Information flow and entropy production in biochemical signal transduction

Workshop on Stochasticity and Fluctuations in Small Systems
30 November 2016, Pohang, Korea

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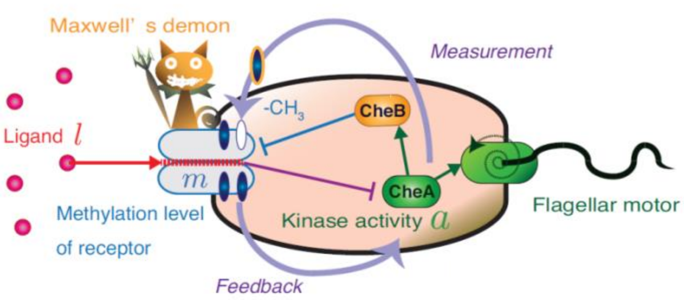

In collaboration with
Sosuke Ito
(Titech & AMOLF)

Outline

- Introduction
- Information and thermodynamics
- Thermodynamics with continuous information flow
- Application to biochemical signal transduction
- Summary

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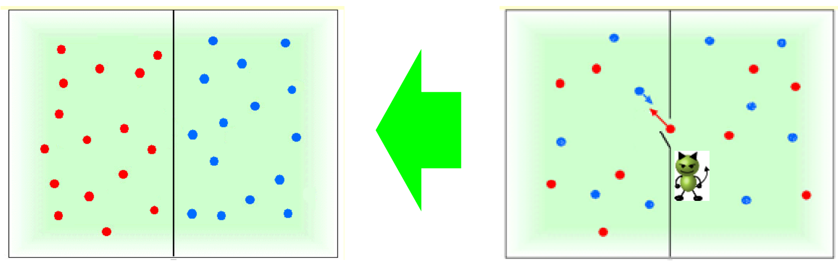
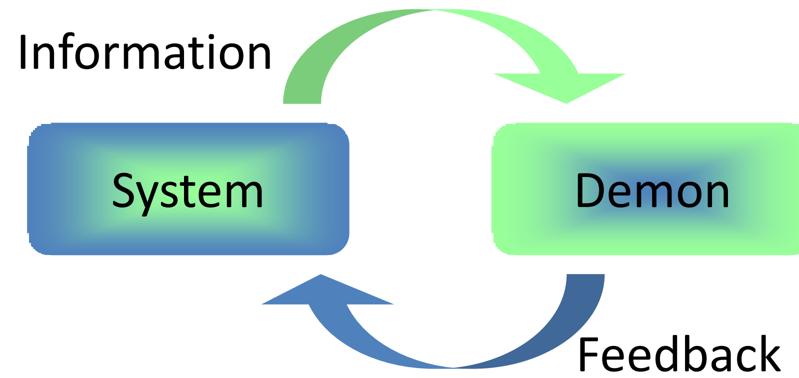
Information Thermodynamics





Information processing at the level of thermal fluctuations

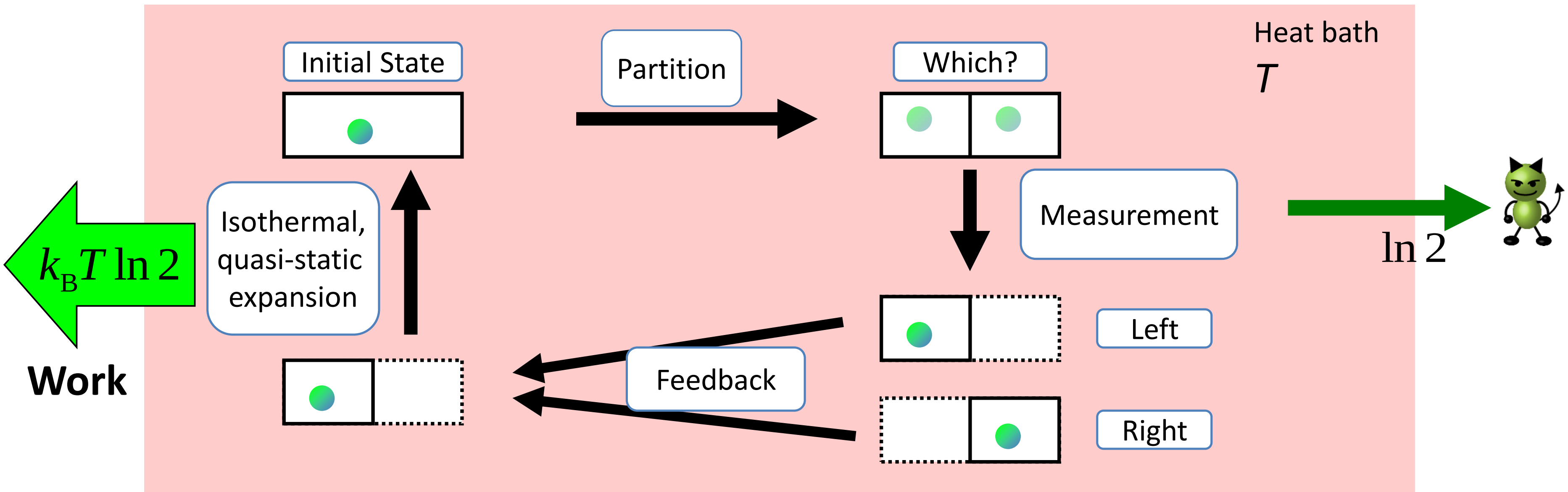
✓ Foundation of the second law of thermodynamics

✓ Application to nanomachines and nanodevices

Review: J. M. R. Parrondo, J. M. Horowitz, & T. Sagawa, *Nature Physics* **11**, 131-139 (2015).

L. Szilard, Z. Phys. **53**, 840 (1929)

Szilard Engine (1929)



Free energy: $F = E - TS$

Increase

Decrease by feedback

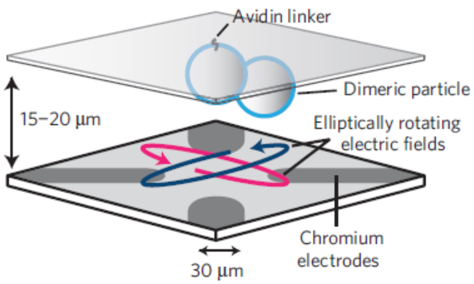
Can control physical entropy by using information

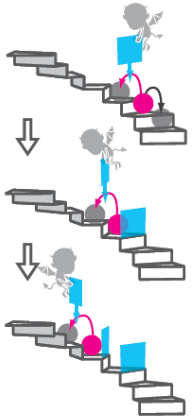
Experimental Realizations

- With a colloidal particle
  Toyabe, TS, Ueda, Muneyuki, & Sano, Nature Physics (2010)

Efficiency: 30%

Validation of $\left\langle e^{-\beta(W-\Delta F)} \right\rangle = \gamma$

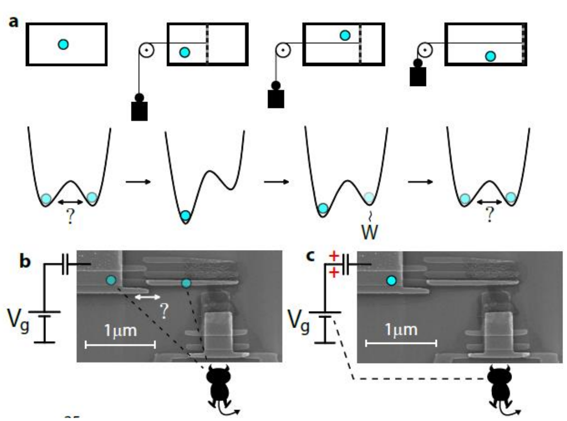




- With a single electron
  Koski, Maisi, TS, & Pekola, PRL (2014)

Efficiency: 75%

Validation of $\left\langle e^{-\beta(W-\Delta F)-I} \right\rangle = 1$



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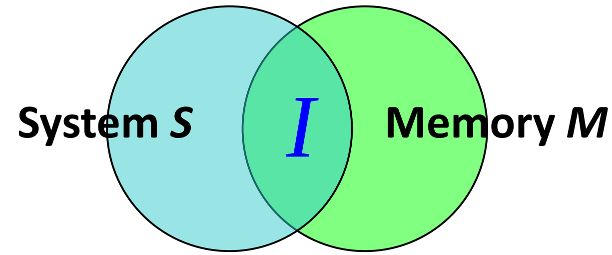
Mutual Information

System S → **Memory M** (measurement device)

Measurement with stochastic errors



$$I(S:M) \equiv H(S) + H(M) - H(SM)$$

Shannon information $H = -\sum_k p_k \ln p_k$

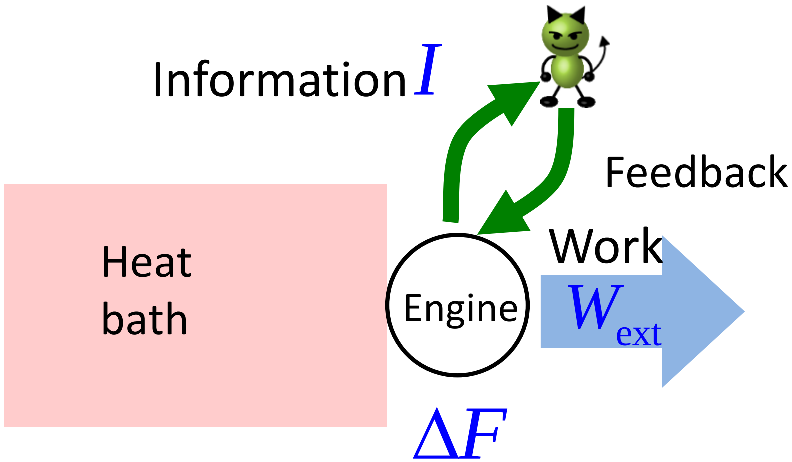
$$0 \leq I \leq H(M)$$

No information

No error

Correlation between S and M

Upper Bound of Extractable Work by Feedback



Assumption:
Initial canonical distribution

TS and M. Ueda, PRL **100**, 080403 (2008).
TS and M. Ueda, PRL **104**, 090602 (2010).

$$W_{\mathrm{ext}} \leq -\Delta F + k_{\mathrm{B}} T I$$

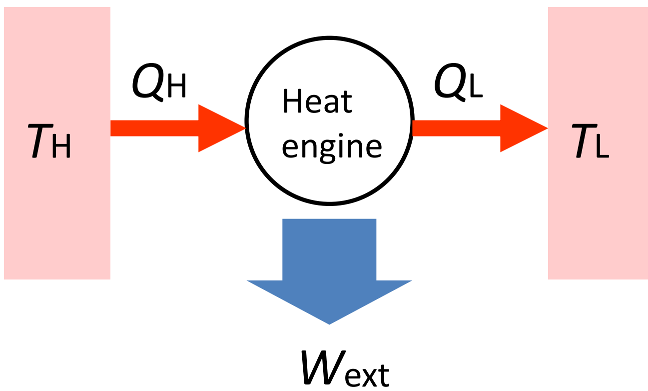
The upper bound of the work extracted by the demon is bounded by the mutual information.

The equality is achieved in the thermodynamically reversible limit

Information Heat Engine

Conventional heat engine:

Heat → Work



Heat efficiency

$$e \equiv \frac{W_{\mathrm{ext}}}{Q_{\mathrm{H}}} \leq 1 - \frac{T_{\mathrm{L}}}{T_{\mathrm{H}}}$$

Carnot cycle

Information heat engine:

Mutual information → Work and Free energy

$$W_{\mathrm{ext}} + \Delta F \leq k_{\mathrm{B}} T I .$$

Szilard engine

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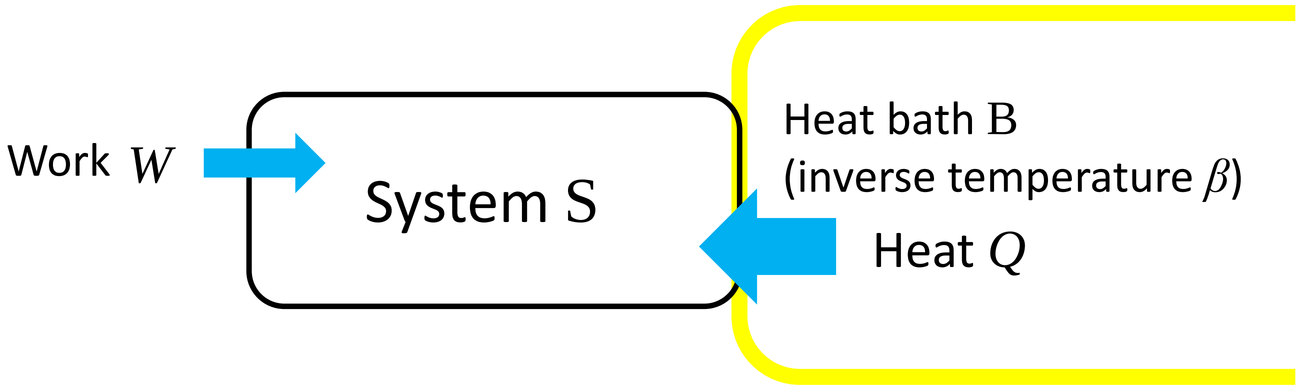
Entropy Production

Stochastic dynamics of system S (e.g., Langevin system)



Entropy production in the total system:

$$\Delta S_{\mathrm{SB}} \equiv \underbrace{\Delta S_{\mathrm{S}}}_{\text{Change in the Shannon entropy of S}} - \beta \underbrace{\langle Q \rangle}_{\text{Averaged heat absorbed by S}}$$

Two Approaches to Continuous Information Flow

- **"Transfer entropy"** approach
  - ✓ Applicable to non-Markovian dynamics
  - ✓ Second law is weaker in Markovian dynamics

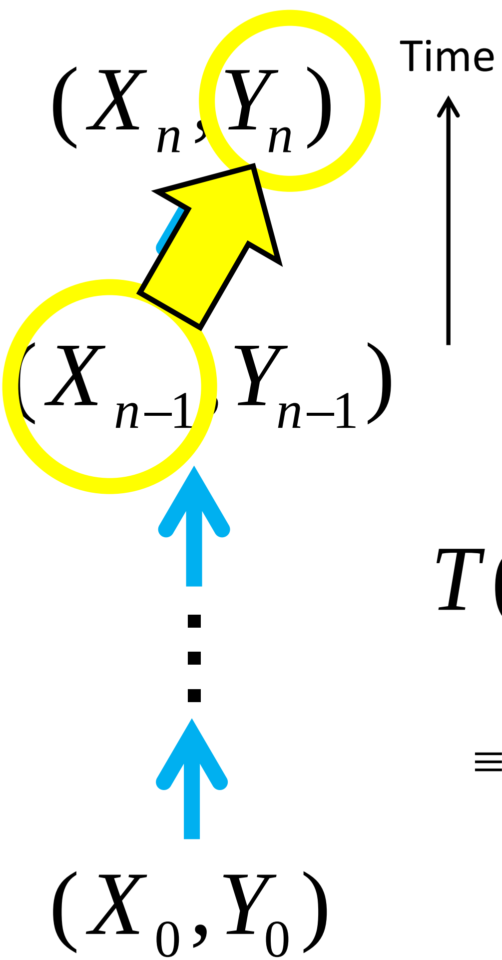
Ito & Sagawa, Phys. Rev. Lett. (2013)

- **"Information flow"** approach
  - ✓ Not applicable to non-Markovian dynamics
  - ✓ Second law is stronger in Markovian dynamics

Second law: Allahverdyan, Dominik & Guenter, J. Stat. Mech. (2009)
Horowitz & Esposito, Phys. Rev. X (2014)
Horowitz & Sandberg, New J. Phys. (2014)
Fluctuation theorem: Shiraishi & Sagawa, Phys. Rev. E (2015)
Rosinberg & Horowitz, EPL (2016)
Onsager reciprocity: Yamamoto, Ito, Shiraishi, & Sagawa, PRE (2016)

Transfer Entropy

Directional information transfer between two systems



Transfer entropy:
Directional information flow
from X to Y
during time n and $n+1$

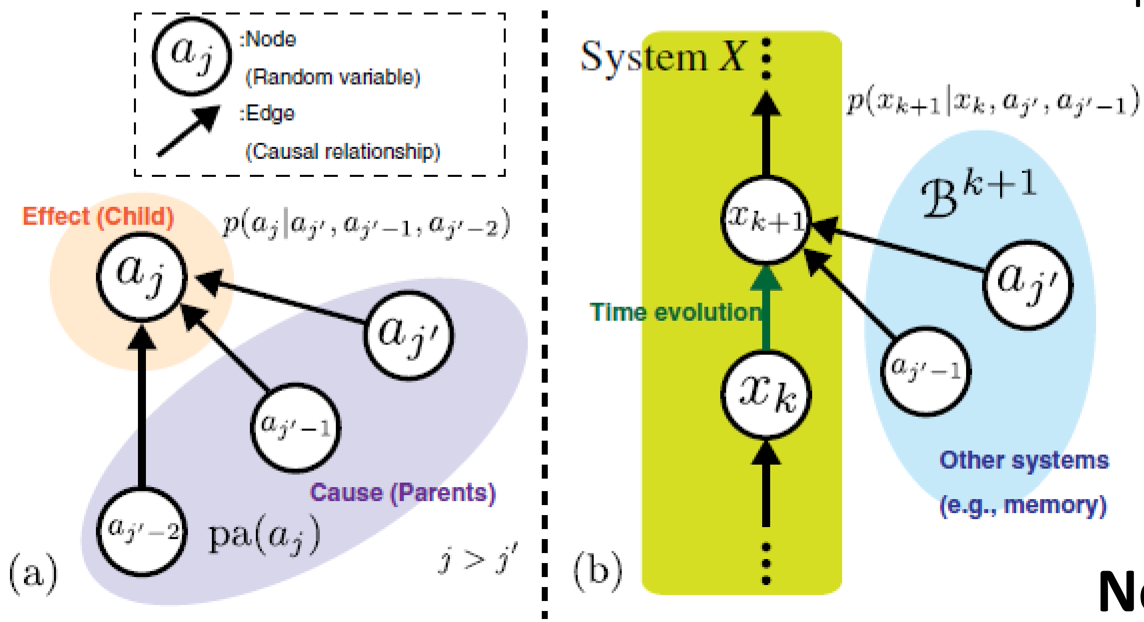
Conditional mutual information

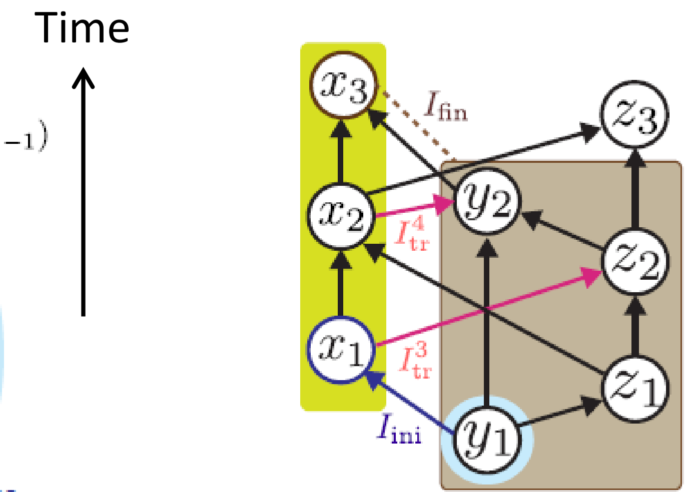
$$T(X_{n-1} \to Y_n) \equiv I\left(X_{n-1} : Y_n \mid Y_{n-1} \cdots Y_0\right)$$

$$\equiv \sum_{x_{n-1}, y_0, \cdots y_n} p(x_{n-1}, y_0, \cdots y_n) \ln \frac{p(x_{n-1}, y_n \mid y_0, \cdots y_{n-1})}{p(x_{n-1} \mid y_0, \cdots y_{n-1})\, p(y_n \mid y_0, \cdots y_{n-1})}$$

T. Schreiber, PRL **85**, 461 (2000)

Many-body Systems with Complex Information Flow





Node: Event

Arrow: Causal relationship

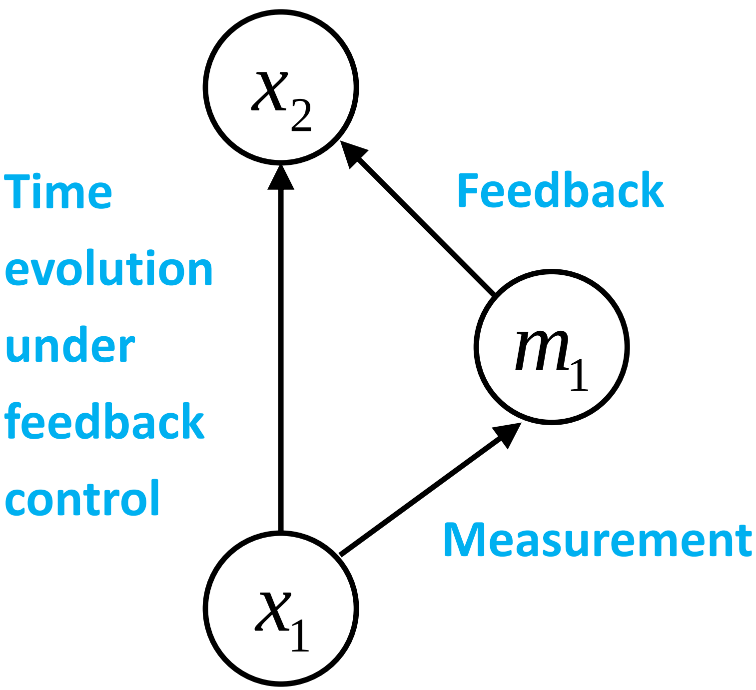
Characterize the dynamics by **Bayesian networks**

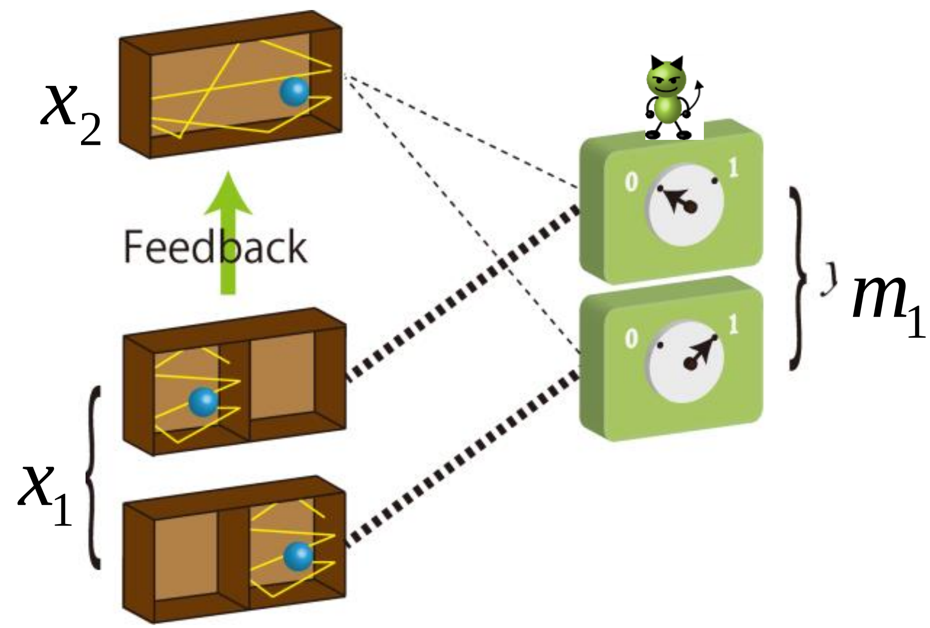
Sosuke Ito & TS, PRL 111, 180603 (2013).

Example: Measurement and Feedback

The joint probability

$$p(x_1)\,p(m_1 \mid x_1)\,p(x_2 \mid m_1, x_1)$$



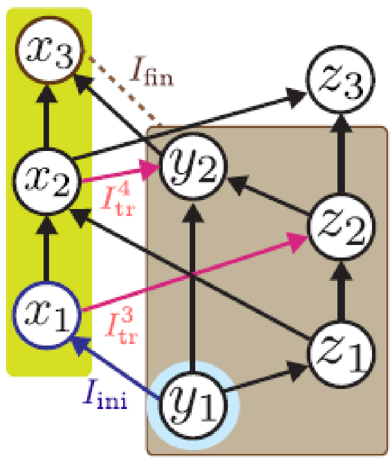


Second Law on Bayesian Networks

$$\Delta S_{\mathrm{XB}} \geq \Theta$$

Informational quantity:

$$\Theta = I_{\mathrm{fin}} - I_{\mathrm{ini}} - \sum_{l} I_{\mathrm{tr}}^{l}$$



ΔS_{XB} **: Entropy production in X and the bath**

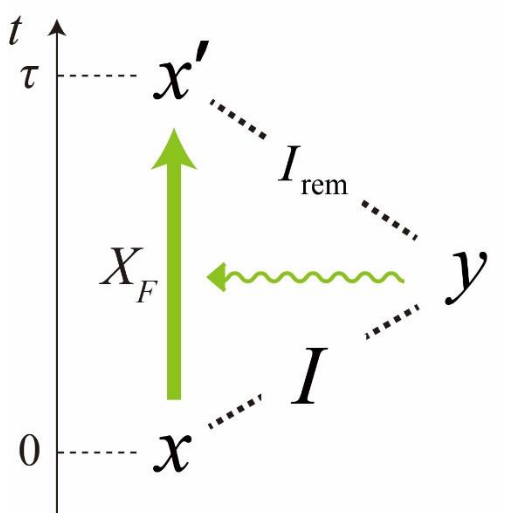
I_{ini} : Initial correlation between X and the other systems

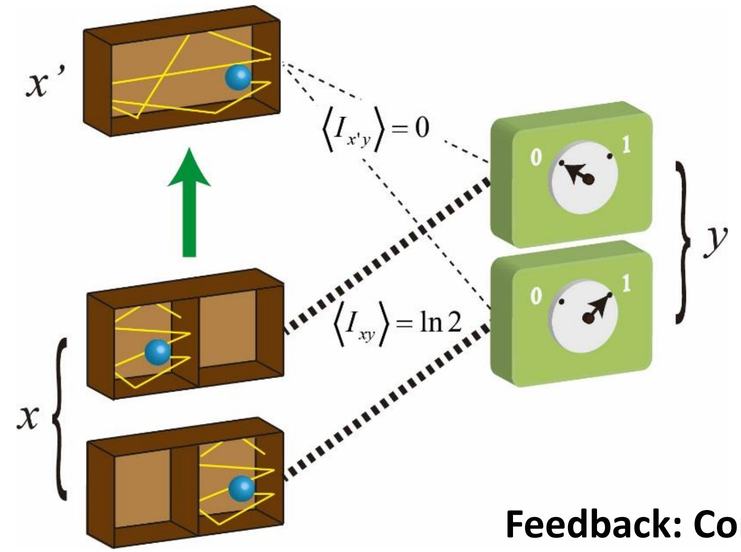
I_{fin} : Final correlation between X and the other systems

$I_{\mathrm{tr}}{}^{l}$: **Transfer entropy** from X to the other systems during the dynamics

Sosuke Ito & TS, PRL 111, 180603 (2013).

Reproduce the Second Law with Feedback





X: Engine
Y: Demon

Feedback: Control protocol depends on the measurement outcome

$$\Delta I \equiv I_{\mathrm{rem}} - I$$

$$\Delta S_{\mathrm{XB}} \geq -\underline{(I - I_{\mathrm{rem}})}$$

(Upper bound of) the correlation that is used by feedback

$$\langle W \rangle \geq \Delta F - k_{\mathrm{B}} T I$$

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Toward Biological Information Processing

What is the role of information in living systems?

Mutual information is experimentally accessible

ex. Apoptosis path: Cheong *et al*. *Science* (2011).

There is no explicit channel coding inside living cells;

Shannon's second theorem is not straightforwardly applicable

Application of information thermodynamics

Barato, Hartich & Seifert, New J. Phys. **16**, 103024 (2014).

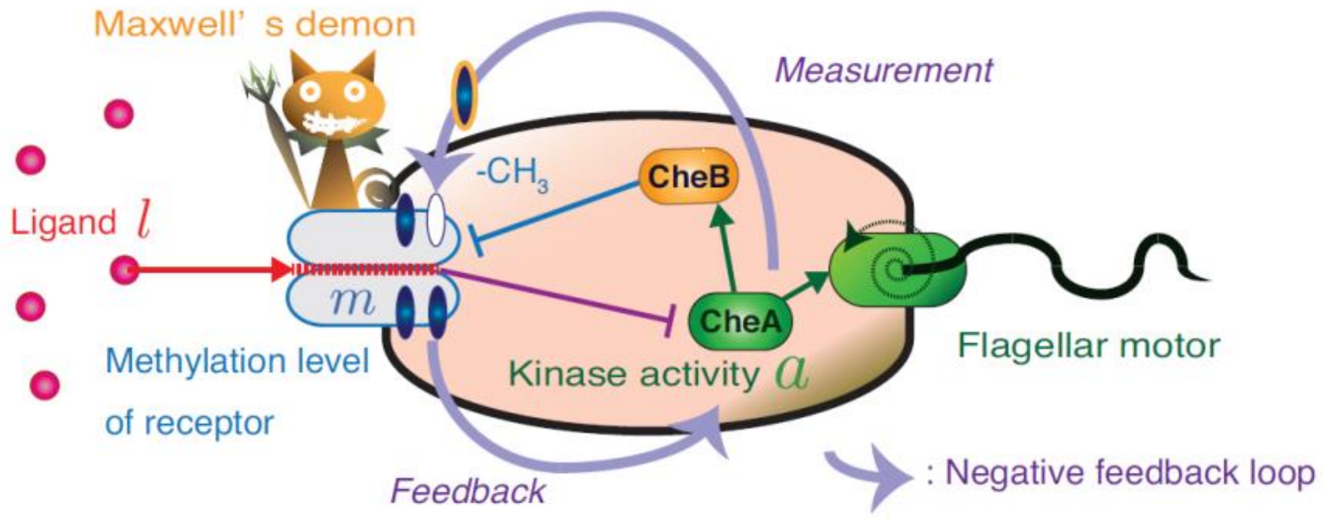
Sartori, Granger, Lee & Horowitz, PLoS Compt. Biol. **10**, e1003974 (2014).

Ito & Sagawa, Nat. Commu. **6**, 7498 (2015).

Our finding:

Relationship between information and the robustness of adaptation

Signal Transduction of *E. Coli* Chemotaxis



E. Coli moves toward food (ligand)

The information about **ligand density** is transferred to the **methylation level** of the receptor, and used for the feedback to the **kinase activity**.

Adaptation Dynamics

2D Langevin model

Y. Tu *et al., Proc. Natl. Acad. Sci. USA* **105**, 14855 (2008).
F. Tostevin and P. R. ten Wolde, *Phys. Rev. Lett.* **102**, 218101 (2009).
F. G. Lan *et al., Nature Physics* **8**, 422 (2012).

$$\dot{a}_t = -\frac{1}{\tau^a}[a_t - \bar{a}_t(m_t, l_t)] + \xi_t^a$$

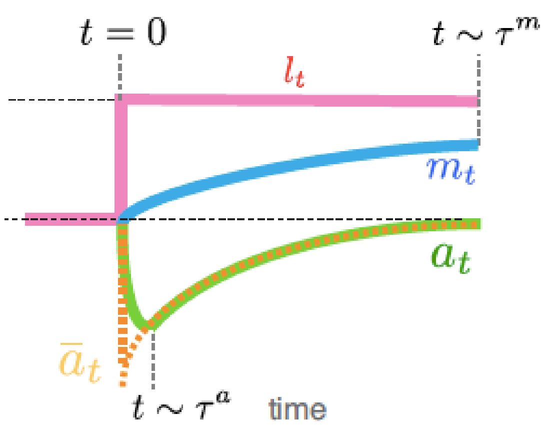
$$\dot{m}_t = -\frac{1}{\tau^m} a_t + \xi_t^m$$

$$\langle \xi_t^x \rangle = 0 \quad \langle \xi_t^x \xi_{t'}^{x'} \rangle = 2T_t^x \delta_{xx'} \delta(t - t')$$

$\bar{a}_t(m_t, l_t) \simeq \alpha m_t - \beta l_t$: stationary value of a_t

$\alpha, \beta > 0$

a_t : kinase activity
m_t : methylation level
l_t : average ligand density
$\tau^m \gg \tau^a > 0$: time constants



Negative feedback loop:

- ✓ Instantaneous change of a_t in response to l_t
- ✓ Memorize l_t by m_t
- ✓ a_t goes back to the initial value

Second Law of Information Thermodynamics

$$dI_t^{\mathrm{tr}} + dS_t^{a|m} \geq \frac{J_t^a}{T_t^a} dt$$

$dS_t^{a|m} := \langle \ln p(a_t|m_t) \rangle - \langle \ln p(a_{t+dt}|m_{t+dt}) \rangle$: Change in the conditional Shannon entropy

$dI_t^{\mathrm{tr}} := I(a_t : m_{t+dt}|m_t)$ **: Transfer entropy**

$\frac{J_t^a}{T_t^a} = \frac{1}{\tau^a T_t^a} \left[T_t^a - \frac{\langle (a_t - \bar{a}_t)^2 \rangle}{\tau^a} \right]$ **: Robustness against the environmental noise**

Upper bound of the robustness is given by the transfer entropy

S. Ito & T. Sagawa, *Nature Communications* **6**, 7498 (2015).

Stationary State

$$\underbrace{\langle (a_t - \bar{a}_t)^2 \rangle} \geq \tau^a T_t^a \left[1 - \underbrace{\frac{dI_t^{\mathrm{tr}}}{dt}} \right]$$

Fluctuation (inaccuracy of information transmission) induced by environmental noise

Transfer entropy

Without feedback： $\langle (a_t - \bar{a}_t)^2 \rangle \geq \tau^a T_t^a$

Exact Expression of Transfer Entropy

If the Langevin equation is linear:

$$dI_t^{\mathrm{tr}} = \frac{1}{2} \ln \left(1 + \boxed{\frac{dP_t}{N_t}} \right)$$

Signal-to-noise ratio

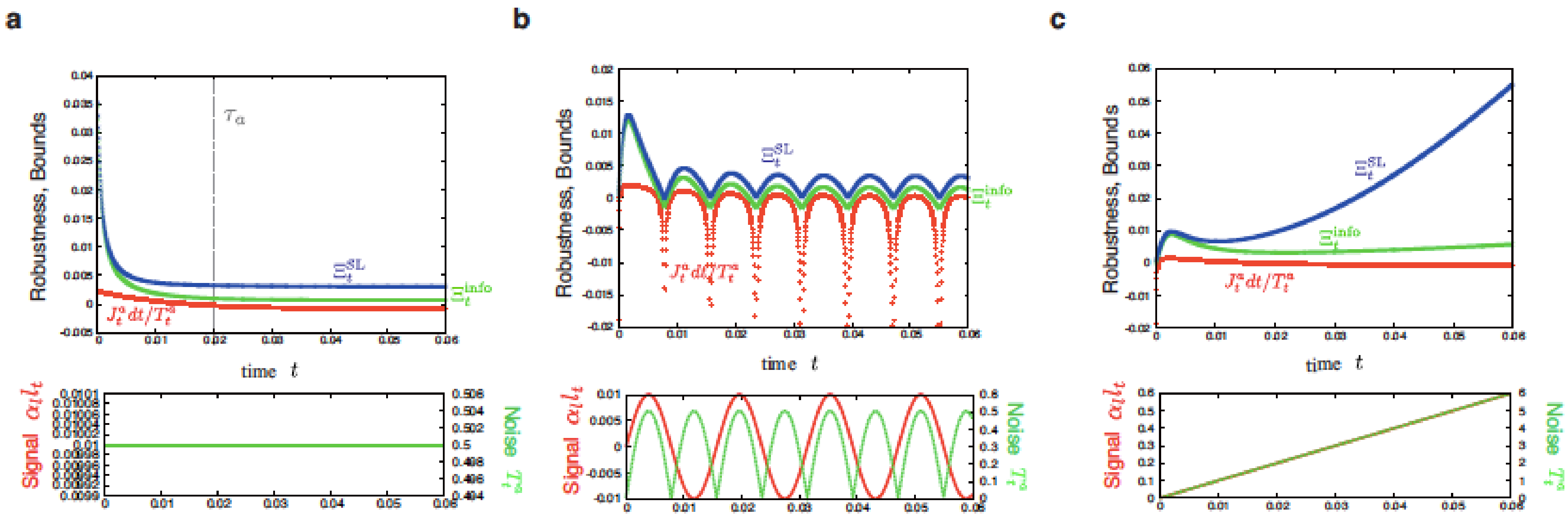
$$dP_t := \frac{(\rho_t^{am})^2 V_t^a}{(\tau^m)^2} dt$$ **: power of the signal from *a* to *m***

$$N_t := 2T_t^m$$ **: noise of *m***

$$V_t^x := \langle x_t^2 \rangle - \langle x_t \rangle^2 \qquad \rho_t^{am} := \frac{\langle a_t m_t \rangle - \langle a_t \rangle \langle m_t \rangle}{\sqrt{V_t^a V_t^m}}$$

Analogous to the Shannon–Hartley theorem

Information-thermodynamic Efficiency



Input ligand signal: a, step function. b, sinusoidal function. c, linear function.

Numerical simulation:

Red: robustness of adaptation

Green: information-thermodynamic bound $\Xi_t^{\rm info}$

Blue: conventional thermodynamic bound $\Xi_t^{\rm SL}$

- ✓ Information thermodynamics gives **a stronger bound**.
- ✓ The adaptation dynamics is inefficient (dissipative) as a conventional thermodynamic engine, but **efficient as an information-thermodynamic engine**.

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Summary

- Second law with transfer entropy on causal networks

S. Ito & T. Sagawa, *Phys. Rev. Lett.* **111**, 180603 (2013).

- Information thermodynamics of biochemical signal transduction
  - ✓ Transfer entropy characterizes the **robustness** of adaptation

S. Ito & T. Sagawa, *Nature Communications* **6**, 7498 (2015).

Review of information thermodynamics:
J. M. R. Parrondo, J. M. Horowitz, & T. Sagawa, *Nature Physics* **11**, 131-139 (2015).

Thank you for your attention!