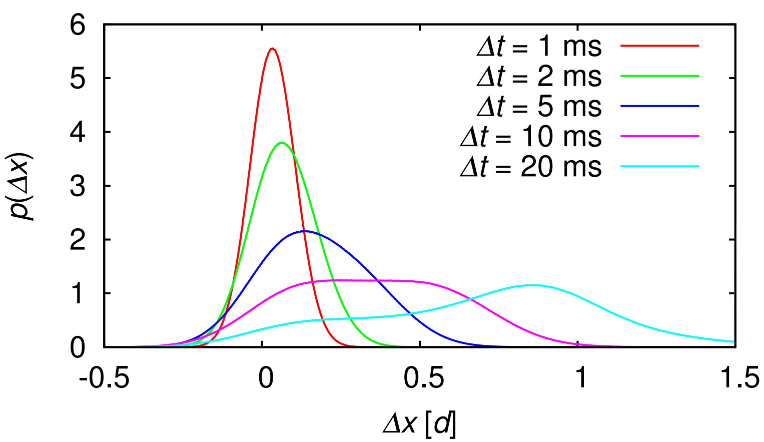
  - probe particle

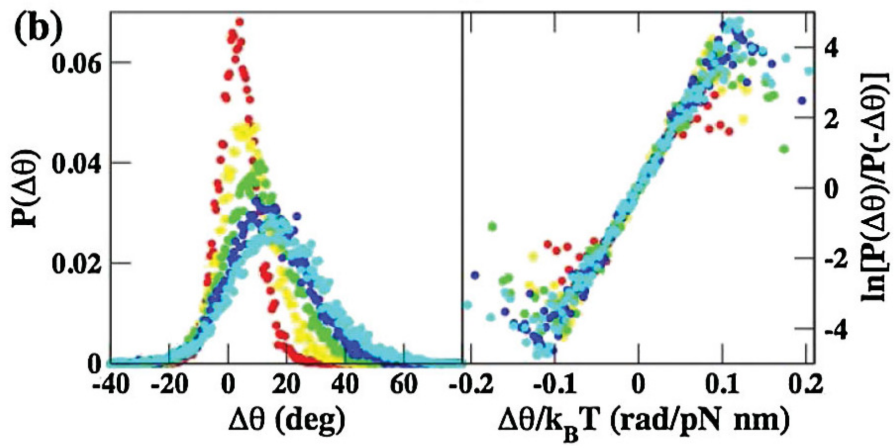
    * $\dot{x} = \mu(-\partial_y V(y) + f^{\text{ex}}) + \zeta$ with $y(\tau) \equiv n(\tau) - x(\tau)$

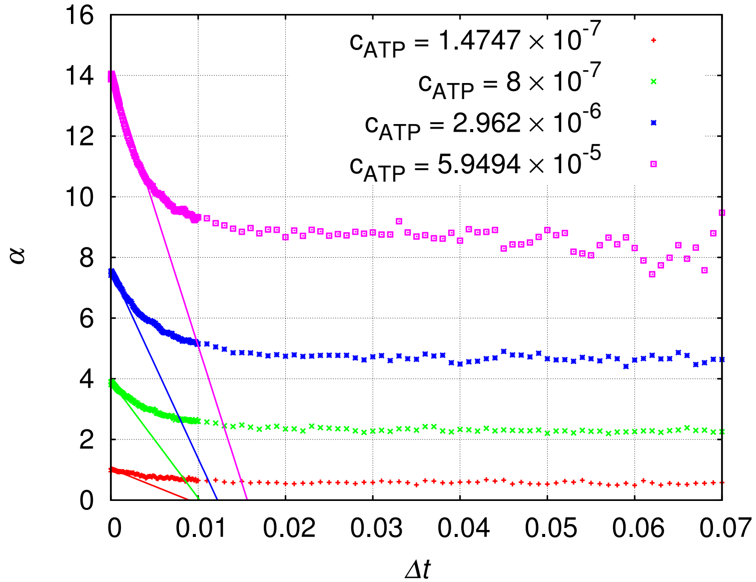
  - motor

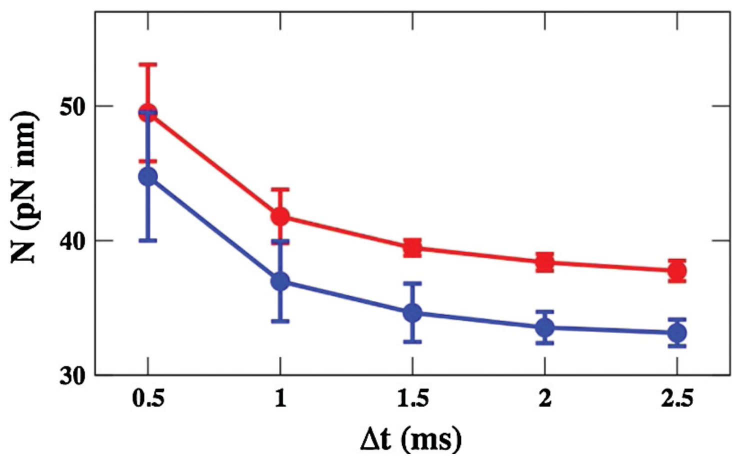
    * $w^+/w^- = \exp[\Delta\mu - V(n+d,x) - V(n,x)]$

- FT-slope from simulations vs experiment



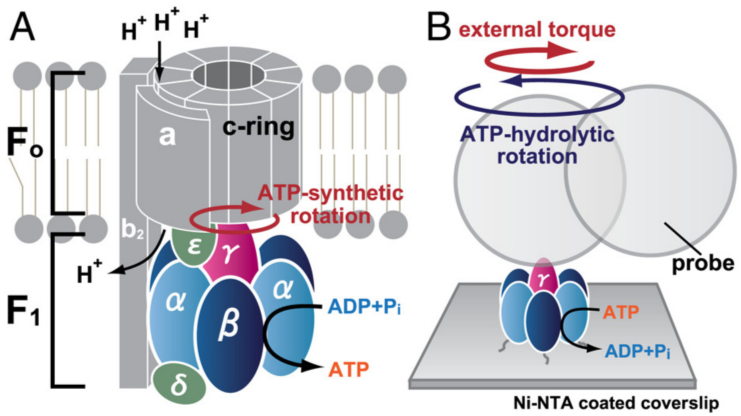


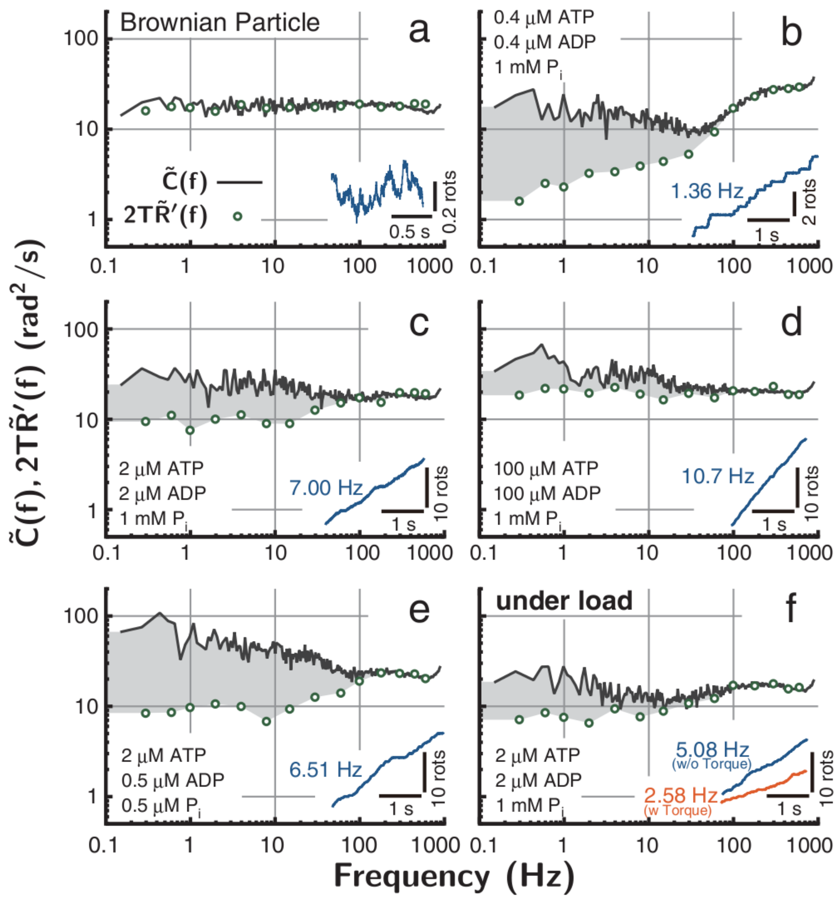




$\Delta t \to 0$ limit yields average force/torque

- Inferring the efficiency of a molecular motor [S. Toyabe et al, PRL 104, 198103 (2010)]

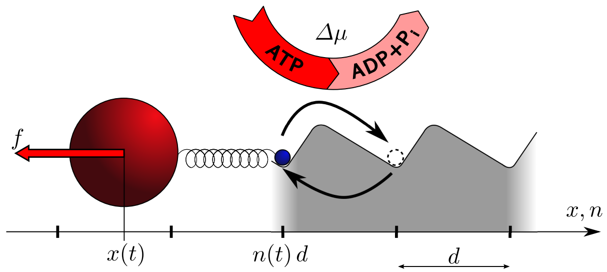




– Harada-Sasa relation [PRL 2006]

$$\mu \dot{Q}_P = v^2 + \int d\omega [C_{\dot{x}}(\omega) - 2k_B T \; \mathrm{Re} R_{\dot{x}}(\omega)]$$

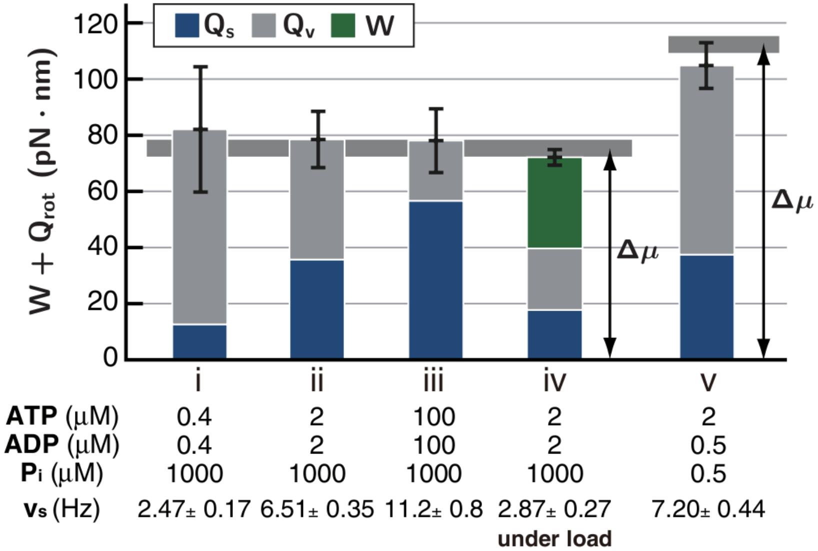
heat from "violation" of fluc-diss-theorem

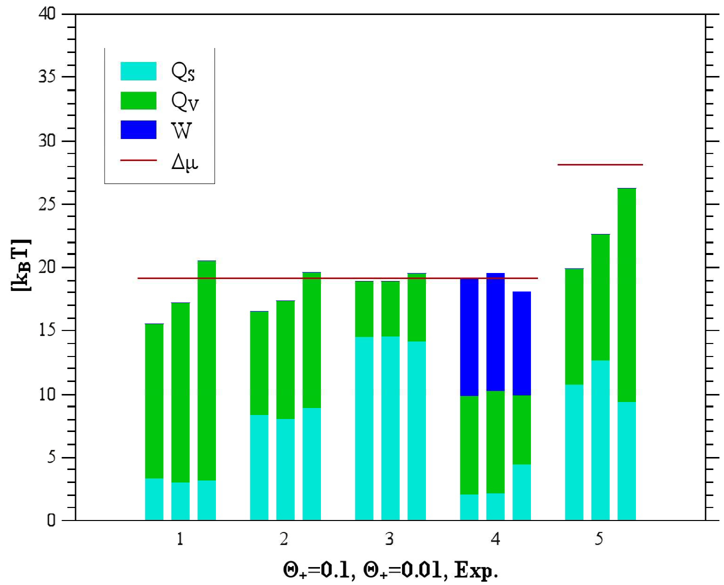


- Comparison:

experiment

theory





[S. Toyabe et al, PRL 104, 198103 (2010)]

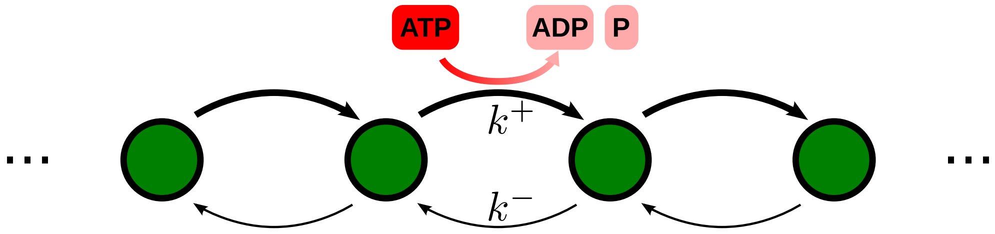
[E. Zimmermann and US, NJP 2012]

- Temporal precision in a finite temperature environment

at 300 K, a precision of 1 sec/day requires at least 6×10^{-11}J/day

- Cost of running a simple clock: ARW

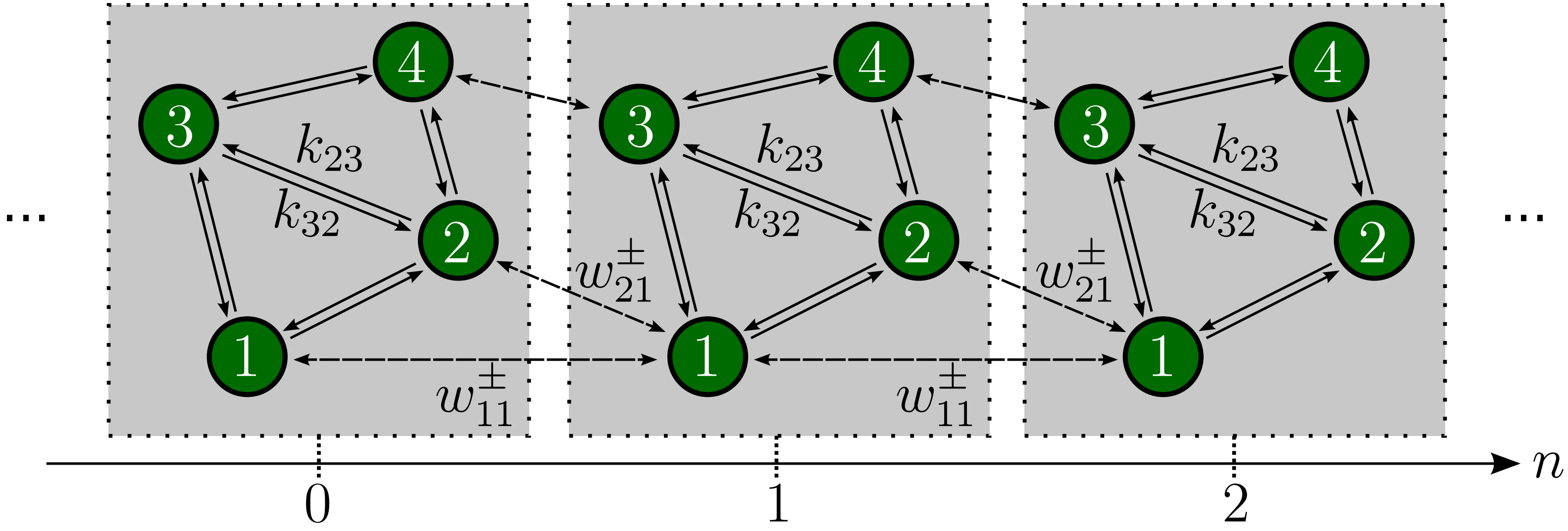
  [AC Barato and US, Phys. Rev. Lett. 114, 158101, 2015]



  - output $n(t)$ with $\langle n \rangle = Jt = (k^+ - k^-)t$
  - variance $\langle (n(t) - \langle n \rangle)^2 \rangle = 2Dt = (k^+ + k^-)t$
  - uncertainty $\epsilon^2 \equiv \text{var}/\text{output}^2 = 2D/J^2 t$
  - th'dyn cost $\mathcal{C} = \sigma t = (k^+ - k^-) \ln(k^+/k^-)t$ with $\sigma \equiv$ rate of entropy production
  - with affinity $\mathcal{A} = k_B T \ \ln(k^+/k^-) = \mu_{\text{ATP}} - \mu_{\text{ADP}} - \mu_{\text{P}}$
  - $\boxed{\mathcal{C}\epsilon^2 = 2\sigma D/J^2 = \mathcal{A} \coth[\mathcal{A}/2k_B T] \geq 2k_B T}$ independent of run time t

- Thermodynamic uncertainty relation holds for general multicyclic processes

  AC Barato and US, Phys. Rev. Lett. 114, 158101, 2015; proof by Gingrich et al, PRL 2016



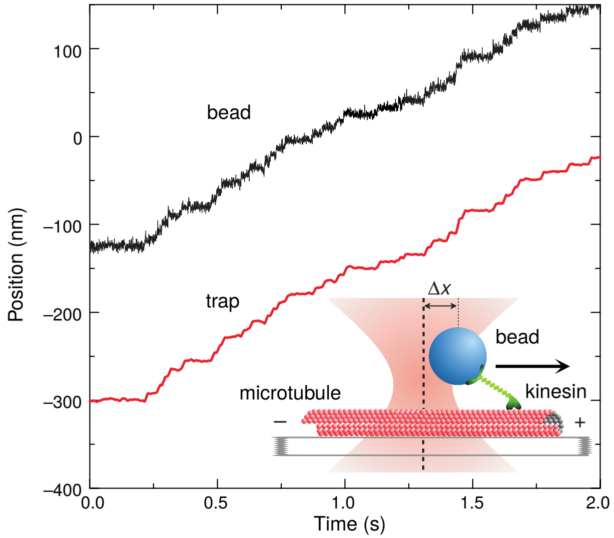
  – $\mathcal{C} \geq 2k_BT/\epsilon^2$ for any th'dyn consistent process at finite T

  – a precision of 1% costs at least 20.000 k_BT

  – inevitable, universal cost of temporal precision (within stationary Markov processes)

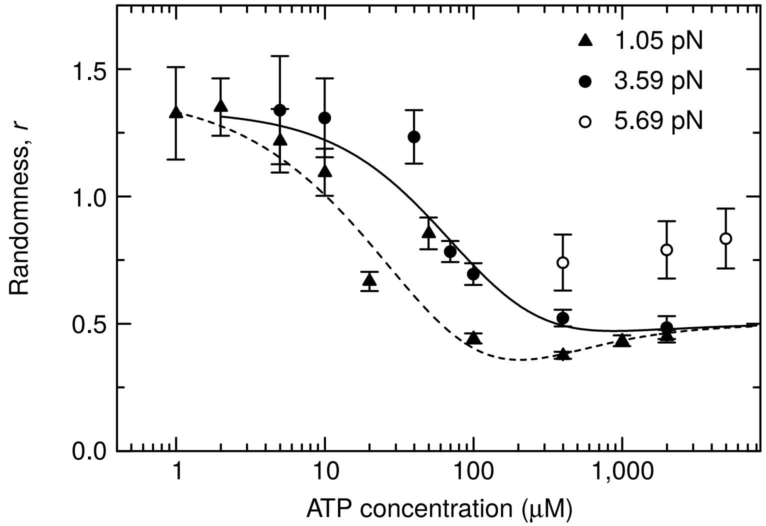
  – for any current $j = \sum_{ij} d_{ij} n_{ij}$ $\sigma \geq j^2/D_j$

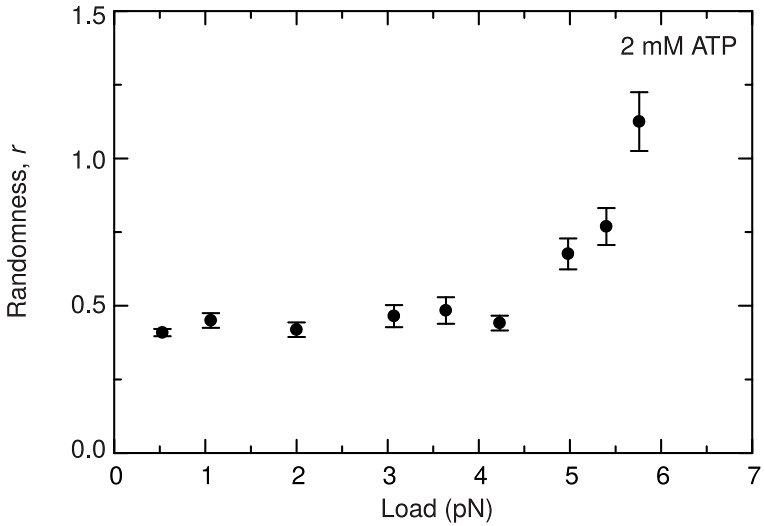
- Thermodynamic inference: Efficiency of a molecular motor



[Visscher et al, Nature, 1999]

- experimental data on
  - velocity v
  - diffusion constant D
  - randomness parameter $r \equiv 2D/v\ell$





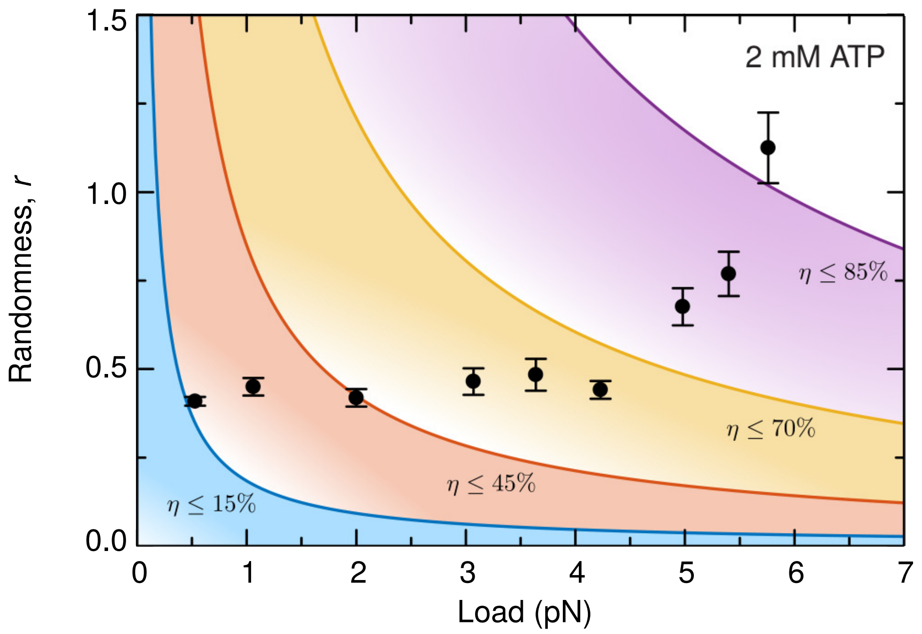
- Thermodynamic inference: Universal bound on the efficiency of molecular machines

  P. Pietzonka, AC Barato, U.S., J Stat Mech, 124004, 2016; U.S., Physica A 504, 176, 2018

  – efficiency

$$\eta \equiv \frac{P^{\rm out}}{P^{\rm in}} = \frac{fv}{\text{unknown}} = \frac{fv}{fv+\sigma} \leq \frac{1}{1+vk_BT/(Df)}$$

  – entropy production rate $\sigma = P^{\rm in} - P^{\rm out} = \text{"chem energy"} - fv \geq v^2/D$



  – independent of the specific chemo-mechanical cycles and of $\Delta\mu$

- Th'dyn' uncertainity relation(s) beyond NESSs?
  - periodic driving with period Ω
    - TUR "fails" in general

      AC Barato and US, PRX 2016
    - for a symmetric protocol $k_{ij}(t) = k_{ij}(\mathcal{T} - t)$

$$\frac{\exp[\Delta S_{\text{per}}] - 1}{t_{\text{per}}} D_j > j^2$$

Proesmans and van den Broeck, EPL 2017

    - a number of "technical" bounds

Barato, Chetrite, Faggionato, Gabrielli, NJP 2018, JStatMech 2019

Proesmans and Horowitz, JStatMech 2019

Koyuk and U.S., JPA 2019

    - operationally accessible version

$$\sigma(\Omega)D(\Omega) \geq [J(\Omega) - \Omega\partial_\Omega J(\Omega)]^2$$

Koyuk and U.S., PRL 2019

  - relaxations towards equilibrium or a NESS

Dechant and Sasa, JStatMech 2018, Liu, Gong and Ueda, arxiv 2019

- A few further generalizations and ramifications
  - underdamped Langevin dynamics
    - TUR "fails" for a finite time $\mathcal{T}$
    - conjectured but not proven for $\mathcal{T} \to \infty$ yet
  - role of a magnetic field — Brandner et al PRL 2018, Chun et al, PRE 2019
  - "generalized" TURs from the fluctuation theorem

    Hasegawa and Van Vu, PRL 2019, Timpanaro et al PRL2019
  - optimal current? (or even the optimal observable?)

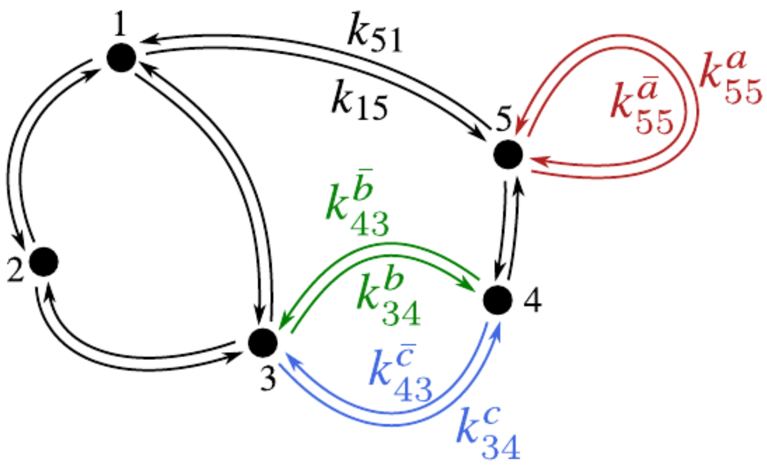
    Polettini et al PRE2016, Busiello and Pigolotti, PRE 2019

    Falasco et al arxiv 2019, Manikandan et al PRL 2020
  - bounds on variance of time-symmetric observables

    Maes PRL 2017, Nardini and Touchette EPJB 2018, Terlizzi and Baiesi, JPA 2019
  - bounds on variance of first-passage times

    Garrahan PRE 2017, Gingrich and Horowitz, PRL 2017
  - open quantum systems ....

- Generalization to time-dependent driving [T Koyuk and U.S., arXiv 2005.02312]

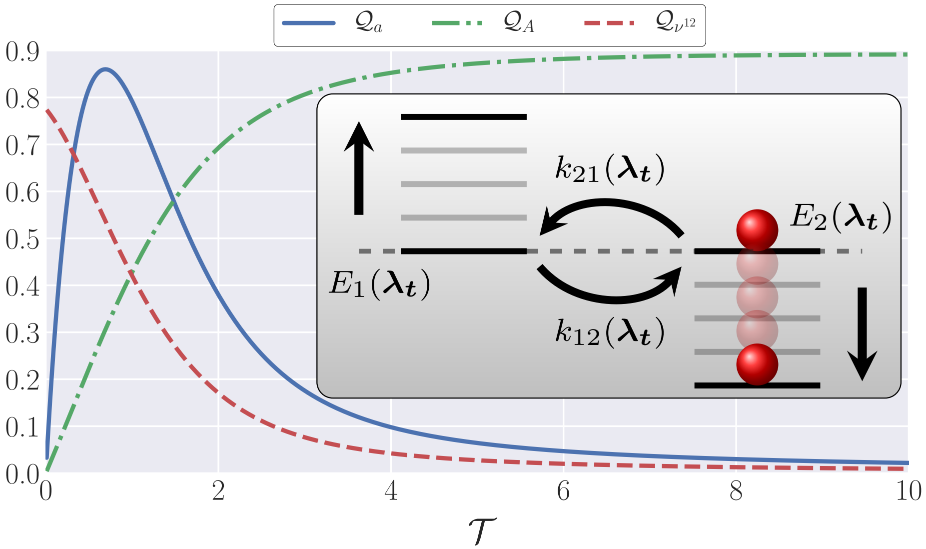


  - network with rates $k_{ij}(\lambda)$ that depend on a driving protocol $\lambda = \lambda(t)$
  - protocol $\lambda(t) = \lambda(vt)$ depends on an experimentally controlable speed parameter v
  - system is driven for a total (observation) time $t = \mathcal{T}$
  - mean current $J(\mathcal{T}, v)$

$$[J(\mathcal{T},v) + \Delta J(\mathcal{T},v)]^2 / D_J(\mathcal{T},v) \leq \sigma(\mathcal{T},v) \quad \text{with} \quad \Delta \equiv \mathcal{T}\partial_{\mathcal{T}} - v\partial_v$$

- Generalization to state observables

  - Example: driven two-state system $k_{12}(vt)$

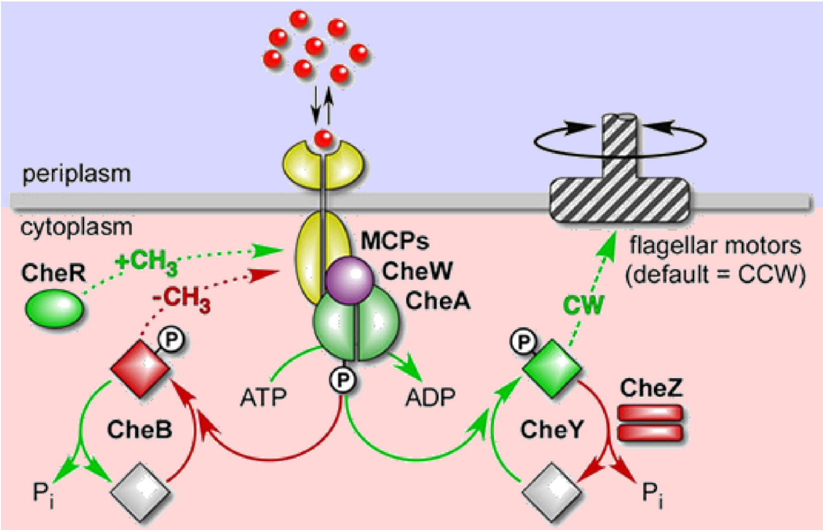


  - observable $a(\mathcal{T}, v) \equiv \delta_{n(\mathcal{T})2}$ at final time [blue]
  - observable $A(\mathcal{T}, v) \equiv \tau_2/\mathcal{T}$ total time spent in state 2 [green]

$$[\Delta X(\mathcal{T}, v)]^2 / D_X(\mathcal{T}, v) \leq \sigma(\mathcal{T}, v) \quad \text{for} \quad X(\mathcal{T}, v) \in \{a(\mathcal{T}, v), A(\mathcal{T}, v)\} \quad \text{with} \quad \Delta \equiv \mathcal{T}\partial_{\mathcal{T}} - v\partial_v$$

  - current $J(\mathcal{T}, v) = [n_{12}(\mathcal{T}, v) - n_{21}(\mathcal{T}, v)]/\mathcal{T}$ [red]

- Information and entropy production in cellular sensing



– Lan et al, Nature Phys. 2012;

Mehta and Schwab PNAS 2012

Information about an external process $\{X(t)\}$ (conc' of a nutrient) is recorded by an internal variable $\{Y(t)\}$ (conc' of phosph'd protein)

Q: Is a rate of information (which one?) acquired about $\{X(t)\}$ related to the thermodynamic cost σ of maintaining the sensory network?

[AC Barato, D Hartich, U.S., PRE 87, 042104, 2013]

[cf: Horowitz & Sandberg NJP 2014, Lang, Fisher, Mora & Mehta PRL 2014,

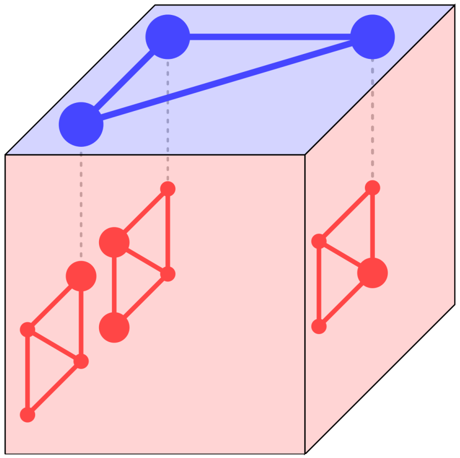
Bo, Del Giudice & Celani JSM 2015,...]

• Framework: Stochastic thermodynamics of bipartite systems

[D. Hartich, AC Barato, U.S., J Stat Mech, P02016, 2014]

– (external) x-jumps $w^{\alpha\beta}$

independent of y



– (internal) y-jumps w_{ij}^{α}

affected by x

– thermodynamic entropy production

$$\sigma = \sigma_x + \sigma_y \geq 0$$

– conditional Shannon entropy

$$H[x|y] = -\sum_{i,\alpha} P_i P(\alpha|i) \ln P(\alpha|i)$$

– learning rate

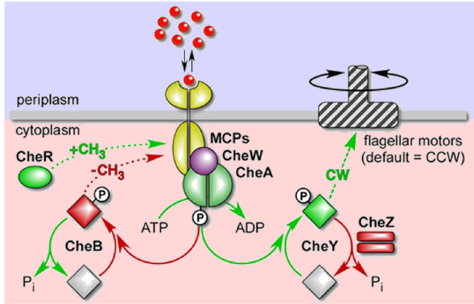
$$\boxed{l_y \equiv -\frac{d}{dt}_{|\text{y}-\text{jumps}} H[x|y] \leq \sigma_y \leq \sigma}$$

– efficiency of learning

$$\boxed{\eta \equiv l_y/\sigma_y \leq 1}$$

– rate of mutual information not bounded by σ_y !

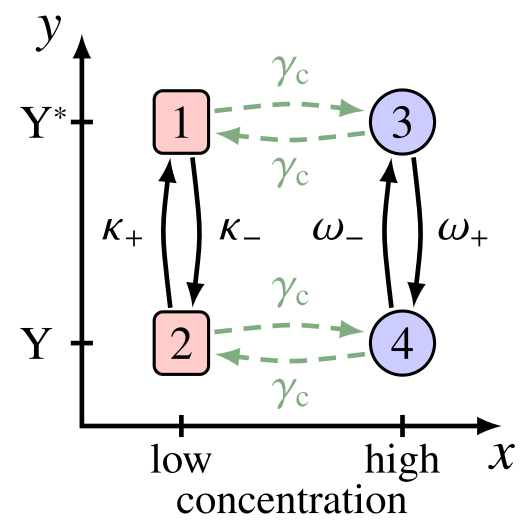
- Efficiency of cellular sensing

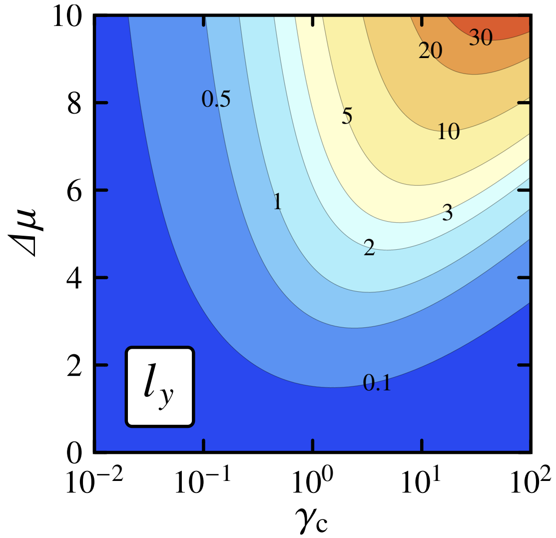


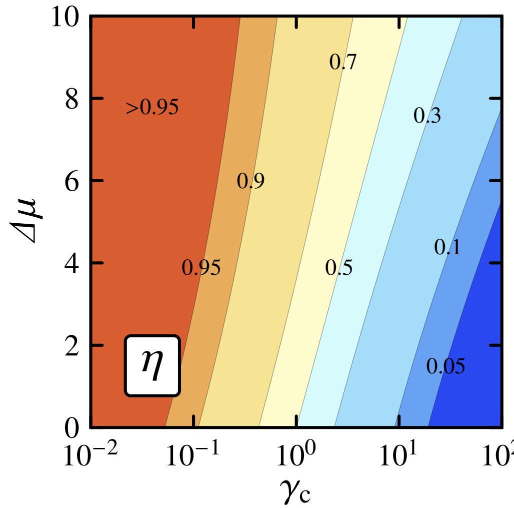
[AC Barato, D Hartich, U.S., NJP **16** 103024, 2014]

Model	ext conc	ligand	activity of rec'r	methyl	Che Y/Y^*
minimal 4-state	$< - - - - - --$	X	$- - - - - - >$	$-$	Y
eq receptor	X	Y_b	Y_a	$-$	$-$
coarse-grained	X	fast	Y_a	$-$	$-$
with adaptation	X	fast	Y_a	Y_m	$-$

- Minimal four state model [AC Barato, D Hartich, U.S., NJP **16** 103024, 2014]







$$Y + ATP \underset{\kappa_-}{\overset{\kappa_+}{\rightleftharpoons}} Y^* + ADP \underset{\omega_-}{\overset{\omega_+}{\rightleftharpoons}} Y + ADP + P_i$$

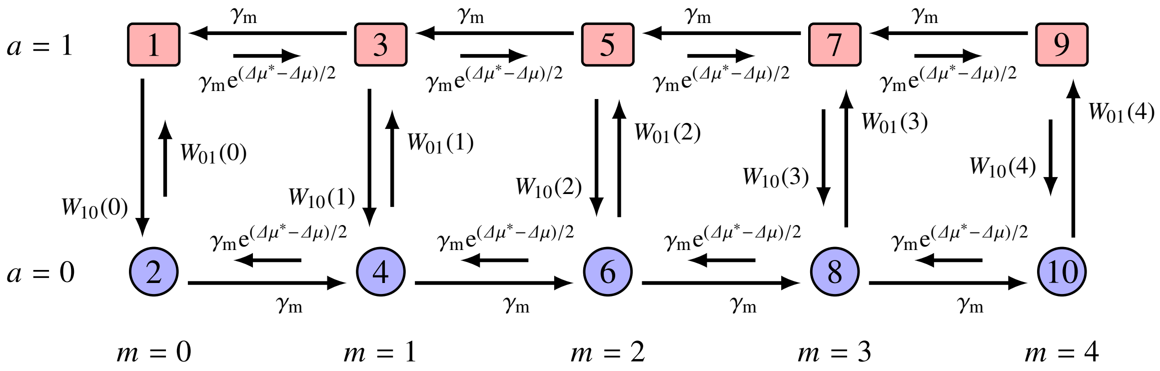
$$\Delta\mu = k_B T \ln(\kappa_+\omega_+/\kappa_-\omega_-)$$

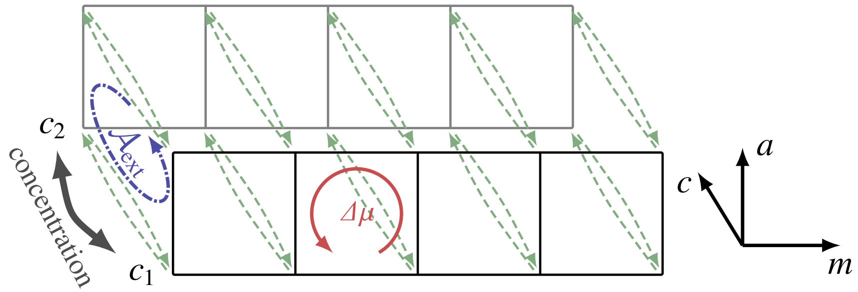
$$\sigma = J\Delta\mu$$

$$l_y = J \ln[P_1 P_4/P_2 P_3]$$

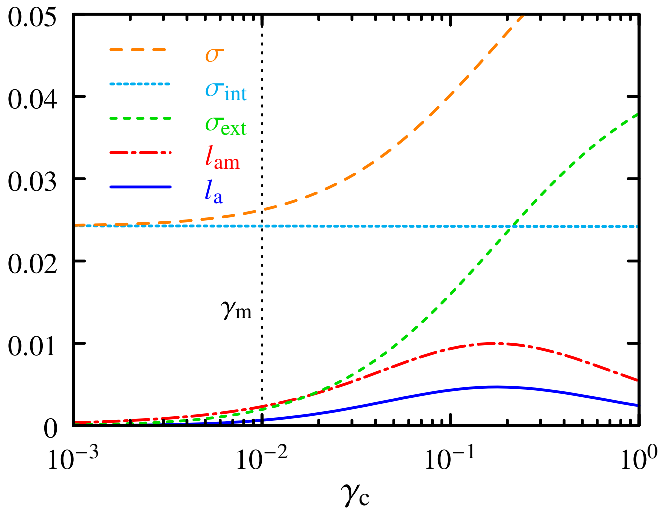
- l_y increases with $\Delta\mu$
- adiabatic case : $\eta \to 1$
- fast external changes: $\eta \to 0$

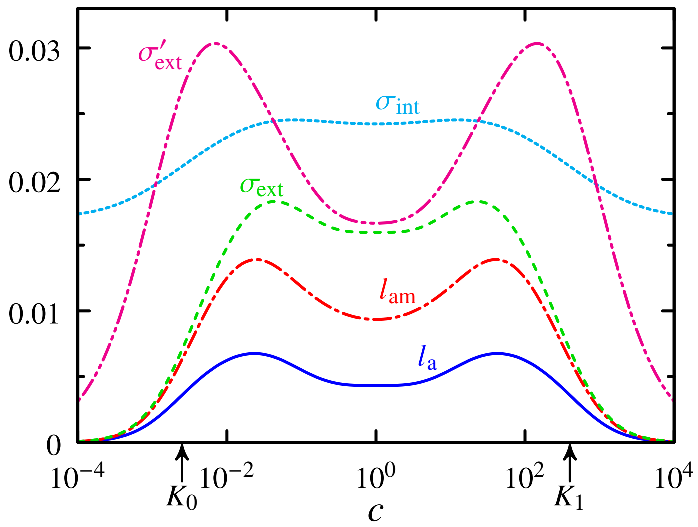
- Model with adaptation [AC Barato, D Hartich, U.S., NJP **16** 103024] 2014

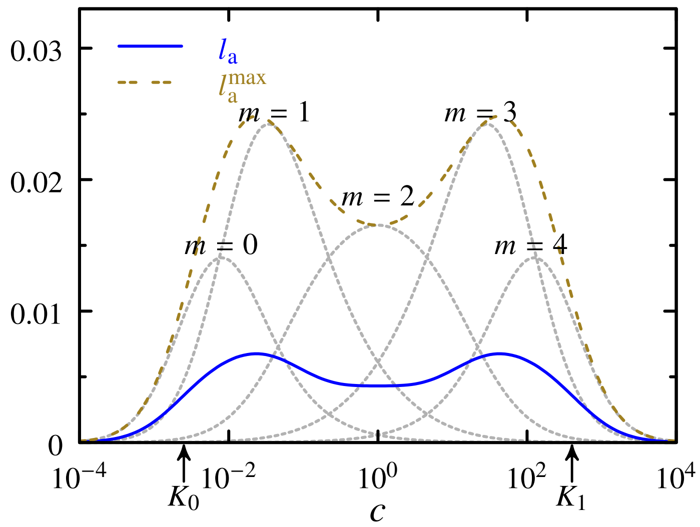




increasing methylation level ⟶







- Stochastic thermodynamics as

  . universal, thermodynamically consistent, quantitative framework

- Universal inequalities (bounds) for thermodynamic inference
  - thermodynamic uncertainty relation provides constraints on
    - ... cost of any process with given precision
    - ... efficiency of any molecular motor (complex)
  - generalization to arbitrary time-dependent driving

- Bipartite approach to information processing in sensing

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