Neural Estimation of **Entropy Production** in **Coarse-Grained Systems** via Trajectory **Snippets** and Application to Molecular *Catenane Motors*

Hyeong-Tark Han[1], Changbeom Hong[1], and Jae-Hyung Jeon[1, 2, 3]

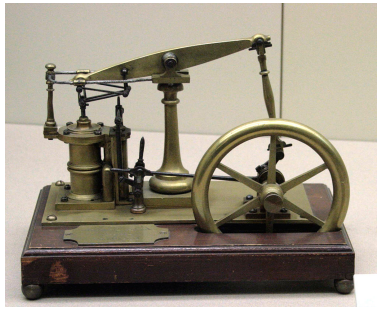
[1]Department of Physics, POSTECH, Pohang
[2]Institute for Theoretical Science, POSTECH, Pohang
[3]Asia Pacific Center for Theoretical Physics, Pohang

NSPCS 2026

Entropy

- Thermodynamics

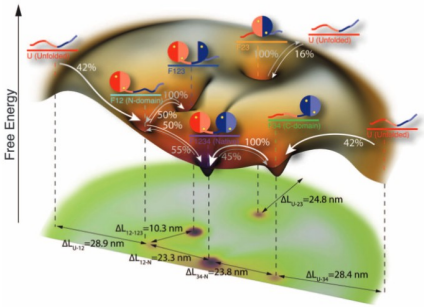
Heat engine



Second law

$$\Delta S = \Delta Q / T \geq 0$$

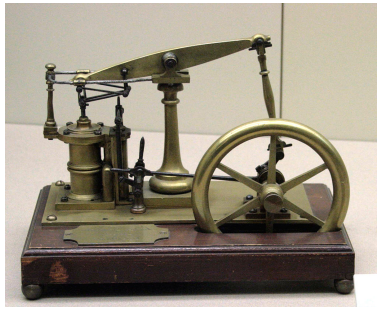
Free energy landscape



Entropy

- Thermodynamics

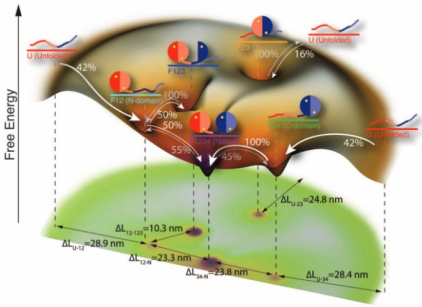
Heat engine



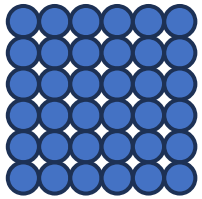
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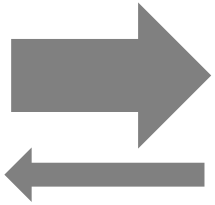
Free energy landscape



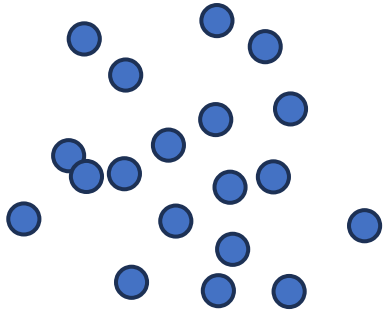
- **Statistical mechanics**



Arrow of time



Irreversibility



U. Seifert, *PRL* (2005)

Irreversibility

- The Kullback—Leibler divergence is equal to **entropy production**.

(Entropy production rate)

$$\sigma = \Delta S/T = \frac{1}{T}\sum_{\zeta} \mathcal{P}(\zeta) \ln \frac{\mathcal{P}[\zeta]}{\mathcal{P}[\tilde{\zeta}]}$$

ζ: trajectory

$\tilde{\zeta}$: time-reversed trajectory

$\mathcal{P}$: path probability



Irreversibility

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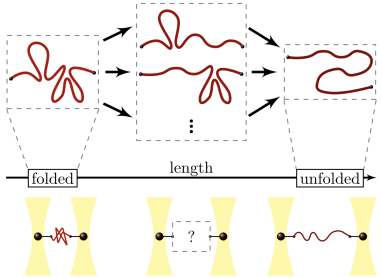
- Proven for many **Markovian** systems.
  - Overdamped **Langevin** equations — J. Kurchan, *J. Phys. A* (1998)
  - **Master** equations — U. Seifert, *PRL* (2005)
  - **Hamiltonian** systems — R. Kawai et al., *PRL* (2007)



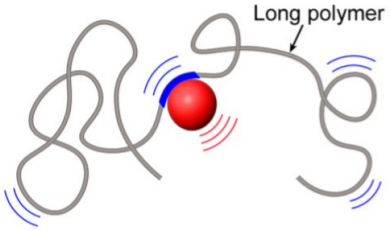
Coarse-grained trajectory (non-Markovian)

Limited observables

Protein folding-unfolding



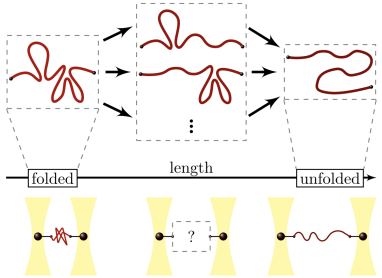
Polymer dynamics



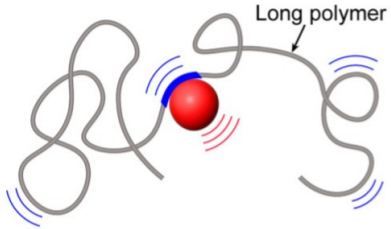
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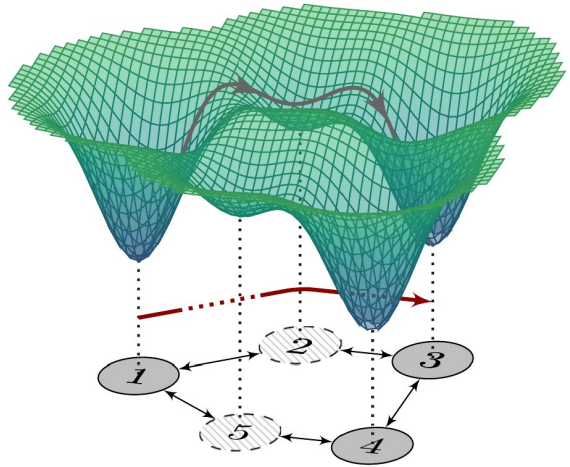


Polymer dynamics



ζ :

Γ :

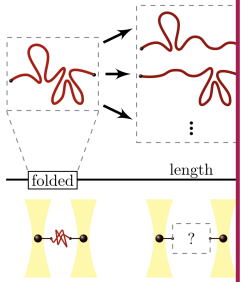


- Non-Markov process
- Non-ergodicity
- Memory effect
- Aging effect

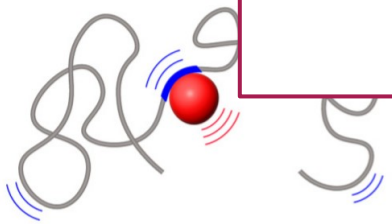
Coarse-grained trajectory (non-Markovian)

Limited obs

Protein folding



Polymer dyn



1. Smaller than true entropy.
2. **Infinitely** long data set needed.
3. **High dimension** of path probability

$$\sigma \geq \sigma_{\mathrm{CG}} \equiv \lim_{T\to\infty} \frac{1}{T} \sum_{\zeta} \mathcal{P}(\Gamma) \ln \frac{\mathcal{P}[\Gamma]}{\mathcal{P}[\tilde{\Gamma}]}$$

É. Roldán *et al.*, *PRL* (2010)

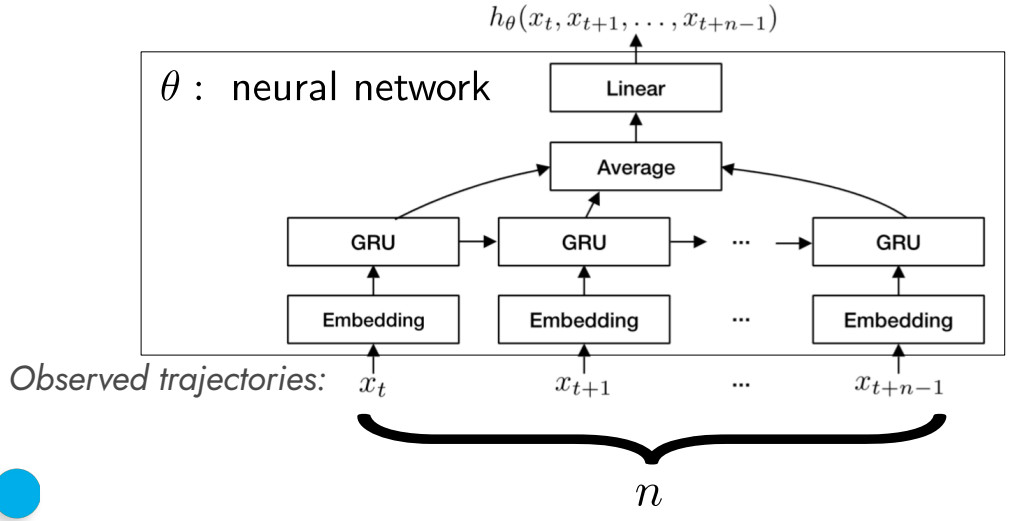
process
city
ect
t

Estimation of entropy via **neural network**

D.-K. Kim, …, **Hawoong Jeong**, *PRL* (2020)

"Maximizing J and increasing n effectively converges ΔS toward σ_{CG}."

$T \to \infty$

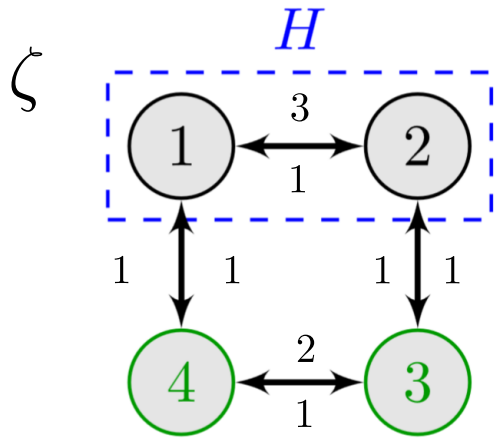


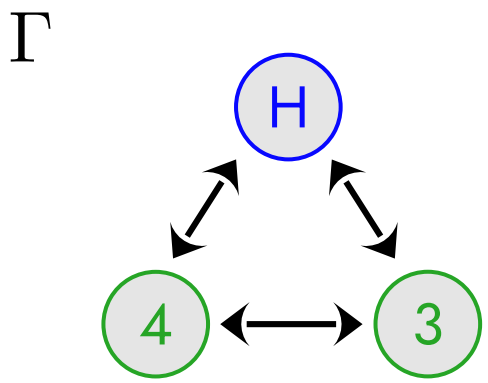
$$\Delta S_\theta(\Gamma) \equiv h_\theta(\Gamma) - h_\theta(\tilde{\Gamma})$$

$$J(\theta) \equiv \langle \Delta S_\theta(\Gamma) - e^{-\Delta S_\theta(\tilde{\Gamma})} \rangle_t$$

$$\hat{\sigma} \equiv \lim_{T\to\infty} \Delta S(\theta^*)/T = \sigma_{\mathrm{CG}}$$

Test: Coarse-grained 4-state Markov chain





$$3 \xrightarrow{t_1} H \xrightarrow{t_2} 4 \xrightarrow{t_3} 3 \xrightarrow{t_4} H \xrightarrow{t_5} \cdots$$

e.g. $n = 3$ $\quad \Gamma_1 = \{3, t_1, H, t_2, 4, t_3\}$

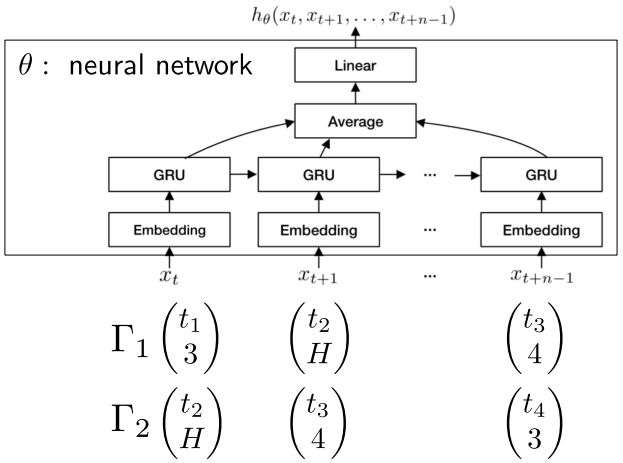
$\Gamma_2 = \{H, t_2, 4, t_3, 3, t_4\}$

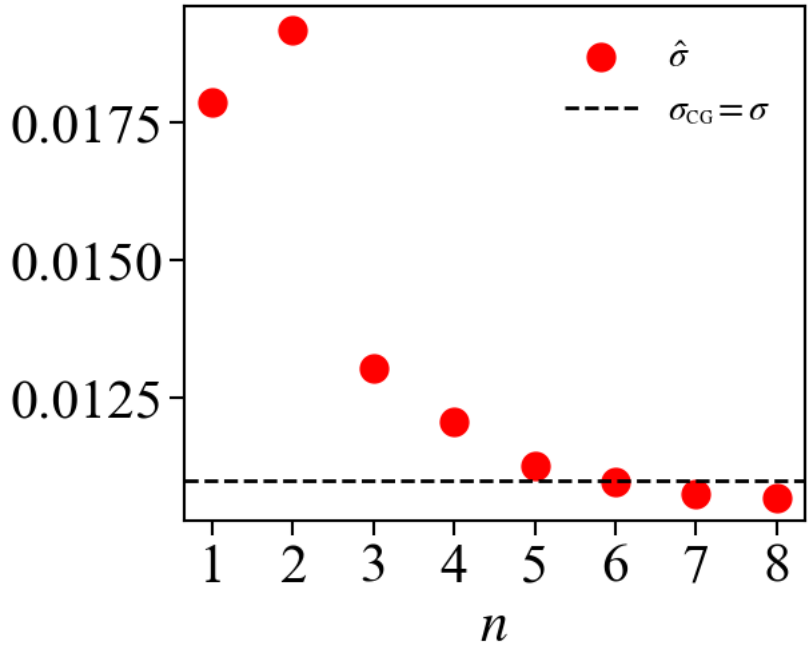
$\cdots$

Test: Coarse-grained 4-state Markov chain

(Number of states=4)

- We should increase n **until** it converges $(n \sim 7)$.
- It can be **greater** than true σ for certain ns.



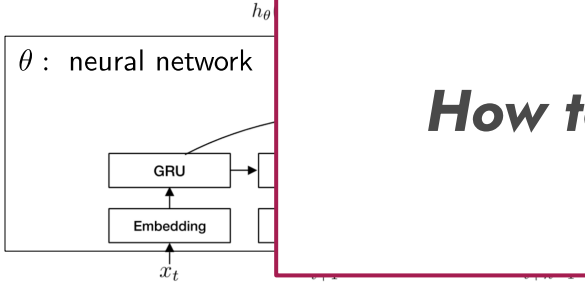


Test: Coarse-grained 4-state Markov chain

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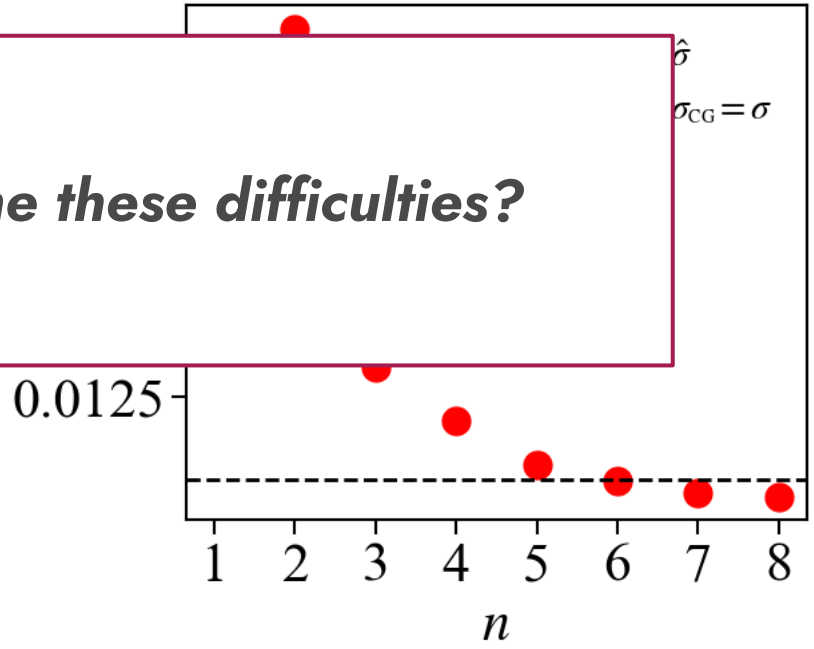
- We should increase n **until** it converges $(n \sim 7)$.
- It can be **greater** than true σ for certain ns.

How to overcome these difficulties?



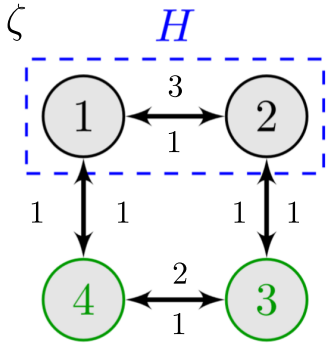
$$\Gamma_1 \begin{pmatrix} t_1 \\ 3 \end{pmatrix} \quad \begin{pmatrix} t_2 \\ H \end{pmatrix} \quad \begin{pmatrix} t_3 \\ 4 \end{pmatrix}$$

$$\Gamma_2 \begin{pmatrix} t_2 \\ H \end{pmatrix} \quad \begin{pmatrix} t_3 \\ 4 \end{pmatrix} \quad \begin{pmatrix} t_4 \\ 3 \end{pmatrix}$$



Snippets J. van der Meer... **Udo Seifert**, *PRL* (2023)

- Γ^s : Sections that result from **cutting** a trajectory at every **Markovian** event



Γ

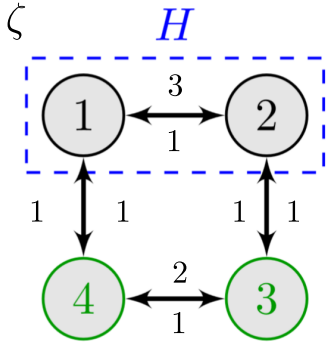
$$3 \xrightarrow{t_1} H \xrightarrow{t_2} 4 \xrightarrow{t_3} 3 \xrightarrow{t_4} H \xrightarrow{t_5} \cdots$$

$$\Gamma_1^s = \{3, t_1, H, t_2, 4, t_3\}$$
$$\Gamma_2^s = \{4, t_3, 3, t_4\}$$
$$\cdots$$

Snippets

J. van der Meer… **Udo Seifert**, *PRL* (2023)

- Γ^s : Sections that result from **cutting** a trajectory at every **Markovian** event



$$\Gamma$$

$$3 \xrightarrow{t_1} H \xrightarrow{t_2} 4 \xrightarrow{t_3} 3 \xrightarrow{t_4} H \xrightarrow{t_5} \cdots$$

$$\Gamma_1^s = \{3, t_1, H, t_2, 4, t_3\}$$
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$$\cdots$$

$$\sigma \geq \sigma_{\mathrm{CG}} \equiv \lim_{T\to\infty} \frac{1}{T} \sum_{\Gamma} \mathcal{P}(\Gamma) \ln \frac{\mathcal{P}[\Gamma]}{\mathcal{P}[\tilde{\Gamma}]}$$

$$= \lim_{T\to\infty} \frac{1}{T} \sum_{n} \sum_{\Gamma_n^s} \mathcal{P}(\Gamma_n^s) \ln \frac{\mathcal{P}[\Gamma_n^s]}{\mathcal{P}[\tilde{\Gamma}_n^s]}$$

$$= \frac{1}{\langle t \rangle} \sum_{I,J,O} p(I,J) \int \mathcal{P}[I,t,O,J] \ln \frac{\mathcal{P}[I,t,O,J]}{\mathcal{P}[\tilde{J},t,\tilde{O},\tilde{I}]}$$

$$+ \frac{1}{\langle t \rangle} \sum_{I,J} p(I,J) \ln \frac{p(J|I)}{p(\tilde{I}|\tilde{J})}$$

$\langle t \rangle$: mean time per snippet

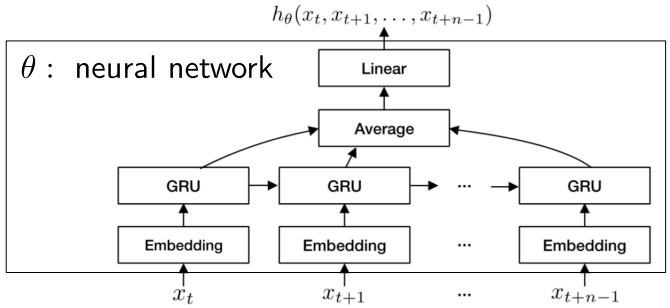
No arbitrary n required

No overestimation

Neural network

Validation of our method

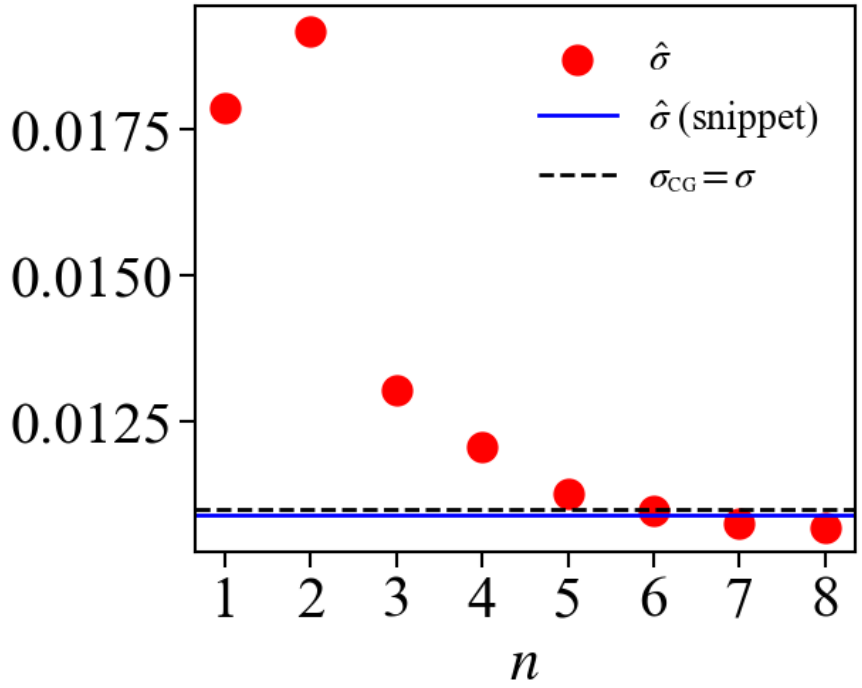
- **Unique** method.
- No **overestimation** for σ.



$$\Gamma_1 \begin{pmatrix} t_1 \\ 3 \end{pmatrix} \quad \begin{pmatrix} t_2 \\ H \end{pmatrix} \quad \begin{pmatrix} t_3 \\ 4 \end{pmatrix}$$

$$\Gamma_2 \begin{pmatrix} t_3 \\ 4 \end{pmatrix} \quad \begin{pmatrix} t_4 \\ 3 \end{pmatrix} \quad \begin{pmatrix} 0 \\ 0 \end{pmatrix}$$

(masking)

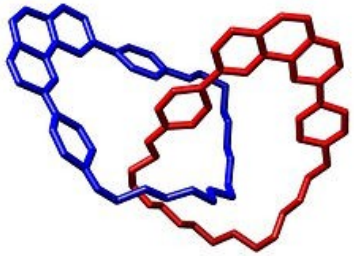


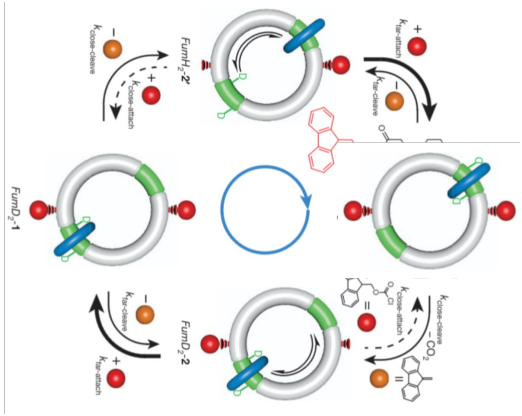
Real world application: *Catenane motors*

- An **autonomous,** *chemically fueled* small-molecule motor
- World's smallest machine

Jean-Pierre Sauvage
2016 Nobel Prize in Chemistry







Full tetrahedral cluster (FTC)

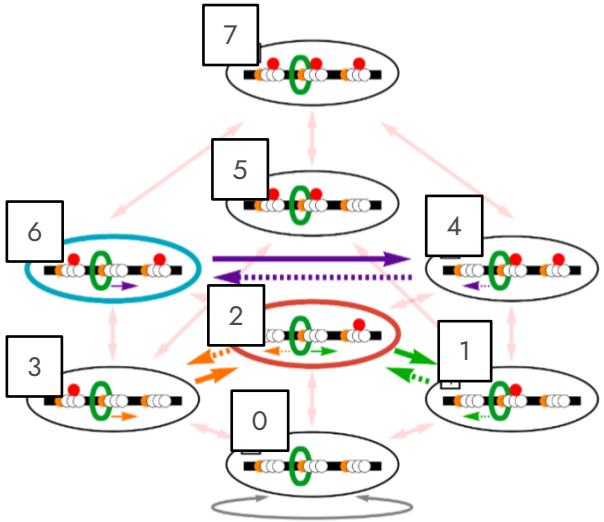
Shuttling ring

R. A Bissell *et al.*, *Nature* (1994)

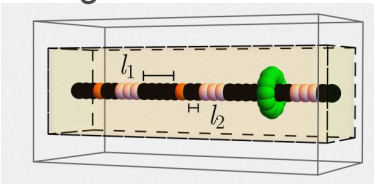
Markovian networks

- The Catenane motor system can be mapped to 8 Markov states.

A. Albaugh *et al.*, *PNAS* (2023)



Langevin simulation



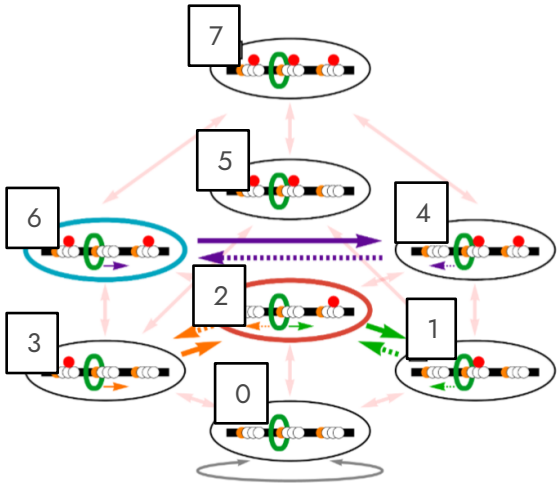
- *All transition rates are known*

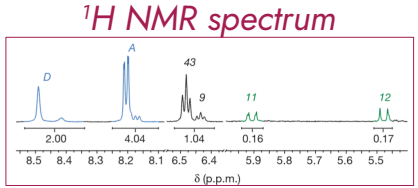


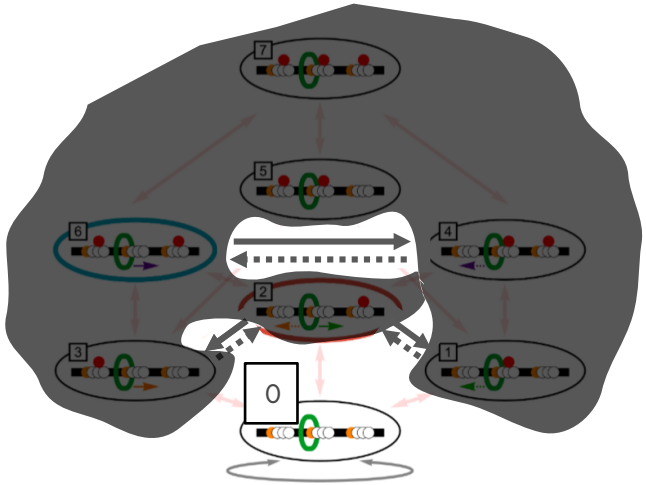
- *True EP can be calculated*

EP estimation after coarse-graining

CG: Only **state 0** and **direction of current** are observable



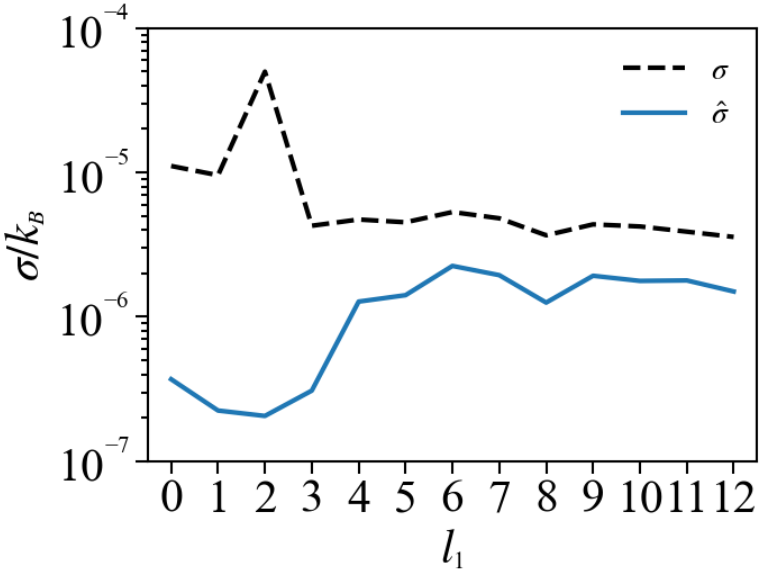




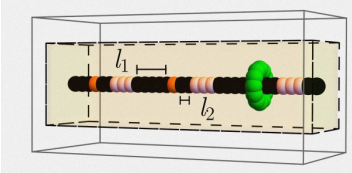
$$\Gamma : \quad 0 \quad t_0^0 \quad t_1^0 \quad 0 \quad t_0^1 \quad t_1^1 \quad t_2^1 \quad t_3^1$$

Results: EP estimation

- We observed similar trend for large l_1 , while **opposite** for short ones

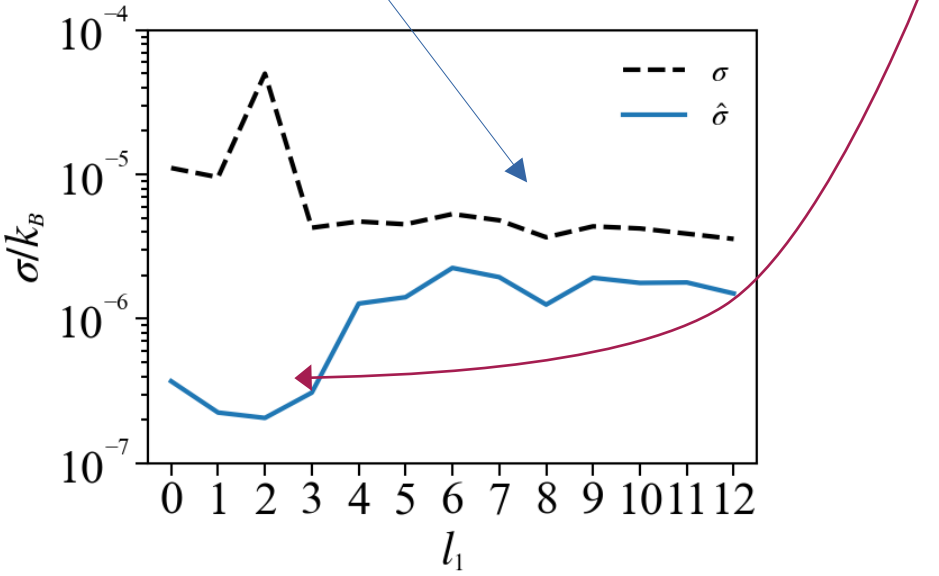


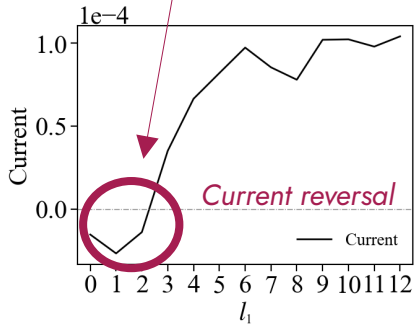
$\sigma \geq \hat{\sigma}$



Results: EP estimation

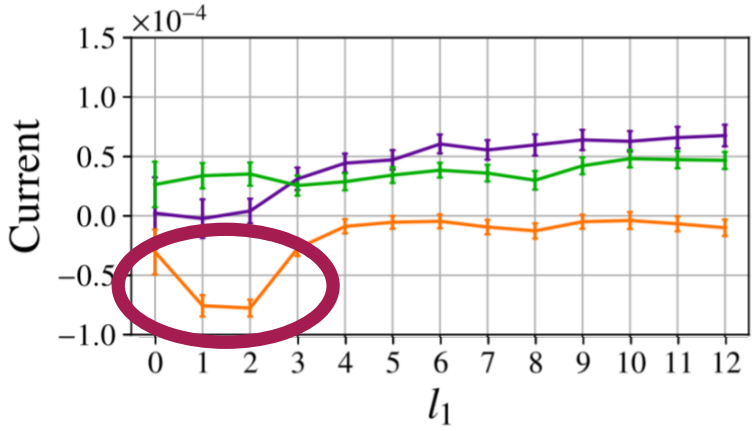
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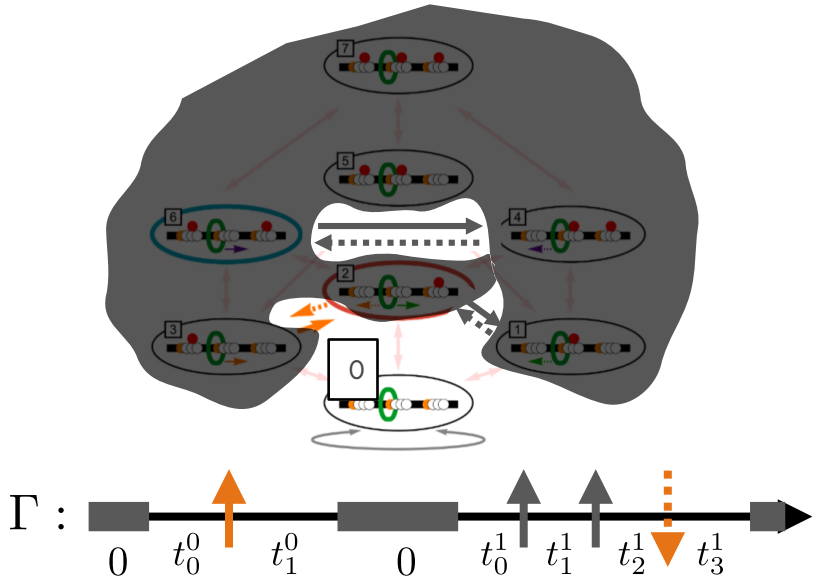




Additional information

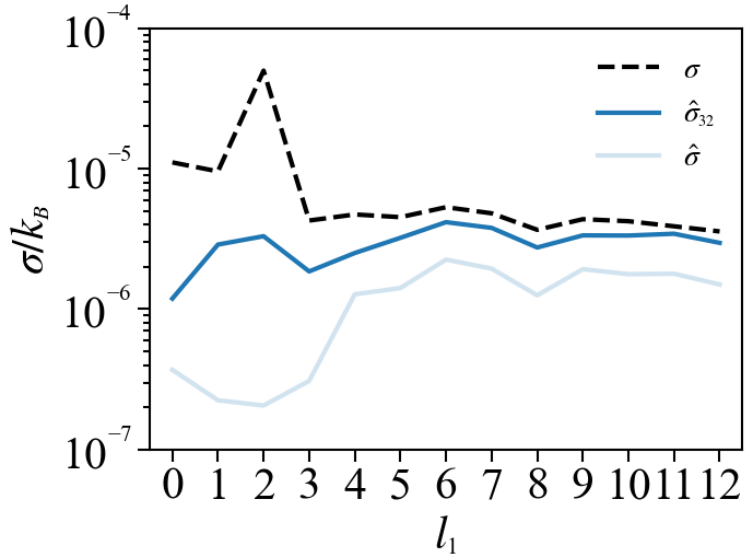
- We can **distinguish the specific current** contributing to the current reversal from others





Additional information

- Similar overall trend across the range.
- Accounting for current reversal is critical.



Summary

- We develop a new neural network method to estimate entropy of non-Markovian systems (coarse-grained trajectories).
- It turns out that the snippet is a key concept to correctly estimate the irreversibility (entropy) of non-Markovian systems using neural networks.
- We validate our neural network method using a 4-state Markov chain model.
- Additionally, we apply our method to the Catenane motor systems, estimating their entropy from observed coarse-grained states.
- For Catenane motors, information of the current reversal is critical to estimating entropy.



Acknowledgments

