Inference and localization of entropy production beyond the thermodynamic uncertainty relation

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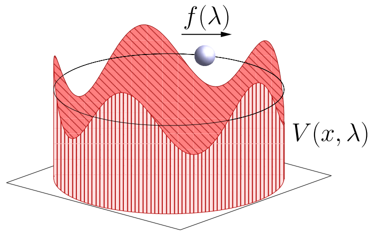
- $\geq$ 2005: ent'production along finite-time trajectories
- $\geq$ 2015: thermodynamic uncertainty relation
- $\geq$ 2023: Markovian events and snippets

* Entropy production in stochastic th'dynamics



  - 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)]: $dw = du + dq$
    - applied work: $dw = f\ dx + \partial_\lambda V(x,\lambda) d\lambda$
    - internal energy : $du = dV$
    - dissipated heat: $dq = dw - du = [-\partial_x V(x,\lambda) + f]dx = T ds^{\text{res}}$
  - total entropy as quantitive measure of broken time reversal symmetry

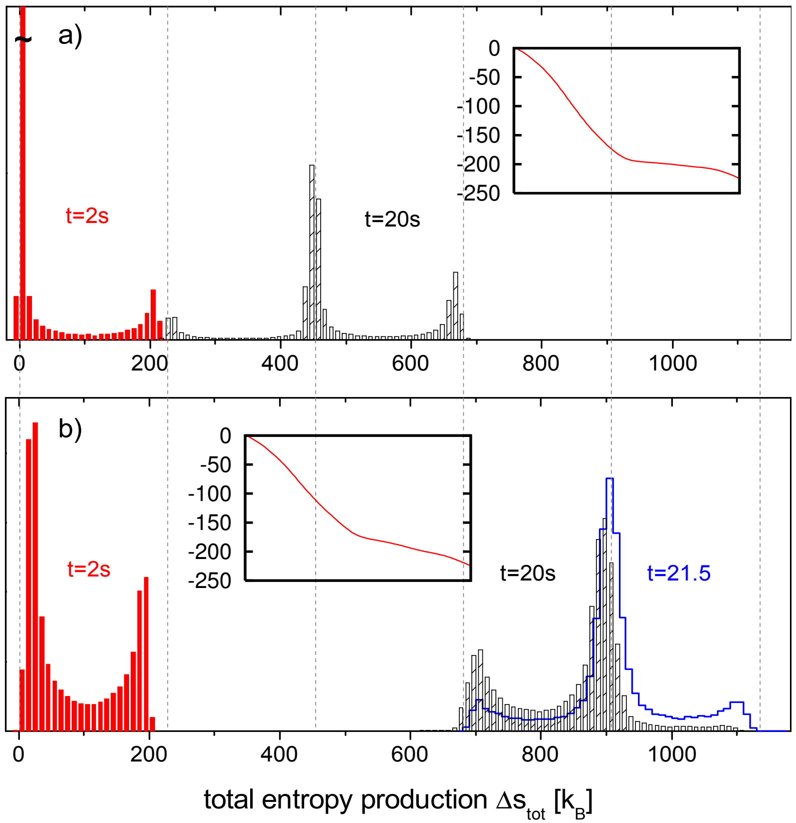
$$x(t) \to \tilde{x}(t) \equiv x(T-t) \qquad \Delta s^{\text{tot}}[x(t)] \equiv \ln[p[x(t)]/\tilde{p}[\tilde{x}(t)]] = \Delta[-\ln p^s(x)] + q/T$$

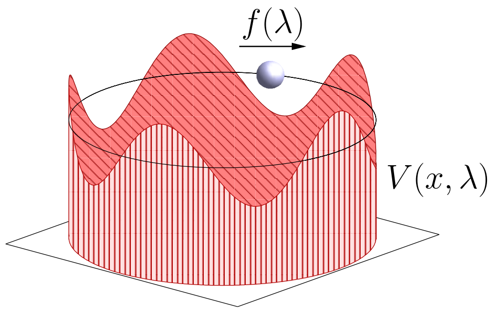
  - IFT for total entropy production $\langle \exp[-\Delta s^{\text{tot}}] \rangle = 1 \Rightarrow \langle \Delta s^{\text{tot}} \rangle \geq 0$ [U.S., PRL 2005]

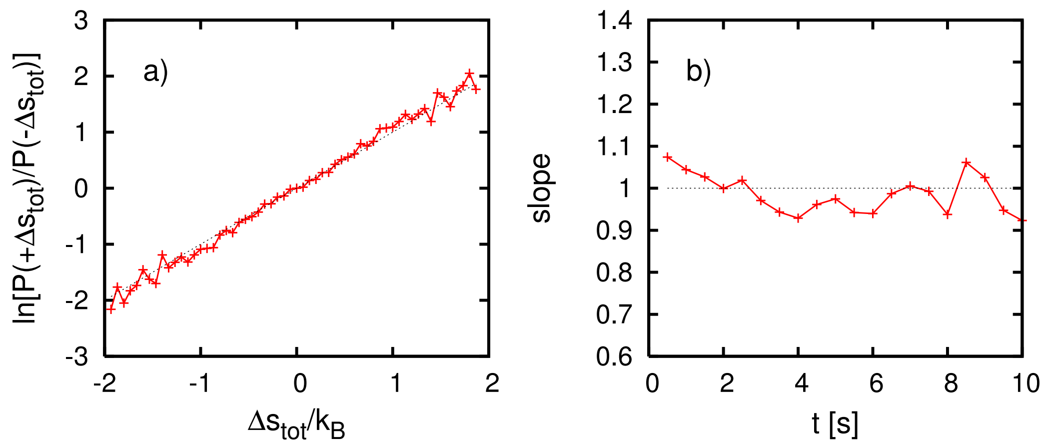
- Fluctuation theorem $p(-\Delta s^{\rm tot})/p(\Delta s^{\rm tot}) = \exp(-\Delta s^{\rm tot})$ in any NESS

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)]



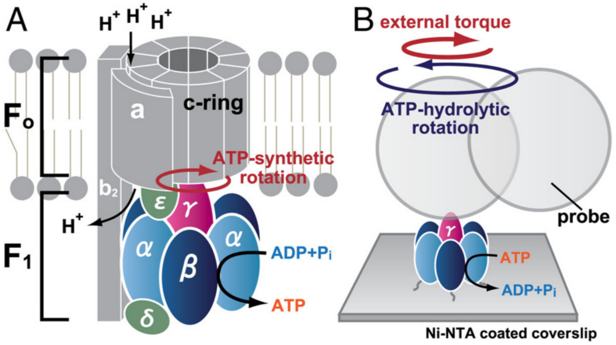


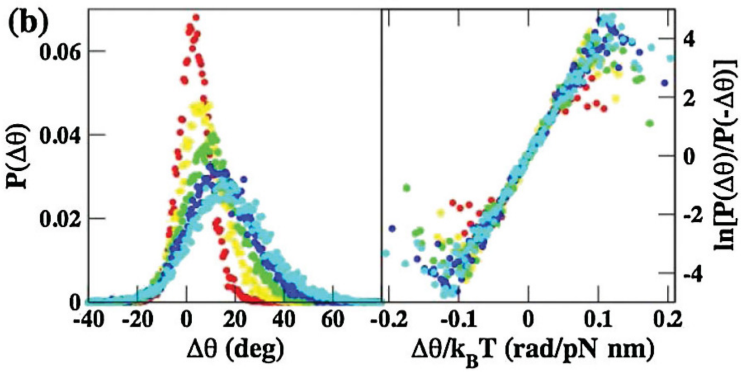


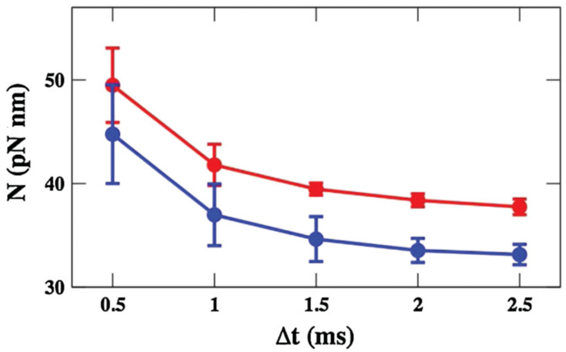
FT-representation

- F1-ATPase and the fluctuation theorem

[K. Hayashi et al, PRL 104, 218103 (2010)]

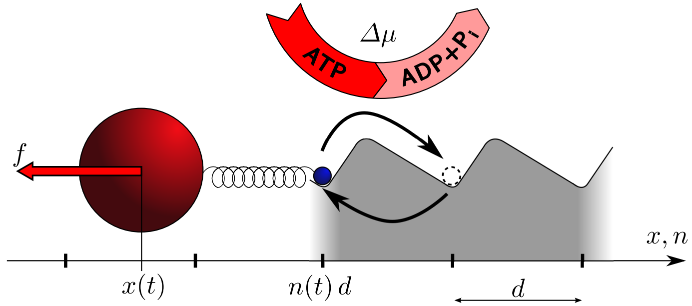


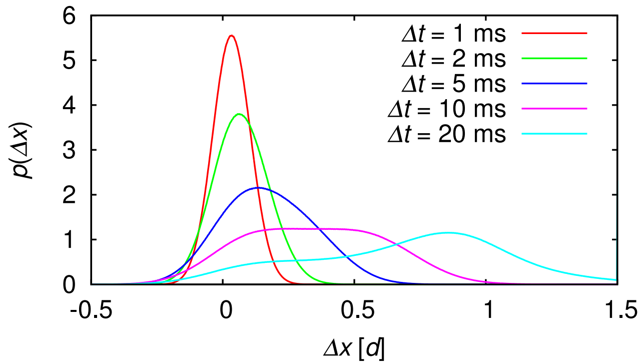


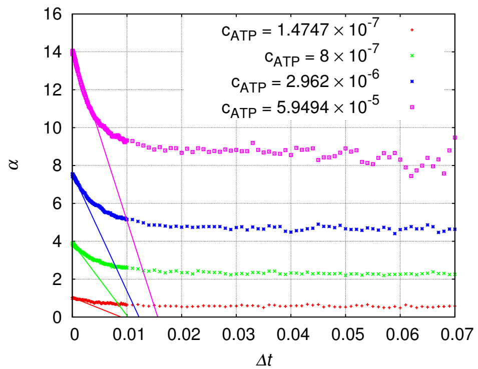


Hybrid model

[E. Zimmermann and U.S., NJP 14, 103023, 2012]







- Two faces of thermodyn' inequalities

$$\boxed{\Delta s^{\text{tot}} > f(\text{"experimentally accessible"})}$$

$\rightarrow$ exp' accessible lower bound on entropy production

$$\boxed{\Delta s^{\text{tot}} > f(\text{"something desirable"})}$$

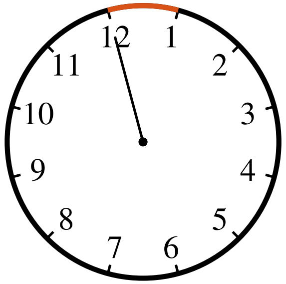
$\rightarrow$ minimal thermodynamic cost of achieving "something desirable"

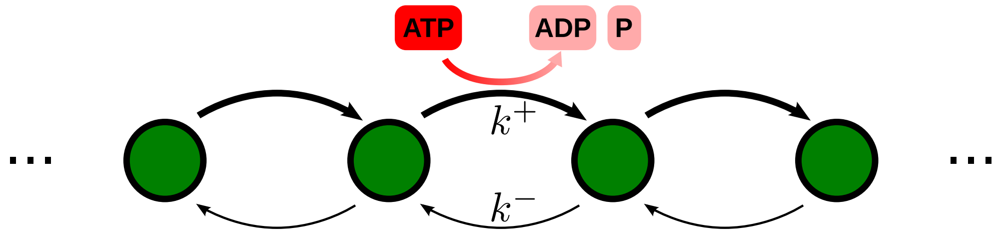
- Temporal precision in an aqueous finite-temperature environment

precision of 1 sec/day will cost 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 $\epsilon^2 \equiv \text{var}/\text{output}^2 = 2D/J^2 t$

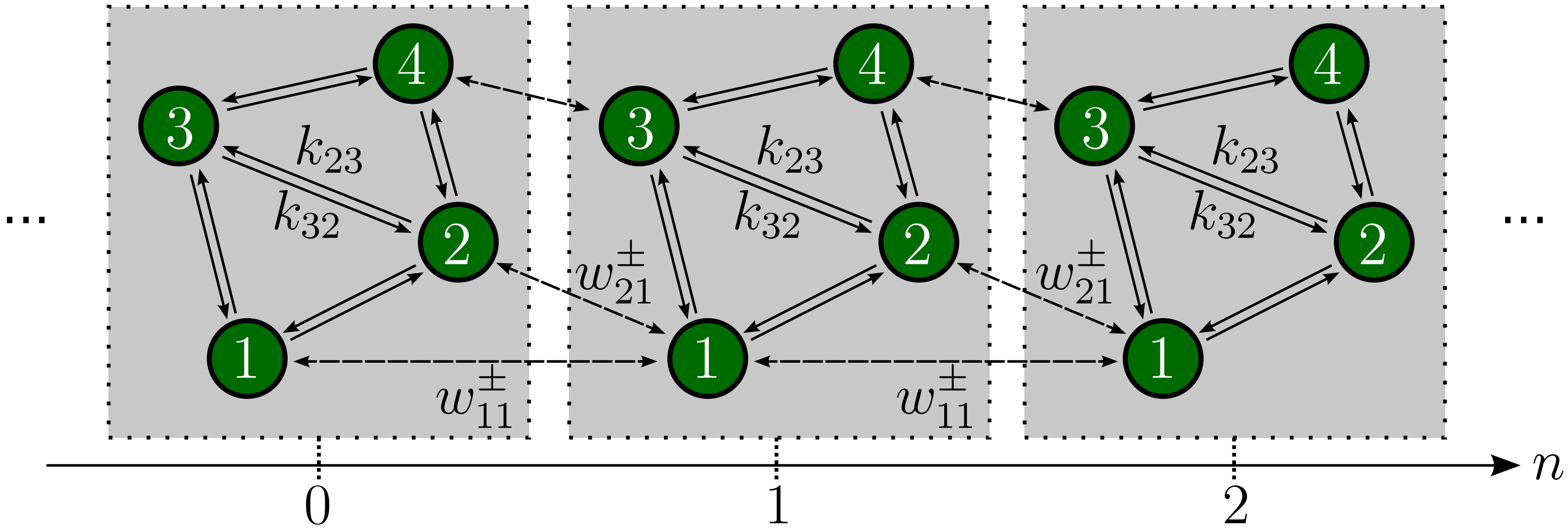
  – th'dyn cost $\mathcal{C} = \sigma t = (k^+ - k^-) \ln(k^+/k^-)t$ with $\sigma \equiv$ rate of entropy production

  – 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 (TUR) holds for general multicyclic processes

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



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

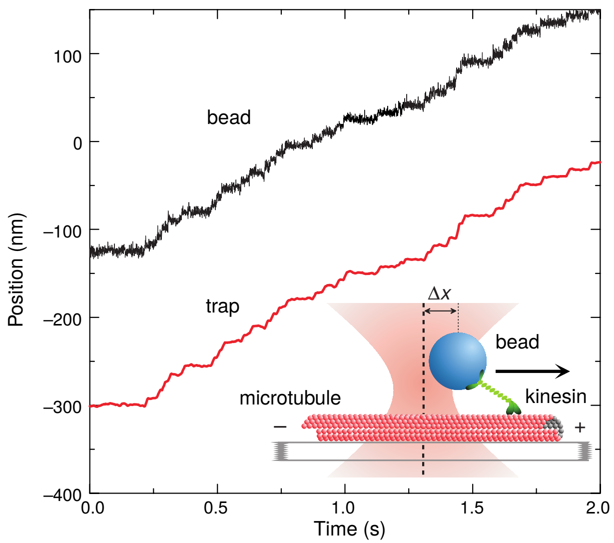
  - a temporal precision of 1% costs at least 20.000 $k_B T$

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

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

  - violated for underdamped Langevin dynamics [P. Pietzonka, PRL 128, 130606, 2022]

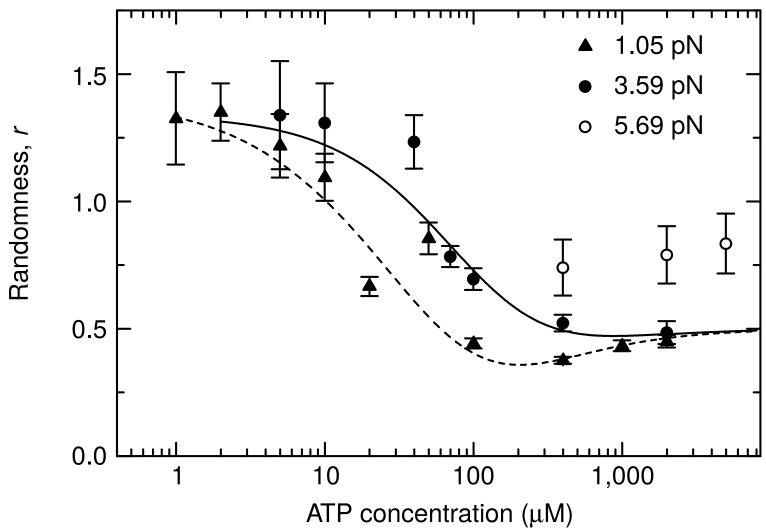
• Thermodynamic inference: Efficiency of a molecular motor

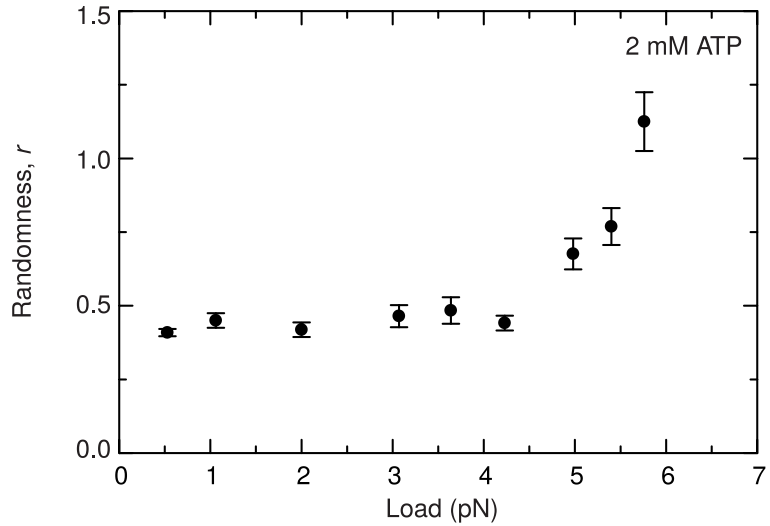


[Visscher et al, Nature, 1999]

– experimental data on

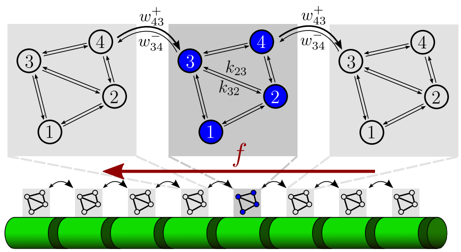
- ∗ velocity v
- ∗ diffusion constant D
- ∗ randomness parameter $r \equiv 2D/v\ell$





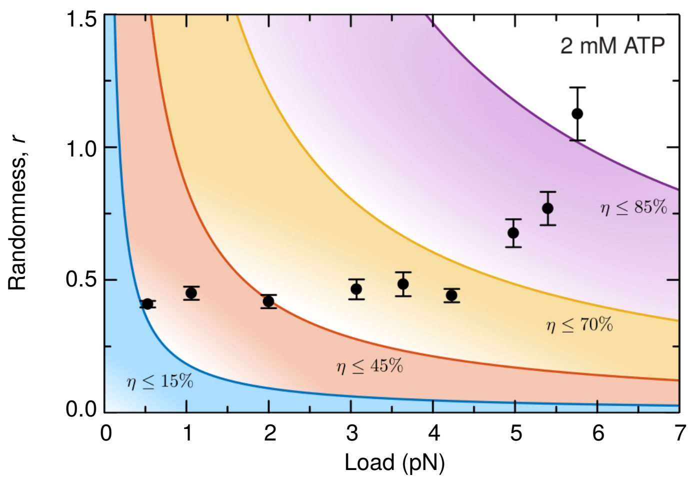
- Thermodynamic inference: Universal bound on the efficiency of molecular machines

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



  - entropy production rate $\sigma = P^{\text{in}} - P^{\text{out}} =$ inacc′ chem energy $- fv \geq v^2/D$
  - efficiency

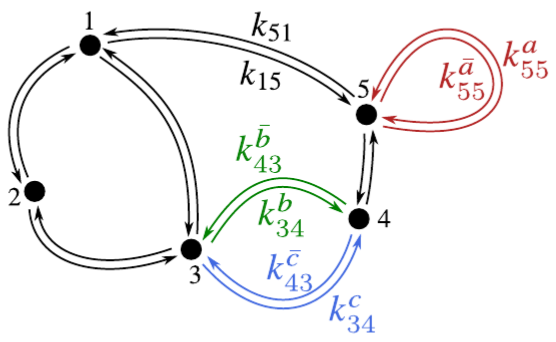
$$\eta \equiv \frac{P^{\text{out}}}{P^{\text{in}}} = \frac{fv}{\text{chem energy}} = \frac{fv}{fv + \sigma} \leq \frac{1}{1 + vk_BT/(Df)}$$



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

- Inference from observing states for time-dependent driving

  [T Koyuk and U.S., Phys. Rev. Lett. 125, 260604, 2020]



  – 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 $t = \mathcal{T}$

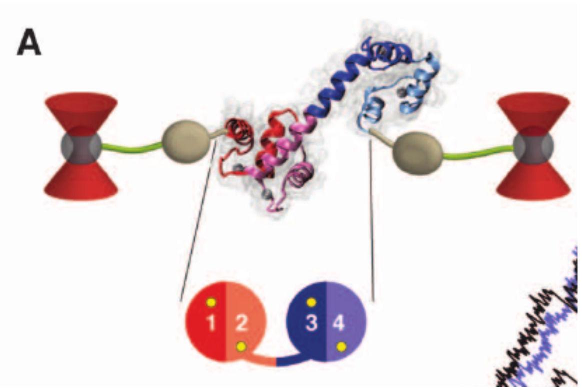
  – observable $A_i(\mathcal{T}, v) \equiv \tau_i/\mathcal{T}$ total time spent in state i

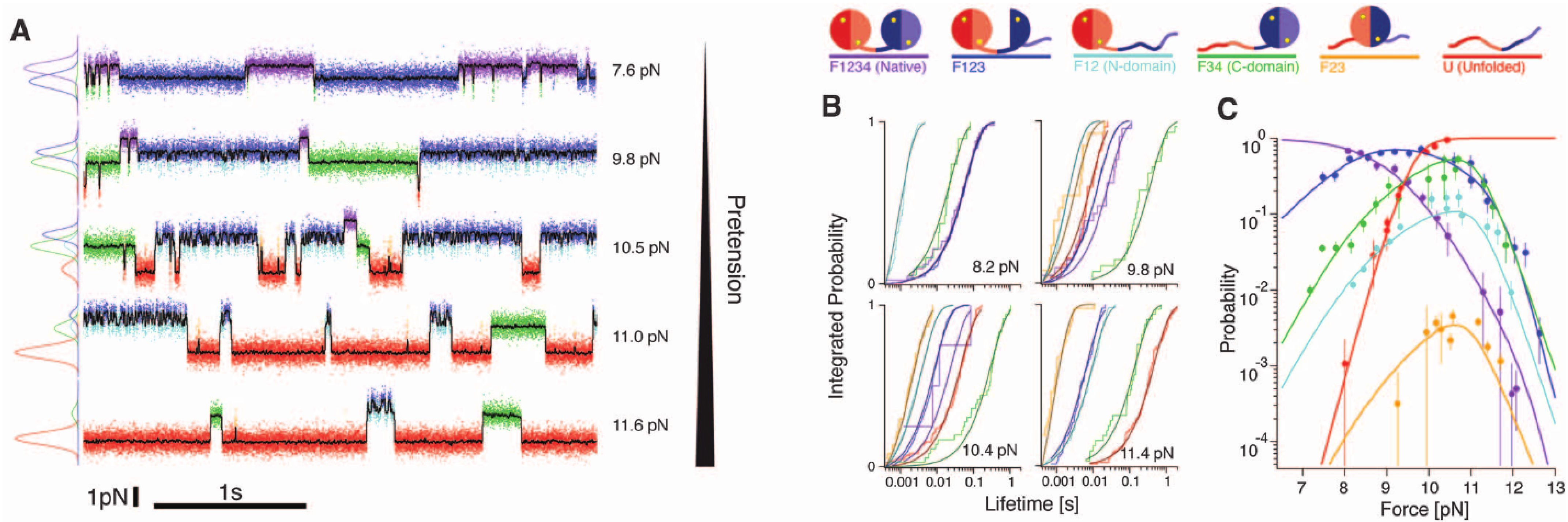
$$\{[\mathcal{T}\partial_{\mathcal{T}} - v\partial_v]\langle A_i(\mathcal{T}, v)\rangle\}^2 / D_{A_i}(\mathcal{T}, v) \leq \sigma(\mathcal{T}, v)$$

  – same for observable $a_i(\mathcal{T}, v) \equiv \delta_{n(\mathcal{T})i}$ state at final time

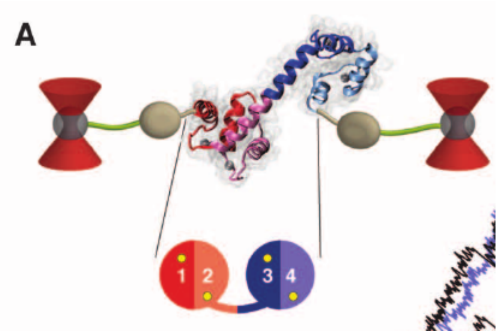
  – [cf for relaxation into eq: K. Liu, Z. Gong, and M. Ueda, PRL 125, 140602 (2020).]

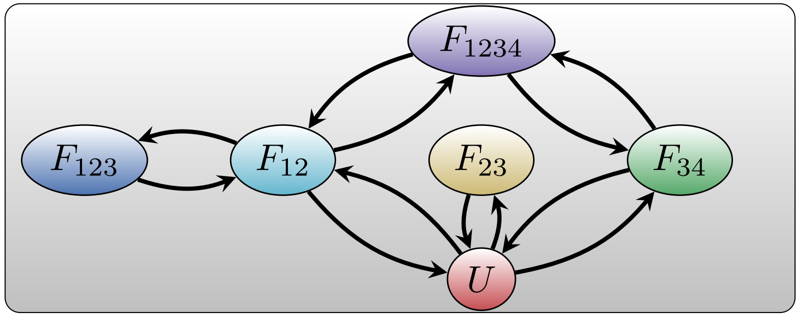
• Biomolecule under a constant force [J. Stigler et al, Science **334** 512 (2011)]

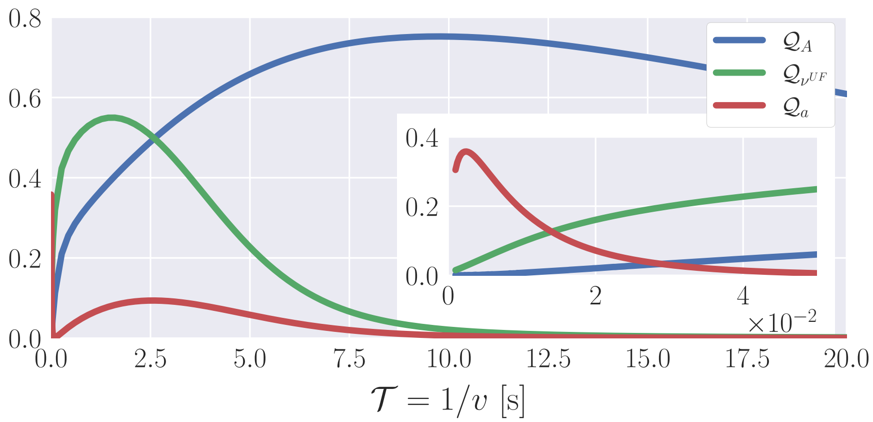




- Application to unfolding of calmodulin under a force-ramp







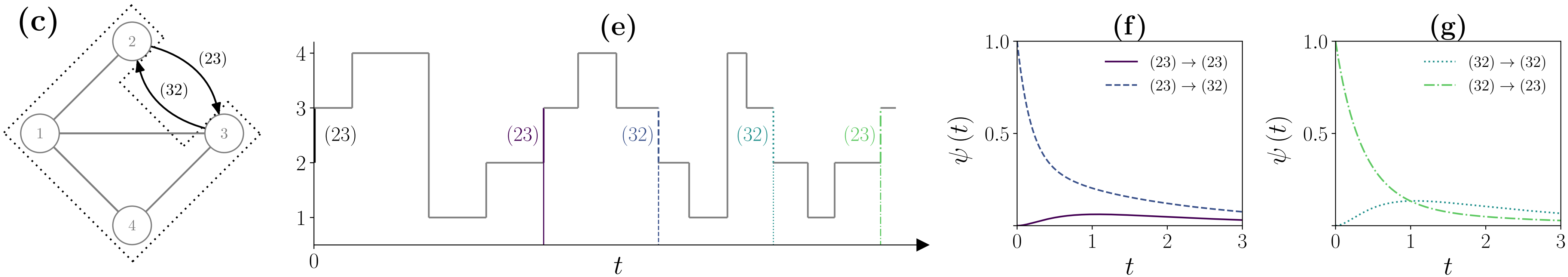
  - force ramp $f(t) = f_0 + vt$
  - observable $a(\mathcal{T}, v) \equiv \delta_{n(\mathcal{T})12}$ at final time [red]
  - observable $A(\mathcal{T}, v) \equiv \tau_U/\mathcal{T}$ total time spent in unfolded state [blue]
  - infer $40 \simeq 80\%$ of entropy production with no model input whatsoever

- NESS: Beyond the TUR: Stronger inference from waiting-time distributions

  Martinez, Bisker, Horowitz, Parrondo, Nat Comm 2019; Skinner and Dunkel, PRL 2021

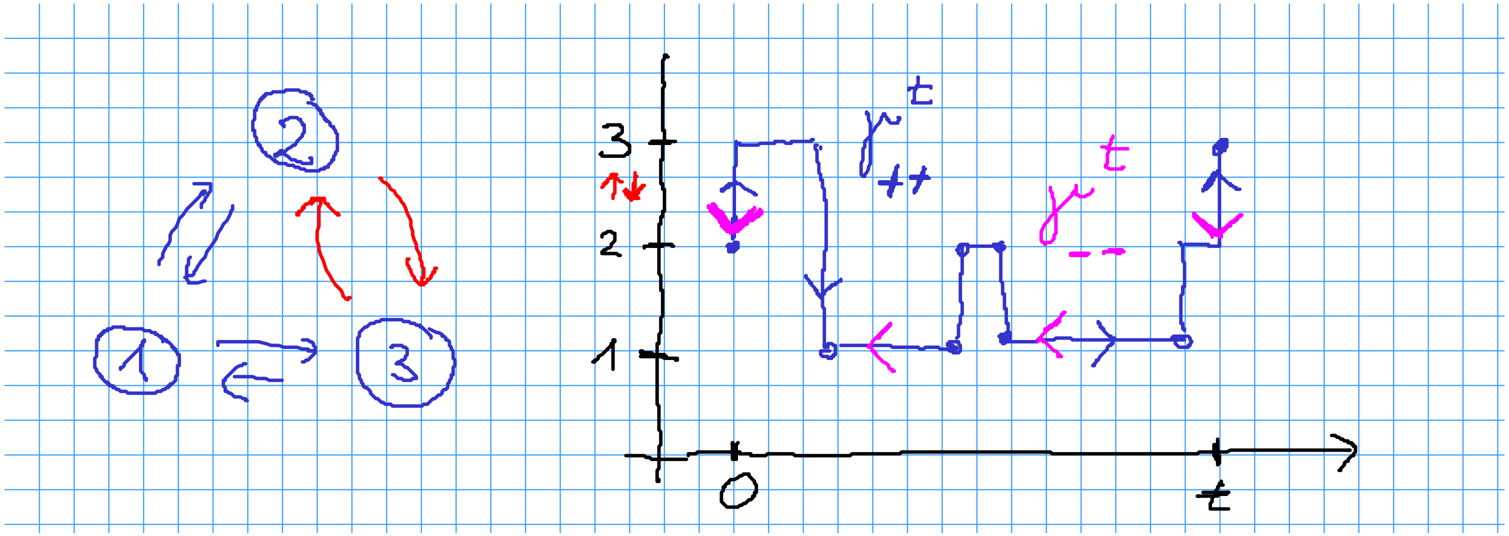
  Ehrich, JSM 2021, Hartich and Godec, PRX 2021, Harunari, Dutta, Polettini, Roldan, PRX 12, 041026, 2022;

  van der Meer, Ertel, U.S., PRX 12, 031025, 2022



  - waiting time between two consecutive transition, e.g., $\psi_{23\to23}(t) \equiv \psi_{++}(t)$
  - ratio of waiting times $a(t) \equiv \ln \psi_{++}(t)/\psi_{--}(t)$

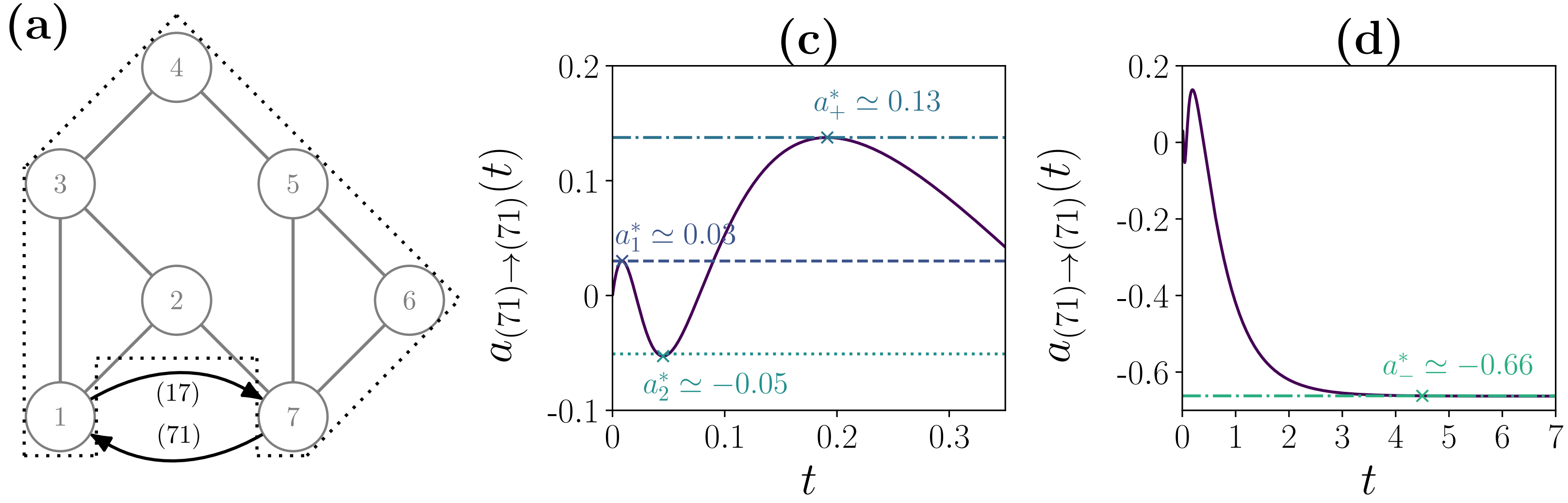
- Unicyclic network with affinity $A_c \equiv \ln \prod_i (k_i^+/k_i^-)$
  - $a(t) \equiv \ln[\psi_{++}(t)/\psi_{--}(t)] = A_c$ [$= \ln p(+|+)/p(-|-)$]
  - observing one link is sufficient to get the ent'prod rate $\sigma = jA_c$, better than TUR



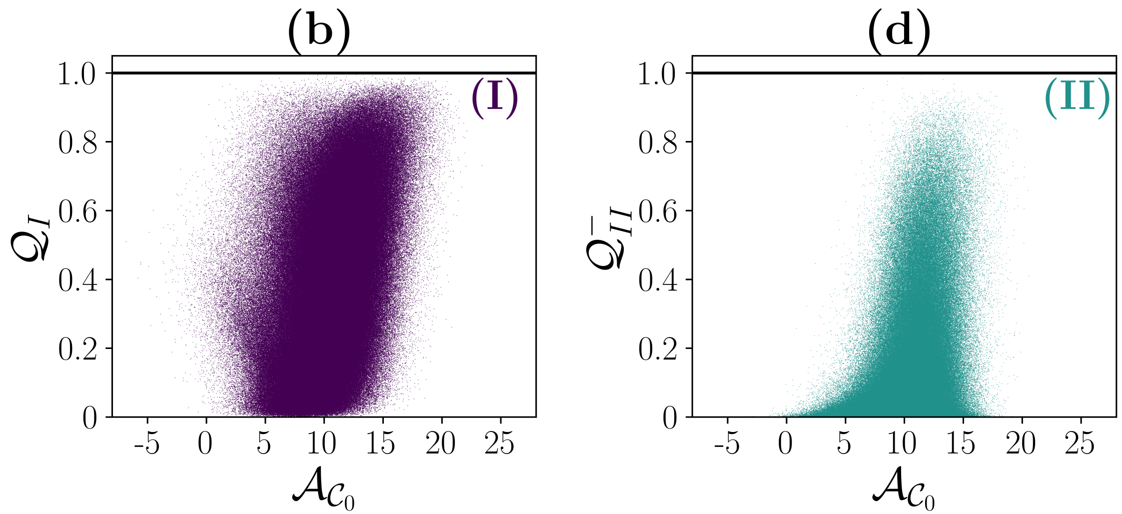
$$\psi_{++}(t) = \sum_{\gamma^t_{+\to+}} p(\gamma^t_{+\to+}| + \text{at } t=0) \;=\; \sum_{\gamma^t_{-\to-}} p(\gamma^t_{-\to-}| - \text{at } t=0)\exp[A_c]$$

$$= \psi_{--}(t)\exp[A_c]$$

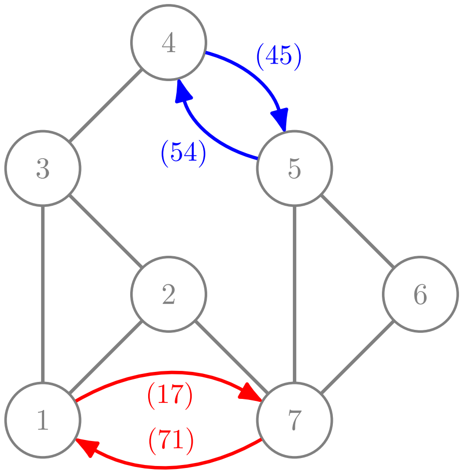
- One observed link in a multicyclic system



- $A_c \equiv \ln \ \prod_{ij\in c}(k_{ij}^+/k_{ij}^-)$
- $a(t\to 0) = A_c$(shortest cycle)
- $\max a(t) \leq \max A_c$
- $\min a(t) \geq \min A_c$



- Several observed links in a multicyclic system



  - mean rate of an I-transition ν_I
  - wt-distributions for consecutive transitions J after I $\psi_{IJ}(t)$
  - lower bound on ent'production

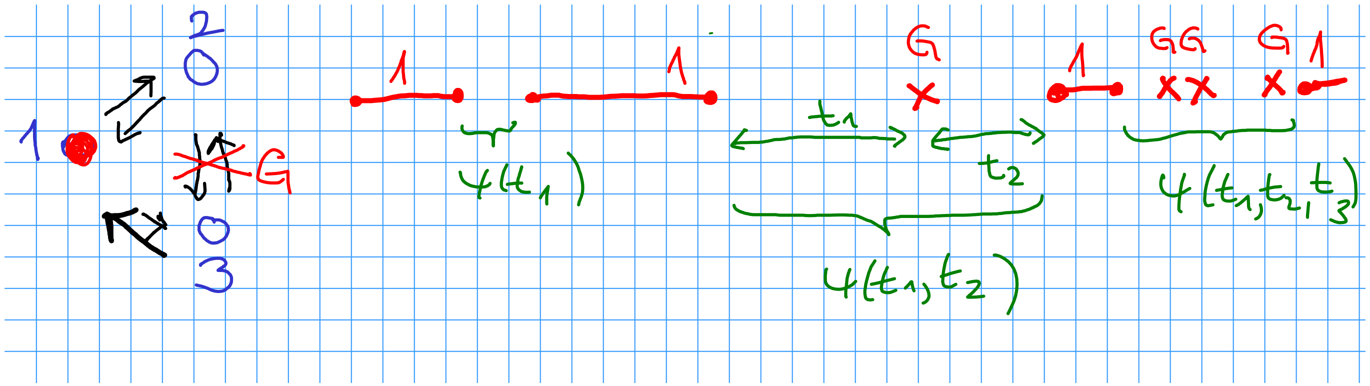
$$\sigma \geq \sum_{IJ} \int_0^\infty dt \nu_I \psi_{IJ}(t) \ln[\psi_{IJ}(t)/\psi_{\tilde{J}\tilde{I}}(t)]$$

  - equality if all $\psi_{IJ}(t)/\psi_{\tilde{J}\tilde{I}}(t)$ are time-independent

- Markovian events and snippets

  [J. van der Meer, J. Degünther, U.S, PRL **130** 257101, 2023]

  – observe only state 1 and transition $G = \{2 \to 3 \text{ or } 3 \to 2\}$



  – waiting time distributions

    * $\psi(t_1) = \sum_{\gamma|1\to1 \text{ with no G}} p[\gamma]$

    * $\psi(t_1,t_2) = \sum_{\gamma|1\to1 \text{ with one G}} p[\gamma]$

  – normalization $1 = \sum_{\gamma|1\to1} p[\gamma] = \int_0^\infty dt_1\ \psi(t_1) + \int_0^\infty dt_1 \int_0^\infty dt_2\ \psi(t_1,t_2) + ...$

  – entropy estimator

$$\sigma \geq \hat{\sigma} = \frac{1}{\bar{t}} \sum_{k>1} \prod_j \int_0^\infty dt_j\ \psi(t_1,...,t_k) \ln[\psi(t_1,...,t_k)/\psi(t_k,...,t_1)]$$

  – infer irreversibility even from time-symmetric events

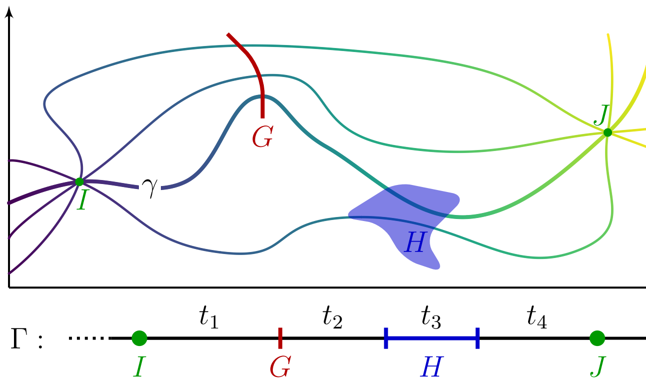
- Generalization to a fluct' coarse-grained ent' production

  [J. Degünther, J. van der Meer, U.S, Phys Rev Res **6**, 023175 (2024)]

  – Markovian events $\{I, J, K, ...\}$ with $p[\gamma_+|I, \gamma_-] = p[\gamma_+|I]$
  – Markovian snippets $\Gamma^s : I \xrightarrow{t,\mathcal{O}} J$ between such events

  – further data $\mathcal{O}$ (like G and H) between such events

  – coarse-grained trajectory
  $\Gamma = (I_0 \xrightarrow{t_1,\mathcal{O}_1} I_1 \xrightarrow{t_2,\mathcal{O}_2} I_2 \xrightarrow{t_3,\mathcal{O}_3} .... \xrightarrow{t_n,\mathcal{O}_n} I_n) = \Gamma_1^s + \Gamma_2^s + ...\Gamma_n^s$
  with weight $\quad p[\Gamma|I_0] = p[\Gamma_1^s|I_0]p[\Gamma_2^s|I_1]p[\Gamma_3^s|I_2]...p[\Gamma_n^s|I_{n-1}]$



  – ent'prod of a Markovian snippet $\qquad \Delta S[\Gamma^s] = \ln\{p(I)p[\Gamma^s|I]/p(J)p[\tilde{\Gamma}^s|\tilde{J}]\}$

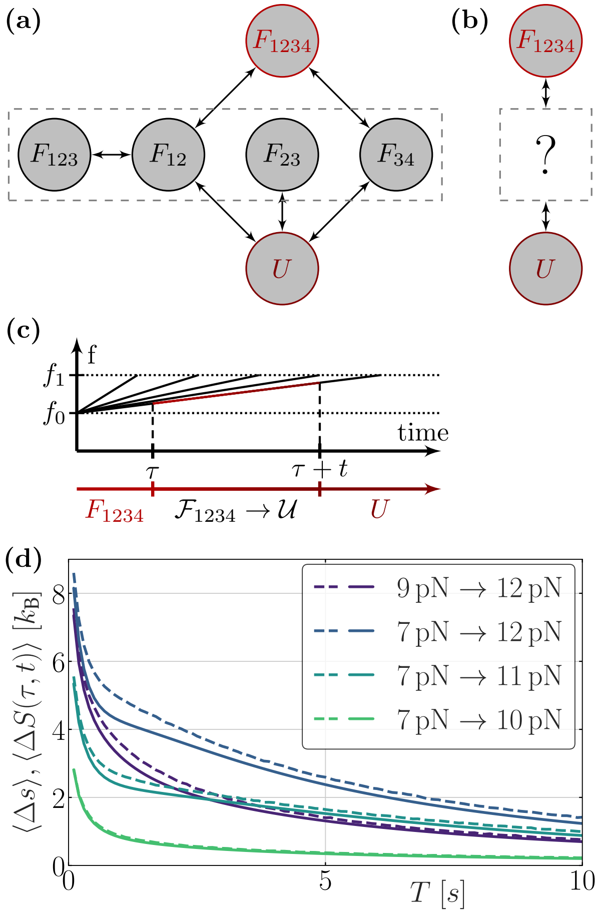
  – ent'prod of a coarse-grained trajectory $\qquad \Delta S[\Gamma] = \sum_i \Delta S_i[\Gamma_i^s]$

    * distribution $p(\Delta S)$ obeys DFT (for even I, J) $\quad p(-\Delta S)/p(\Delta S) = e^{-\Delta S}$
    * th'dyn'ly consistent bound $\Delta S[\Gamma] \leq \langle \Delta s[\gamma] | \Gamma \rangle$ from IFR $e^{-\Delta S[\Gamma]} = \langle e^{-\Delta s[\gamma]} | \Gamma \rangle$

  – recover similar structure for $\Delta S[\Gamma]$ as we had in 2005 for $\Delta s[\gamma]$

- Localization of ent'production for time-dependent driving in time and "space"

  [J. Degünther, J. van der Meer, U.S, PNAS, e2405371121, 2024]



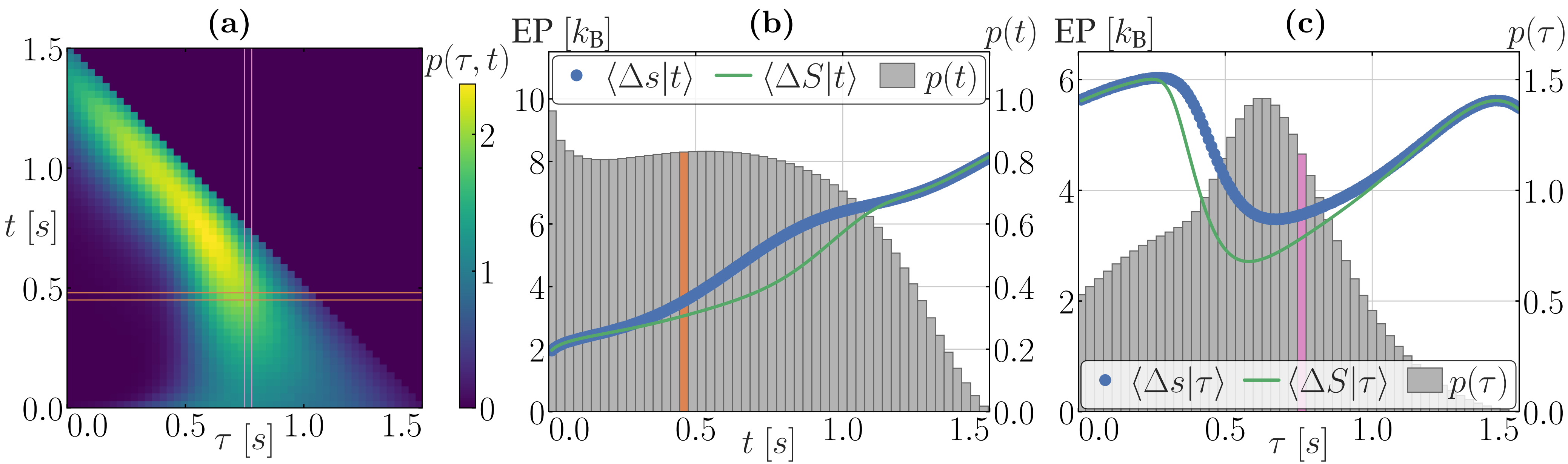
– unfolding of calmodulin under a force ramp

– leaving F_{1234} and entering U is observable

– mean ent'prod only of unfolding events

- Time-resolved entropy production

$p(\tau, t)$ entropy production of unfolding events



as a function of the duration t ... of the onset τ

– quite good estimate (green/blue)

– early starters and late ones are rare and expensive

- stochastic thermodynamics established as

  . universal, thermodynamically consistent, quantitative framework

- thermodynamic uncertainty relation provides a universal constraint on

  - ... the dispersion of any current in terms of the overall ent'prod rate
  - ... the cost of temporal precision
  - ... efficiency of any molecular motor (-complex)

- thermodynamic inference based on waiting times and Markovian events/snippets

  - reveals hidden properties of biochemical/-physical/-molecular systems
  - allows localizations of ent'production in space and time

- acknowledgments

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