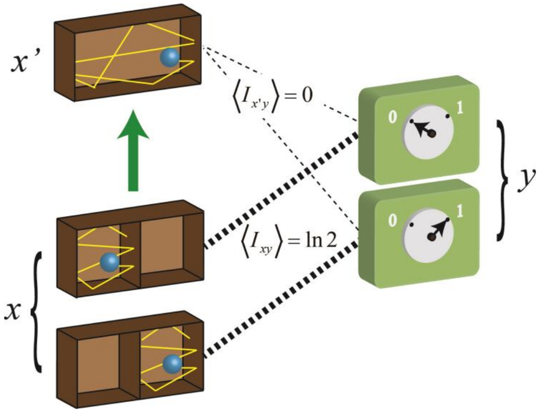
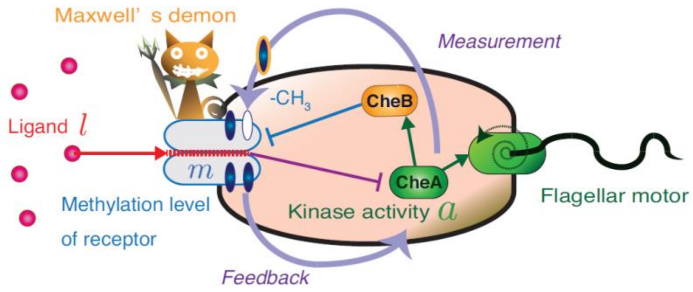
Maxwell's Demon in Biochemical Signal Transduction





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New Frontiers in Non-equilibrium Physics 2015

28 July 2015, YITP, Kyoto

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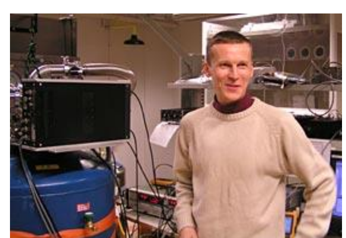

Outline

Review of previous results

- Introduction
- Information and entropy
- Information thermodynamics: a general framework
- Paradox of Maxwell's demon

- Thermodynamics of autonomous information processing
- Application to biochemical signal transduction

Today's main part!

- Summary

Outline

- **Introduction**
- Information and entropy
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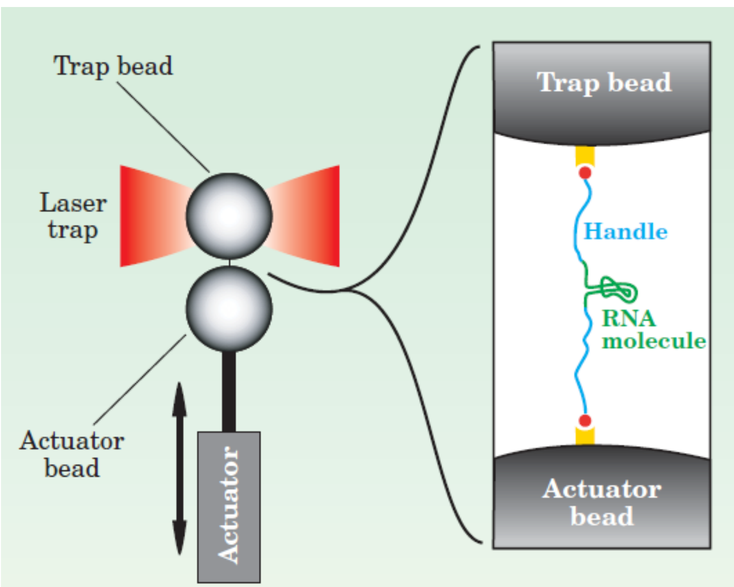
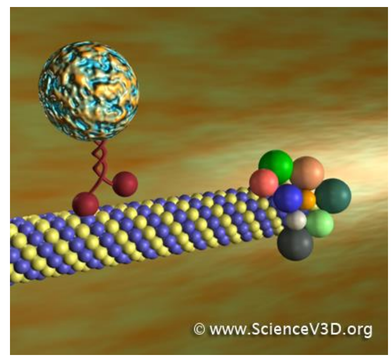
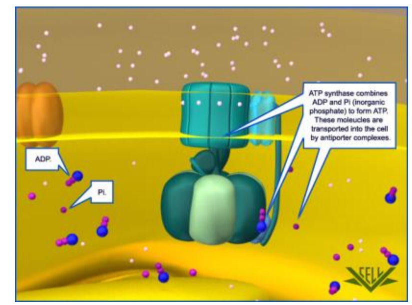
Thermodynamics in the Fluctuating World

Thermodynamics of small systems with large heat bath(s)

➡ Thermodynamic quantities are fluctuating!



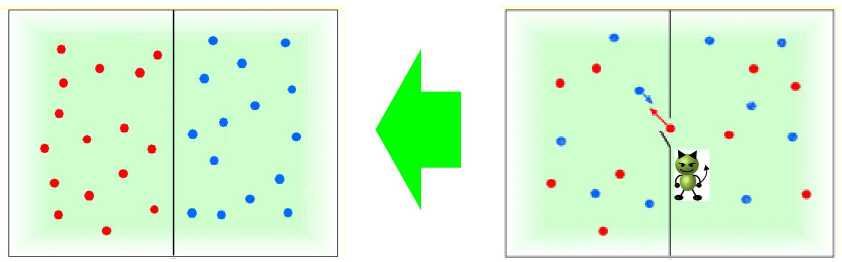


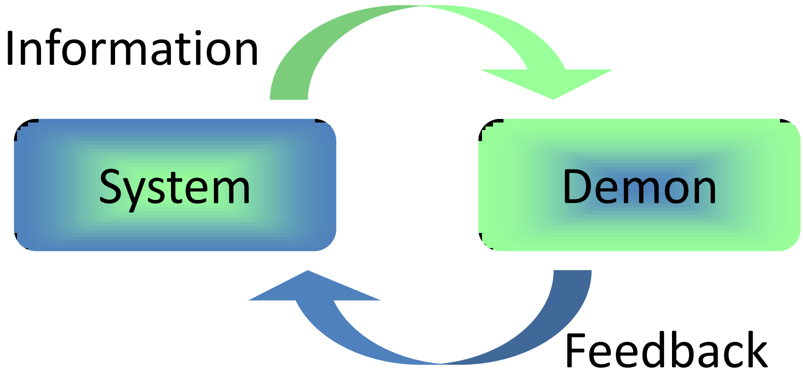


✓ **Second law** $\langle W \rangle \geq \Delta F$

✓ **Nonlinear & nonequilibrium relations**

Information Thermodynamics





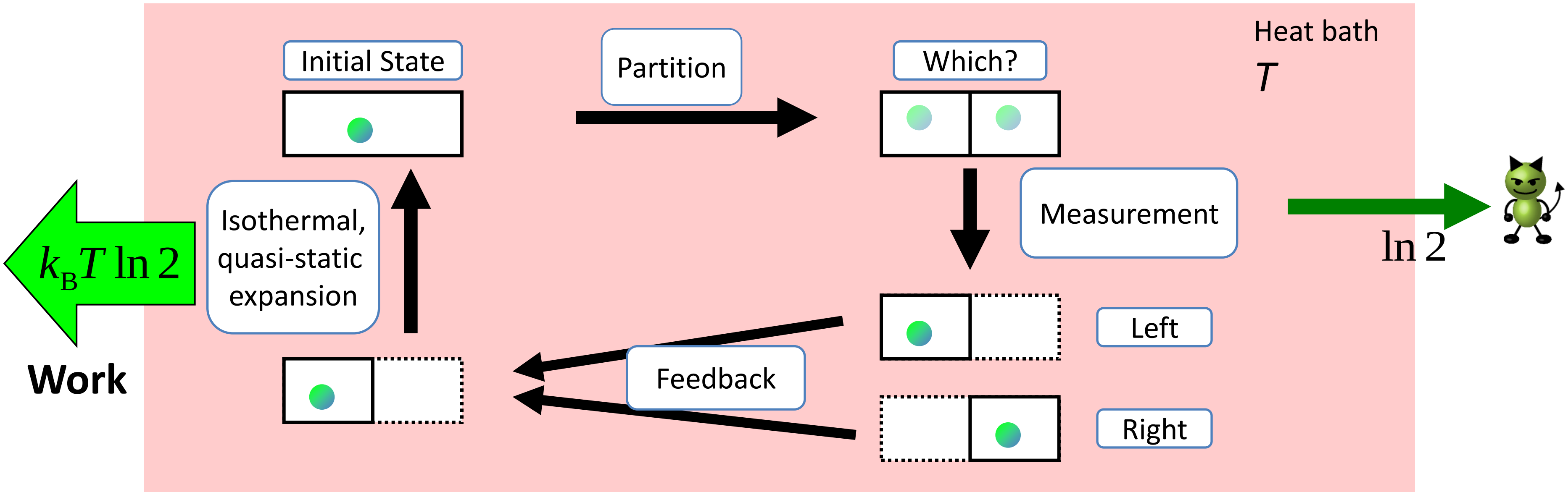
Information processing at the level of thermal fluctuations

- ✓ 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: $F = E - TS$

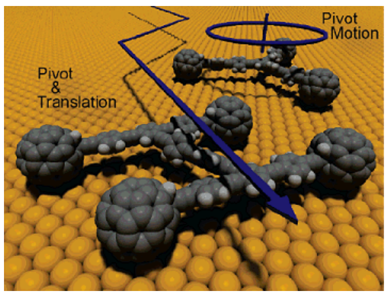
Increase (F)

Decrease by feedback (S)

Can control physical entropy by using information

Information Heat Engine

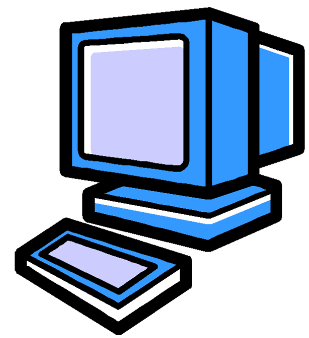
System
(Working engine)



Information

Feedback

Memory
(Controller)



Free energy / work

Entropic cost

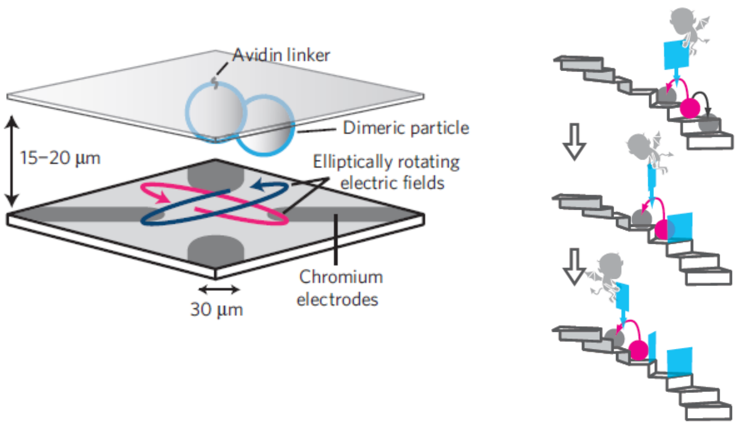
✓ **Can increase the system's free energy even if there is no energy flow between the system and the controller**

Experimental Realizations

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

  Efficiency: 30%

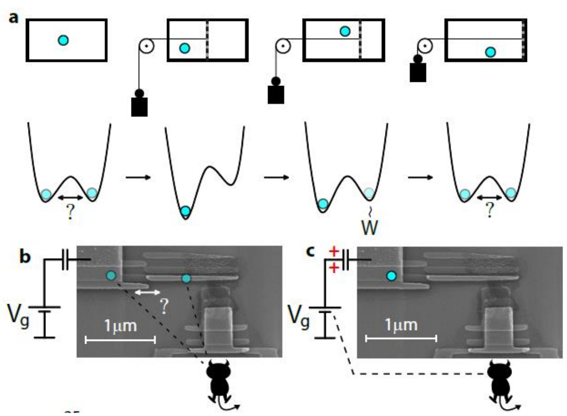
  Validation of $\left\langle e^{-\beta(W-\Delta F)} \right\rangle = \gamma$



- 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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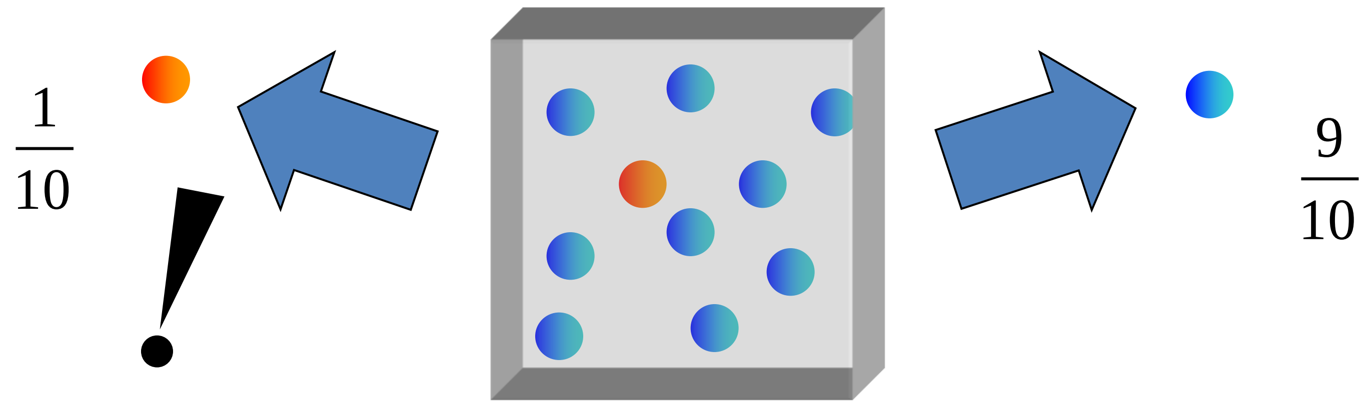
Shannon Information



Information content with event k: $\ln \frac{1}{p_k}$

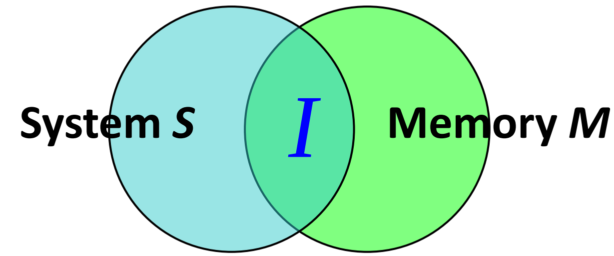
Average

Shannon information: $H = \sum_k p_k \ln \frac{1}{p_k}$

Mutual Information

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

Measurement with stochastic errors

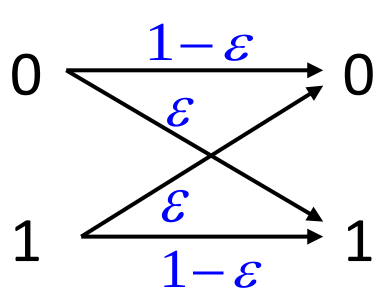


$$I(S:M) \equiv H(S) + H(M) - H(SM)$$

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

No information

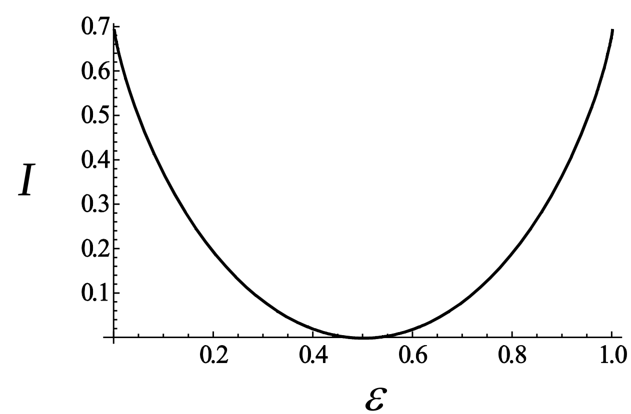
No error



Ex. Binary symmetric channel

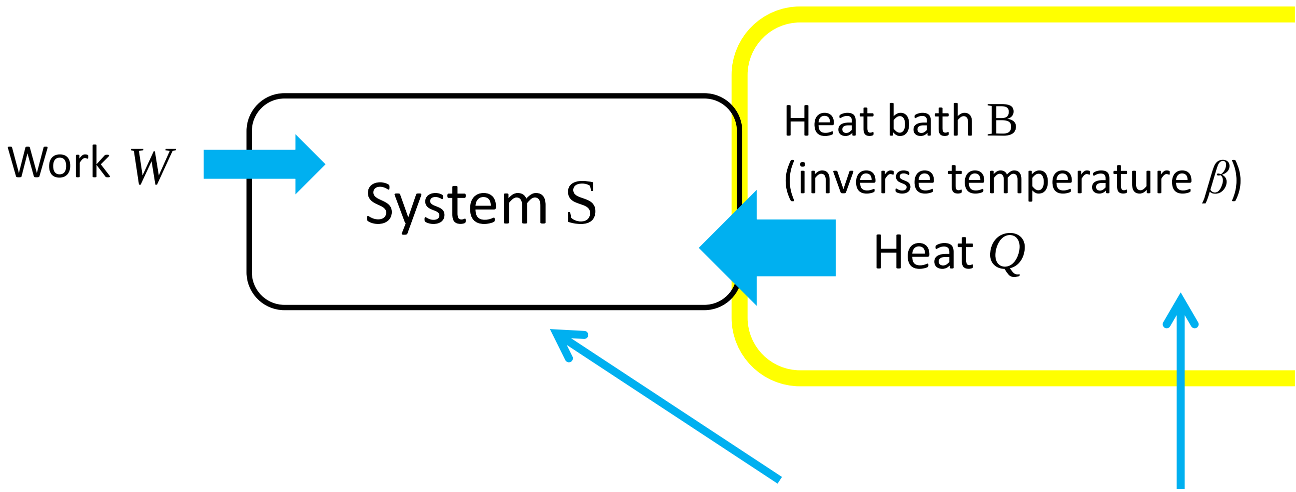
Correlation between S and M

$$I = \ln 2 + \varepsilon \ln \varepsilon + (1-\varepsilon)\ln(1-\varepsilon)$$



Entropy Production

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



Entropy production in the total system: $$\Delta S_{\mathrm{SB}} \equiv \Delta S_{\mathrm{S}} - \beta \langle Q \rangle$$

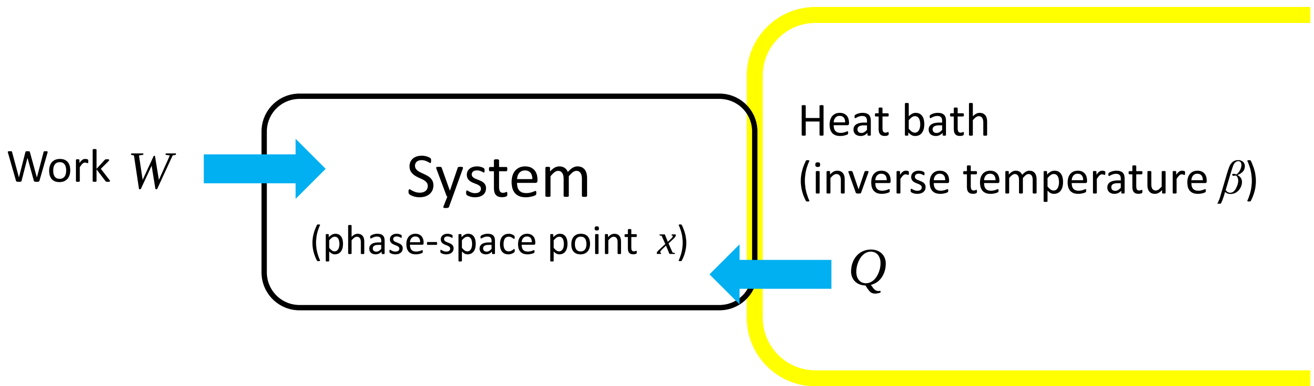
Change in the Shannon entropy of S (ΔS_{S})

Averaged heat absorbed by S ($\beta \langle Q \rangle$)

If the initial and the final states are canonical distributions: $$\Delta S_{\mathrm{SB}} = \beta \left(\langle W \rangle - \Delta F \right)$$

Free-energy difference (ΔF)

Stochastic Entropy Production



Stochastic entropy production along a trajectory of the system from time 0 to τ

$$\Delta s_{\rm SB} \equiv \Delta s_{\rm S} - \beta Q$$

$$\Delta s_{\rm S} \equiv s_{\rm S}[x(\tau),\tau] - s_{\rm S}[x(0),0] \qquad s_{\rm S}[x,t] \equiv -\ln P[x,t]$$

$$\langle \Delta s_{\rm S} \rangle = \Delta S_{\rm S}$$

$P[x,t]$: probability distribution at time t

If the initial and the final states are canonical distributions: $\Delta s_{\rm SB} = \beta(W - \Delta F)$

Integral Fluctuation Theorem and Jarzynski Equality

Integral fluctuation theorem

$$\left\langle e^{-\Delta s_{\mathrm{SB}}} \right\rangle = 1$$

Seifert, PRL (2005), …

for any initial and final distributions

Second law can be expressed by an **equality** with full cumulants

➡ The second law of thermodynamics (Clausius inequality)

$$\left\langle \Delta s_{\mathrm{SB}} \right\rangle \geq 0 \quad \Leftrightarrow \quad \Delta S_{\mathrm{S}} \geq \beta \langle Q \rangle$$

Jarzynski equality

Jarzynski, PRL (1997)

$$\Delta s_{\mathrm{SB}} = \beta (W - \Delta F) \quad \Rightarrow \quad \left\langle e^{-\beta W} \right\rangle = e^{-\beta \Delta F} \quad \Rightarrow \quad \langle W \rangle \geq \Delta F$$

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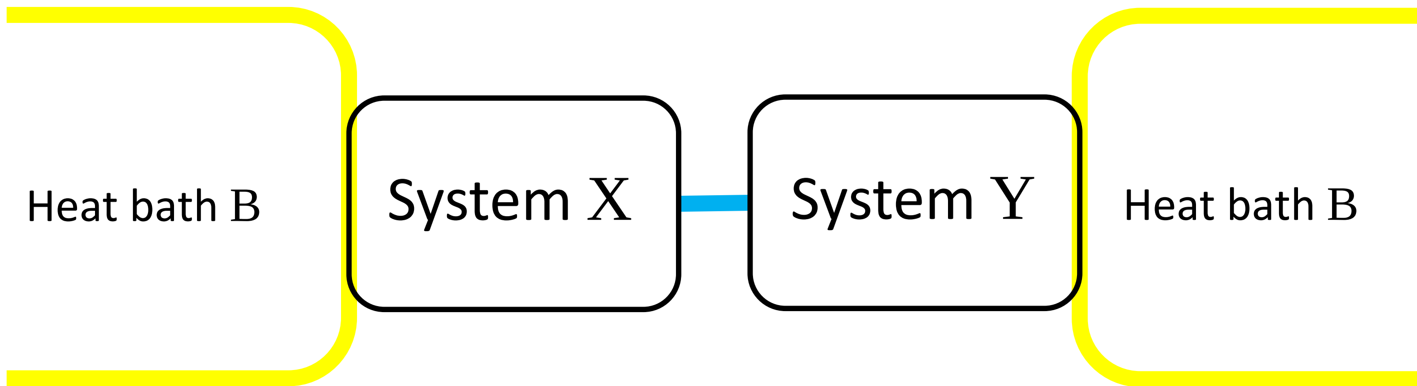
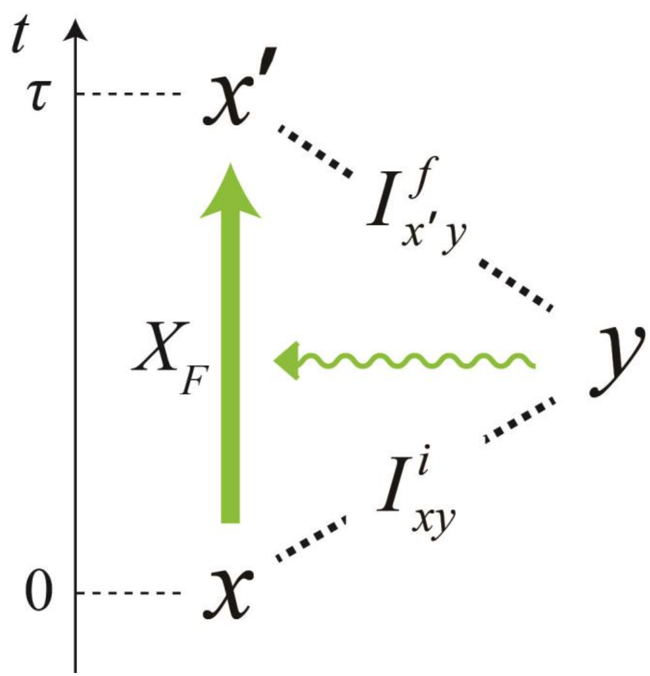
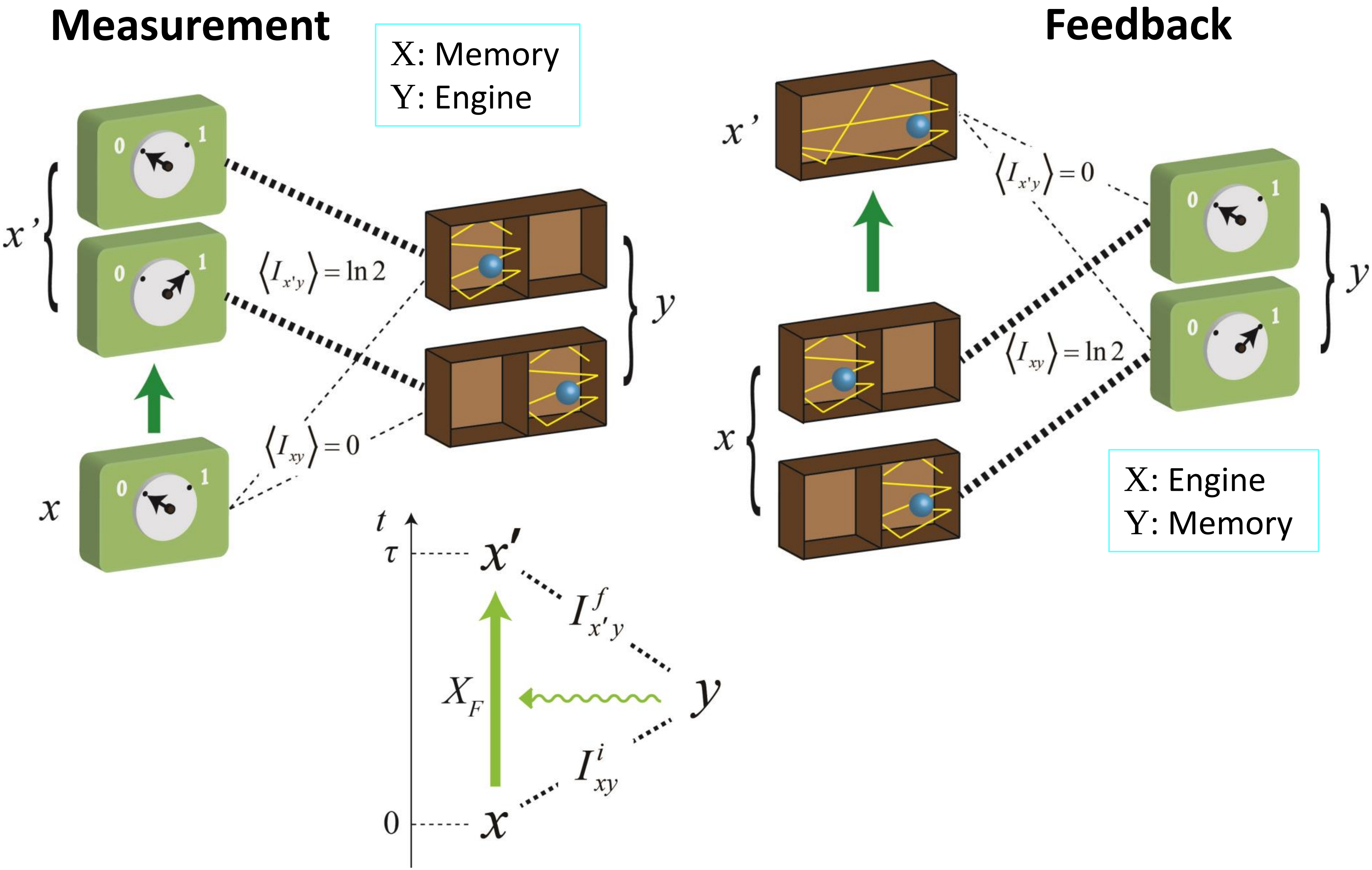
Setup





Time evolution of X
under the influence of Y with
initial and final correlations

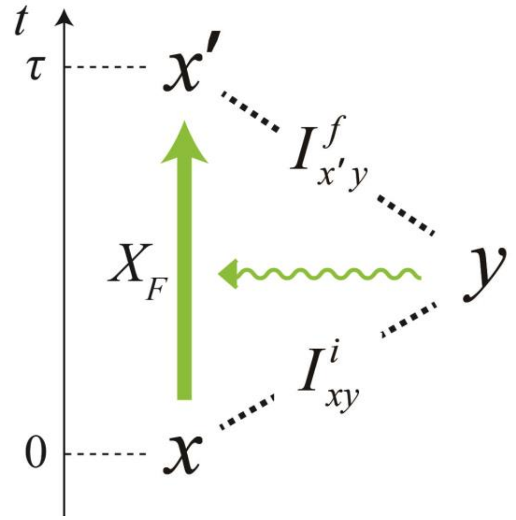
Special Cases: Measurement and Feedback



Stochastic Entropy and Mutual Information

Entropy increase in XB

$$\Delta s_{\mathrm{XB}} \equiv \Delta s_{\mathrm{X}} - \beta Q_{\mathrm{X}}$$



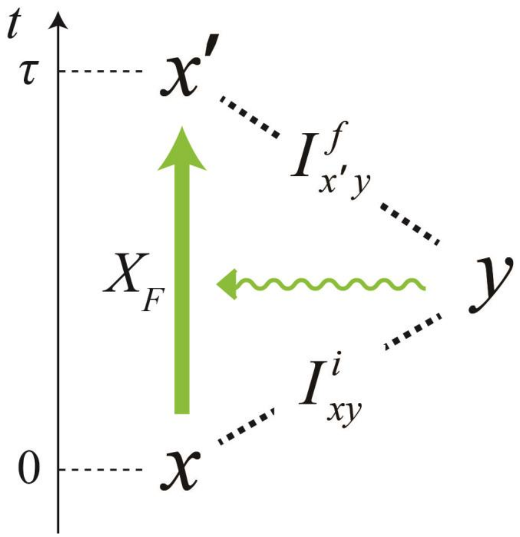
Initial correlation

$$I^i_{xy} \equiv \ln \frac{P[x,y]}{P[x]P[y]} \quad \Rightarrow \quad \langle I^i_{xy} \rangle = \int dx dy P[x,y] \ln \frac{P[x,y]}{P[x]P[y]}$$

Final correlation

$$I^f_{x'y} \equiv \ln \frac{P[x',y]}{P[x']P[y]} \quad \Rightarrow \quad \langle I^f_{x'y} \rangle = \int dx' dy P[x',y] \ln \frac{P[x',y]}{P[x']P[y]}$$

Decomposition of Entropy Production



Total entropy production in XYB

$$\Delta s_{\mathrm{XYB}} = \Delta s_{\mathrm{XB}} - \Delta I$$

$$\Delta s_{\mathrm{XYB}} \equiv \Delta s_{\mathrm{XY}} - \beta Q_{\mathrm{X}}$$

$$\Delta s_{\mathrm{XB}} \equiv \Delta s_{\mathrm{X}} - \beta Q_{\mathrm{X}}$$

$$\Delta I \equiv I^f_{x'y} - I^i_{xy}$$

$$\Delta s_{\mathrm{XY}} = \Delta s_{\mathrm{X}} + \cancel{\Delta s_{\mathrm{Y}}} - \Delta I$$

$$= \Delta s_{\mathrm{X}} - \Delta I$$

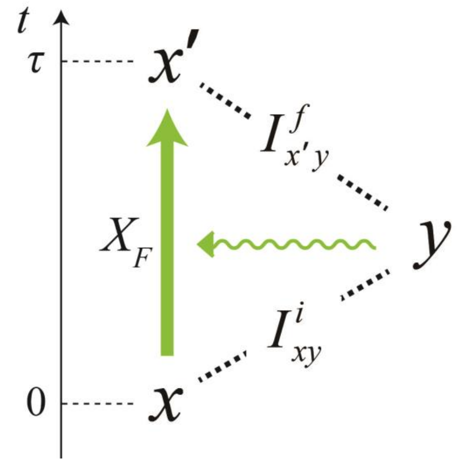
Fluctuation Theorem

Integral fluctuation theorem

$$\Delta s_{\mathrm{XYB}} = \Delta s_{\mathrm{XB}} - \Delta I$$

$$\left\langle e^{-\Delta s_{\mathrm{XYB}}} \right\rangle = 1$$

$$\Leftrightarrow \quad \left\langle e^{-\Delta s_{\mathrm{XB}} + \Delta I} \right\rangle = 1$$

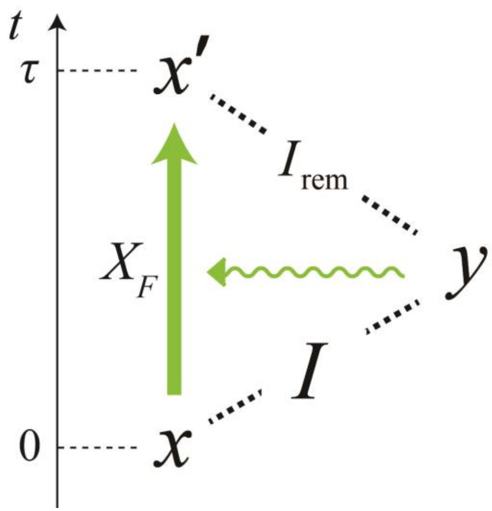


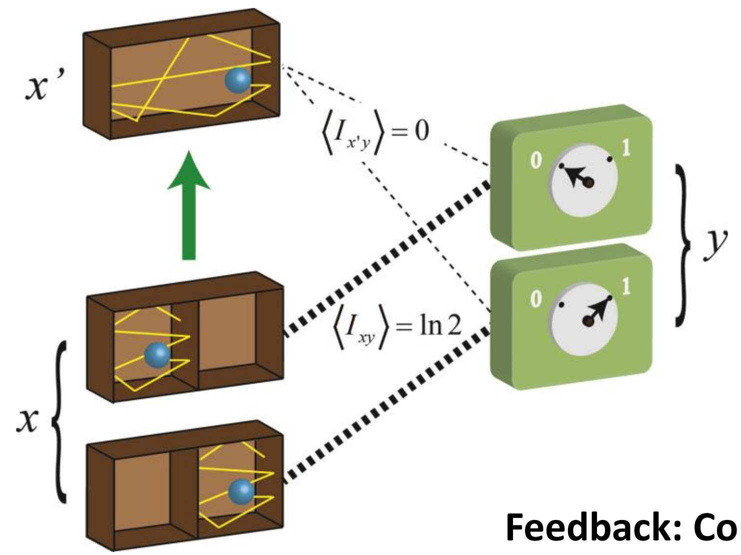
Second law $\left\langle \Delta s_{\mathrm{XYB}} \right\rangle \geq 0$

$$\Leftrightarrow \quad \left\langle \Delta s_{\mathrm{XB}} \right\rangle \geq \left\langle \Delta I \right\rangle$$

TS and M. Ueda, Phys. Rev. Lett. **109**, 180602 (2012).

Special Case 1: Feedback Control





X: Engine
Y: Memory

Feedback: Control protocol depends on the measurement outcome

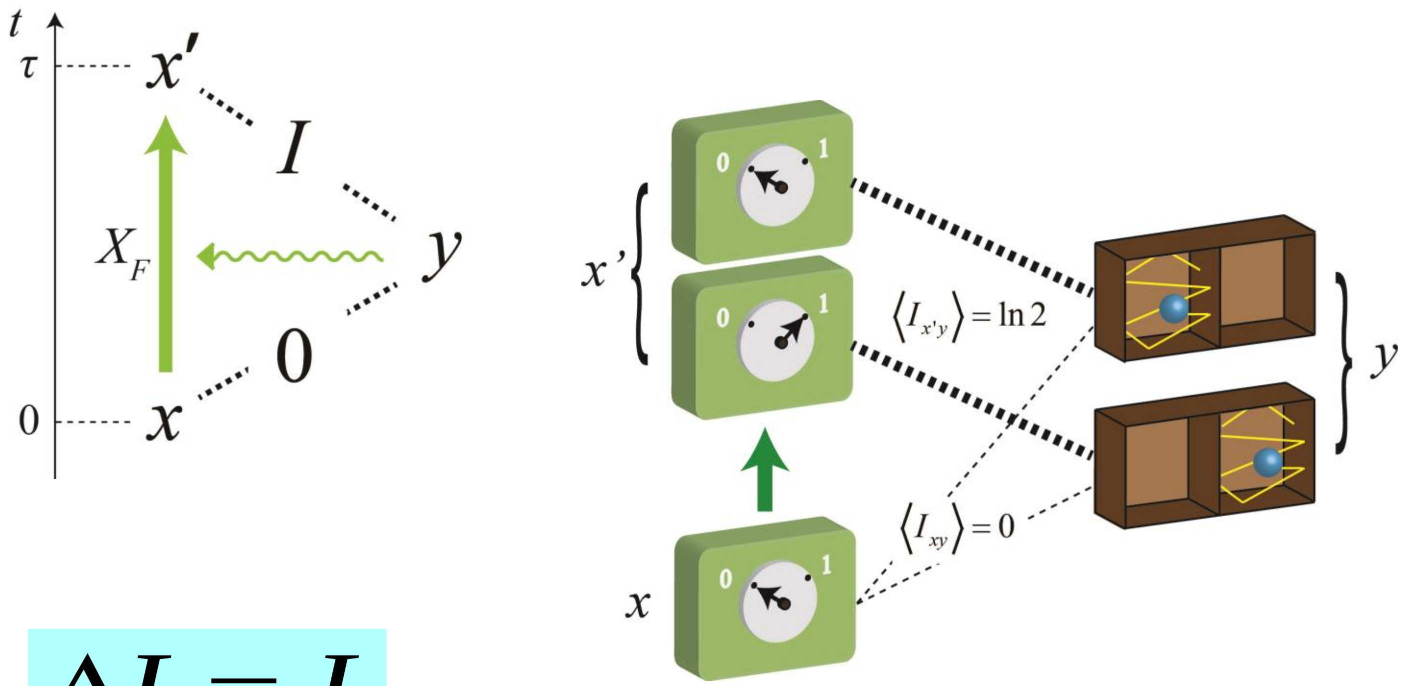
$$\Delta I \equiv I_{\text{rem}} - I$$

$$\Rightarrow \left\langle e^{-\Delta s_{\text{XB}} + (I_{\text{rem}} - I)} \right\rangle = 1 \qquad \Rightarrow \langle \Delta s_{\text{XB}} \rangle \geq -\langle I - I_{\text{rem}} \rangle$$

$$\Rightarrow W_{\text{ext}} \leq -\Delta F + k_{\text{B}} T \langle I \rangle$$

F : equilibrium free energy

Special Case 2: Measurement

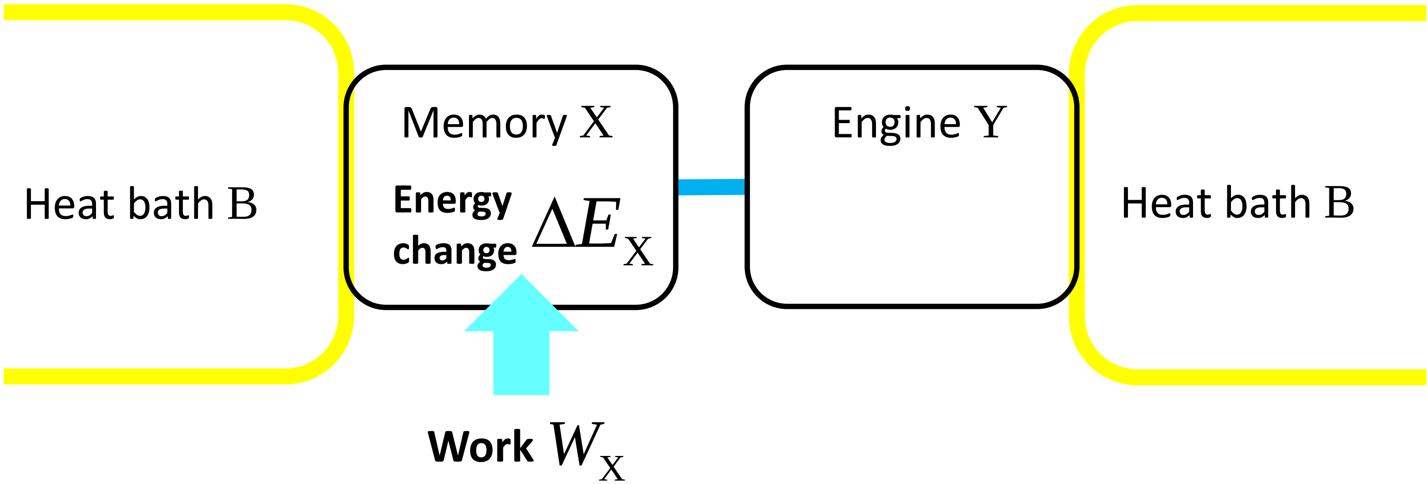


X: Memory
Y: Engine

$$\Delta I \equiv I$$

$$\Rightarrow \left\langle e^{-\Delta s_{\mathrm{XB}}+I} \right\rangle = 1 \quad \Rightarrow \left\langle \Delta s_{\mathrm{XB}} \right\rangle \geq \left\langle I \right\rangle$$

Minimal Energy Cost for Measurement



$$\langle \Delta s_{\mathrm{XB}} \rangle \geq \langle I \rangle \quad \Rightarrow \quad \beta \langle W_{\mathrm{X}} \rangle \geq \beta \langle \Delta E_{\mathrm{X}} \rangle - \langle \Delta s_{\mathrm{X}} \rangle + \langle I \rangle$$

Change in the nonequilibrium free energy of only X

Additional energy cost to obtain information

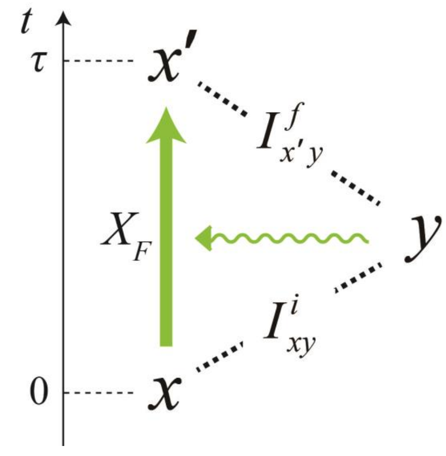
Information is not free

TS and M. Ueda, Phys. Rev. Lett. **109**, 180602 (2012).

General Principle of Information Thermodynamics

$$\left\langle e^{-\Delta s_{\mathrm{XB}}+\Delta I} \right\rangle = 1$$

$$\Rightarrow \quad \langle \Delta s_{\mathrm{XB}} \rangle \geq \langle \Delta I \rangle$$



Feedback:

$$\left\langle e^{-\Delta s_{\mathrm{XB}}+(I_{\mathrm{rem}}-I)} \right\rangle = 1$$

$$\Rightarrow \quad \langle \Delta s_{\mathrm{XB}} \rangle \geq -\langle I - I_{\mathrm{rem}} \rangle$$

Measurement:

$$\left\langle e^{-\Delta s_{\mathrm{XB}}+I} \right\rangle = 1$$

$$\Rightarrow \quad \langle \Delta s_{\mathrm{XB}} \rangle \geq \langle I \rangle$$

Unified formulation of measurement and feedback

TS and M. Ueda, PRL **109**, 180602 (2012).

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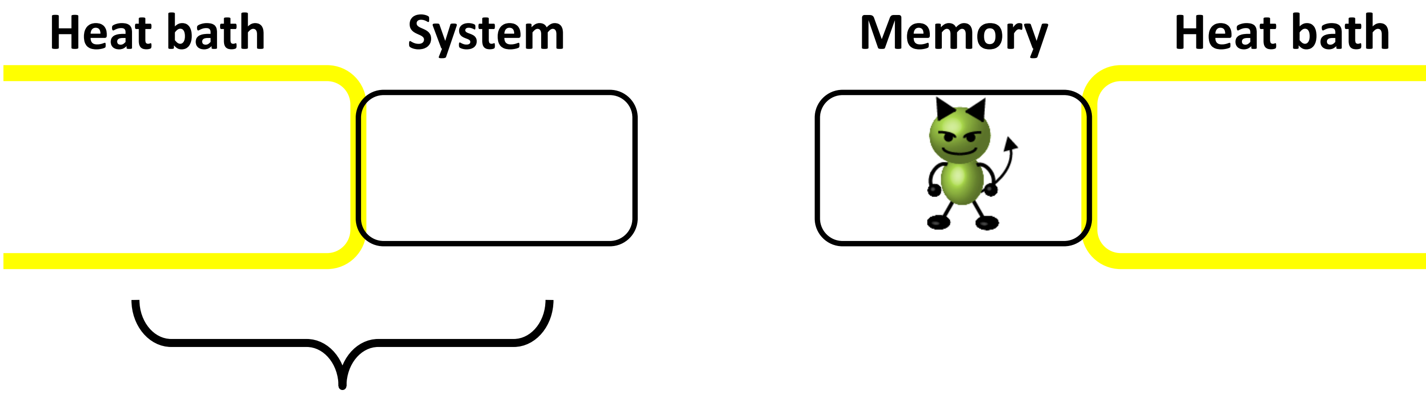
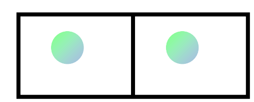
Problem



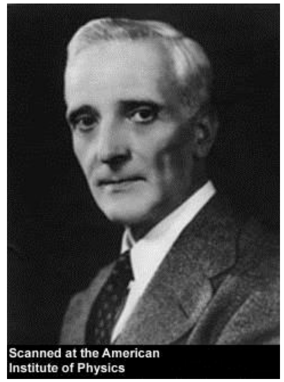
What compensates for the entropy decrease here?

For Szilard engine, $\langle \Delta s_{\mathrm{SB}} \rangle = -\ln 2$



Conventional Arguments

Measurement process



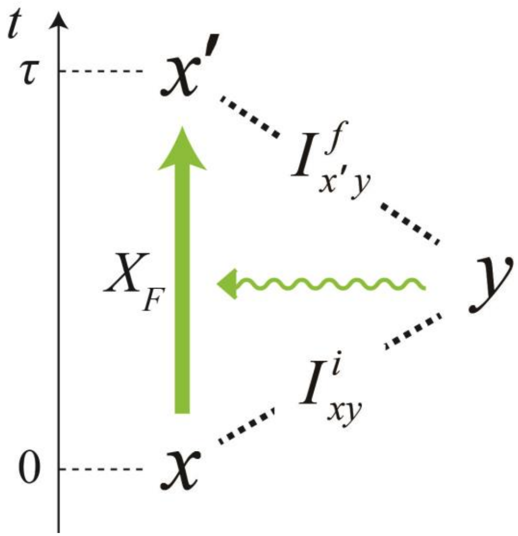
Brillouin

Erasure process
(From Landauer principle)

Bennett
&
Landauer

Widely accepted since 1980's

Total Entropy Production



Total entropy production in XYB

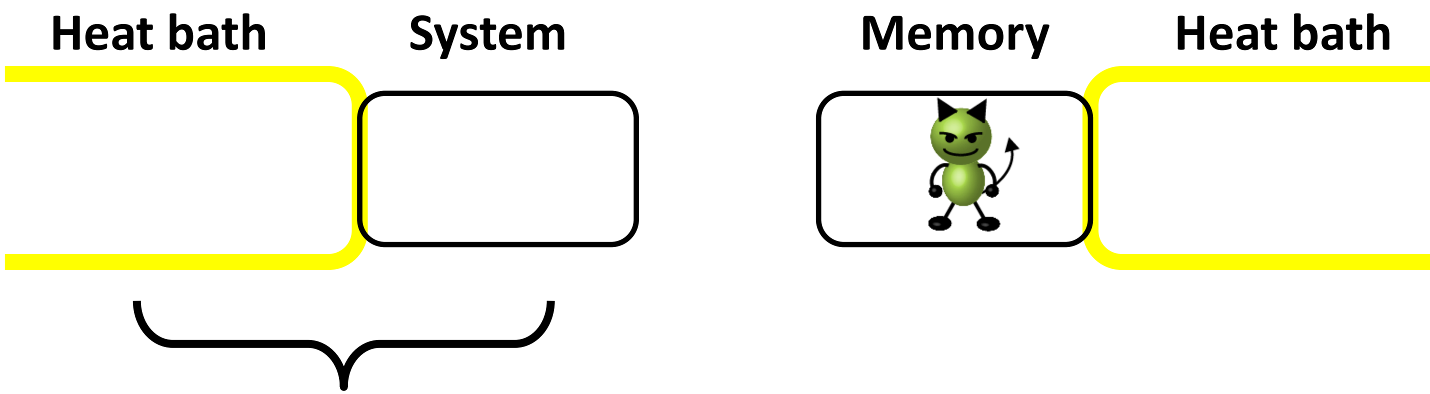
$$\Delta s_{\mathrm{XYB}} \equiv \Delta s_{\mathrm{XY}} - \beta Q_{\mathrm{X}}$$
$$= \Delta s_{\mathrm{XB}} - \Delta I$$

$$\langle \Delta s_{\mathrm{XB}} \rangle \geq \langle \Delta I \rangle \quad \Leftrightarrow \quad \langle \Delta s_{\mathrm{XYB}} \rangle \geq 0$$

Equality: thermodynamically reversible

If the mutual information is taken into account, the total entropy production is always nonnegative for each process of measurement or feedback.

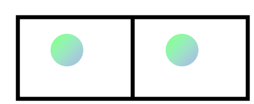
Revisit the Problem



What compensates for the entropy decrease here?

Mutual-information change compensates for it.

For Szilard engine, $\langle \Delta s_{\mathrm{SB}} \rangle = -\ln 2$



$$\langle \Delta s_{\mathrm{SMB}} \rangle = \langle \Delta s_{\mathrm{SB}} \rangle + \langle I \rangle = -\ln 2 + \ln 2 = 0$$

Key to Resoluve the Paradox

- Maxwell's demon is consistent with the second law for measurement and feedback processes **individually**
  - The mutual information is the key
- We don't need the Landauer principle to understanding the consistency

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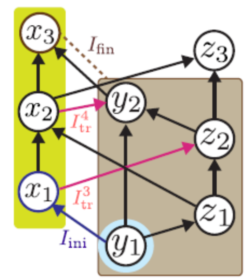
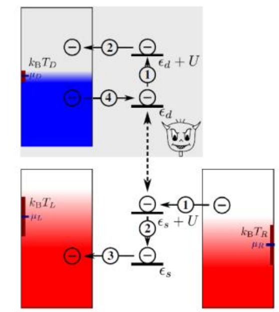
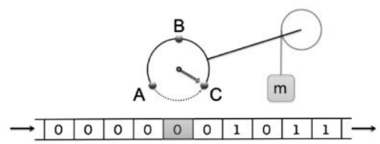
Thermodynamics of Autonomous Information Processing

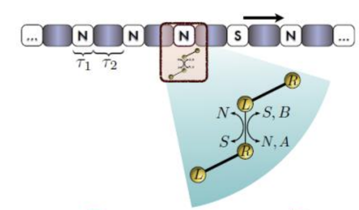
- **Second law & fluctuation theorem**
  Allahverdyan, Dominik & Guenter, J. Stat. Mech. (2009)
  Hartich, Barato, & Seifert, J. Stat. Mech. (2014)
  Horowitz & Esposito, Phys. Rev. X (2014)
  Horowitz & Sandberg, New J. Phys. (2014)
  Shiraishi & Sagawa, Phys. Rev. E (2015)
  Ito & Sagawa, Phys. Rev. Lett. (2013)

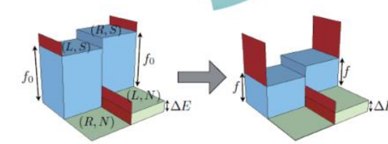






- **Models of autonomous Maxwell's demons**
  Mandal & Jarzynski, PNAS (2012)
  Mandal, Quan, & Jarzynski, Phys. Rev. Lett. (2013)
  Strasberg, Schaller, Brandes, & Esposito Phys. Rev. Lett. (2013)
  Horowitz, Sagawa, & Parrondo, Phys. Rev. Lett. (2013)
  Shiraishi, Ito, Kawaguchi & Sagawa, New J. Phys. (2015)





Toward deeper understanding of information nanomachines

Two Approaches

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

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

➡ But we derived a stronger version! **(Poster by Ito)**

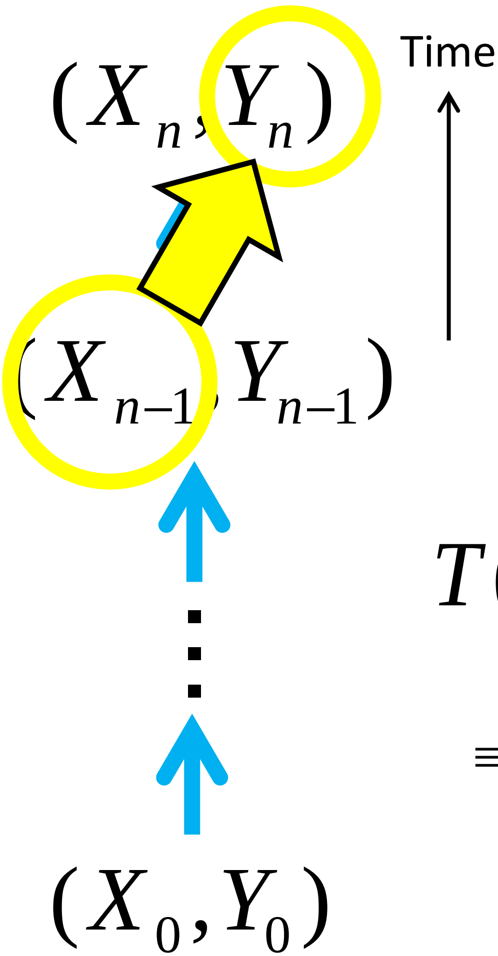
- **"Information flow"** approach
  - ✓ Not applicable to non-Markovian dynamics
  - ✓ Second law is stronger in Markovian dynamics

Second law: Allahverdyan, Dominik & Guenter, J. Stat. Mech. (2009)
Hartich, Barato, & Seifert, J. Stat. Mech. (2014)
Horowitz & Esposito, Phys. Rev. X (2014)
Horowitz & Sandberg, New J. Phys. (2014)

Fluctuation theorem: Shiraishi & Sagawa, PRE (2015) ➡ **Poster by Shiraishi**

Transfer Entropy

Directional information transfer between two systems



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

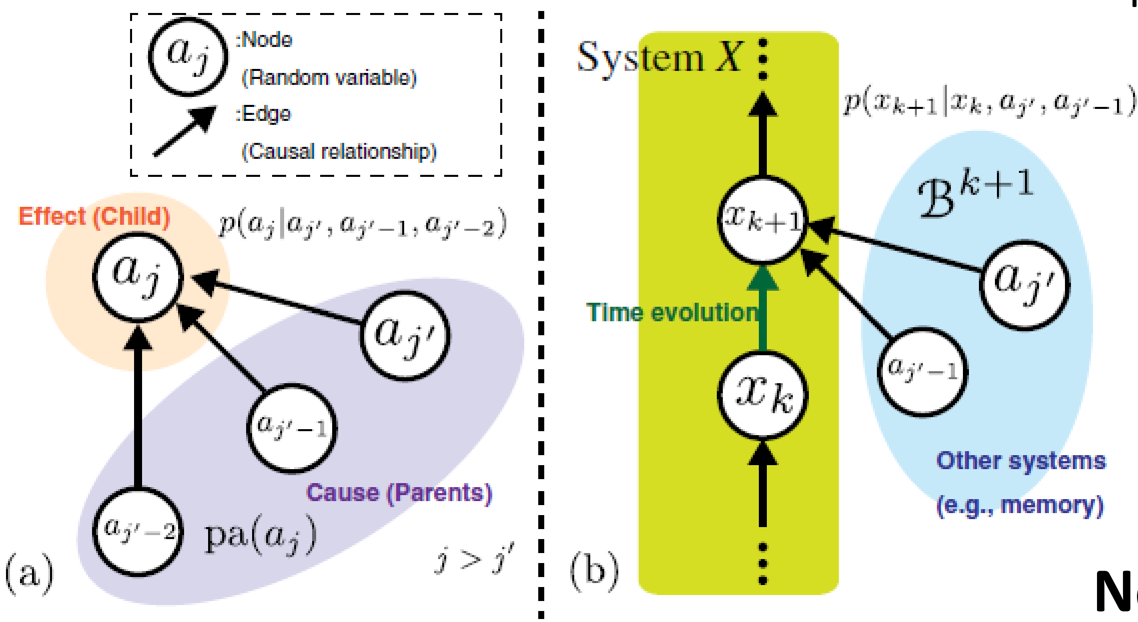
Conditional mutual information

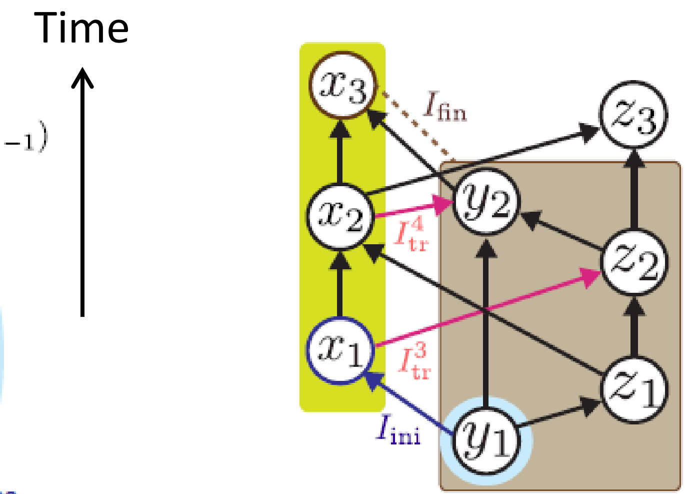
$$T(X_{n-1} \to Y_n) \equiv I\left(X_{n-1} : Y_n \mid Y_{n-1} \cdots Y_0\right)$$

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

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

Many-body Systems with Complex Information Flow





Node: Event

Arrow: Causal relationship

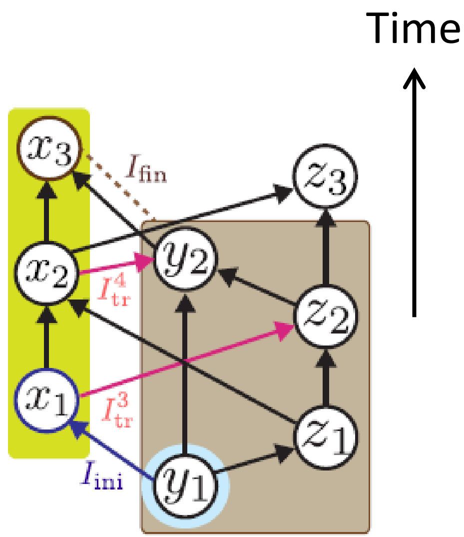
Characterize the dynamics by **Bayesian networks**

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

Second Law on Bayesian Networks

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

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



S. Ito & T. Sagawa, PRL 111, 180603 (2013)

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

I_{ini} : Initial mutual information between X and other systems

I_{fin} : Final mutual information between X and other systems

I_{tr}^{l} : **Transfer entropy** from X to other systems

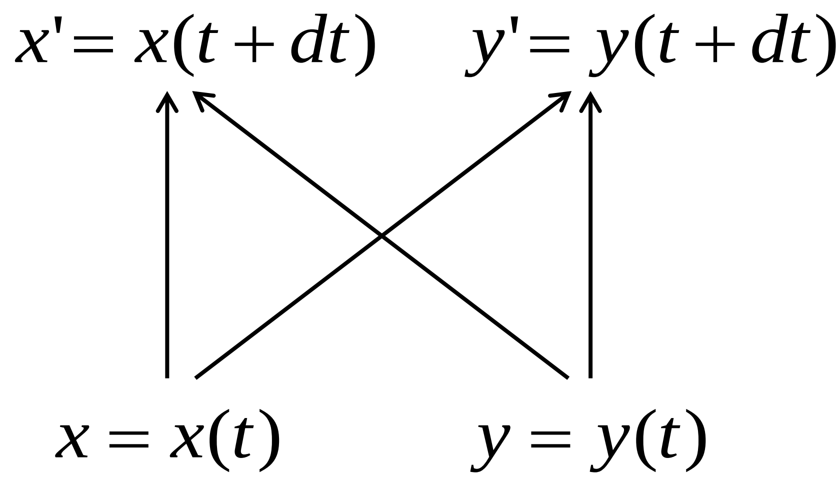
Information Flow VS Transfer Entropy

Infinitesimal transition of coupled Langevin system

$$\dot{x}(t) = f(x(t), y(t)) + \xi_x(t)$$

$$\dot{y}(t) = g(x(t), y(t)) + \xi_y(t)$$

$\langle \xi_x(t)\xi_y(t) \rangle = 0$: independent noise



Stronger: $\langle s(x') - s(x) - \beta Q \rangle \geq \langle \underline{I(x':y) - I(x:y)} \rangle$

Information flow

Weaker: $\langle s(x') - s(x) - \beta Q \rangle \geq \langle I(x':y') - I(x:y) - \underline{I(x:y'|y)} \rangle$

Transfer entropy

⇔ $\langle s(x'|y') - s(x|y) - \beta Q \rangle \geq -\underline{\langle I(x:y'|y) \rangle}$

Outline

- Introduction
- Information and entropy
- Information thermodynamics: a general framework
- Paradox of Maxwell's demon

- Thermodynamics of autonomous information processing
- **Application to biochemical signal transduction**

- Summary

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;

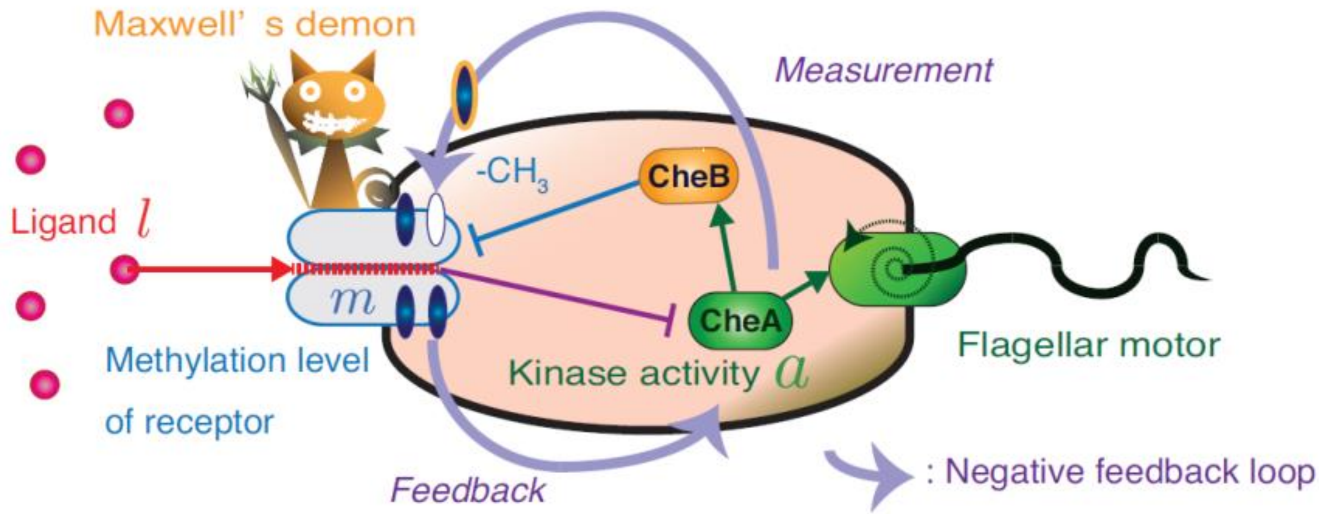
Shannon's second theorem is not straightforwardly applicable

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).

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

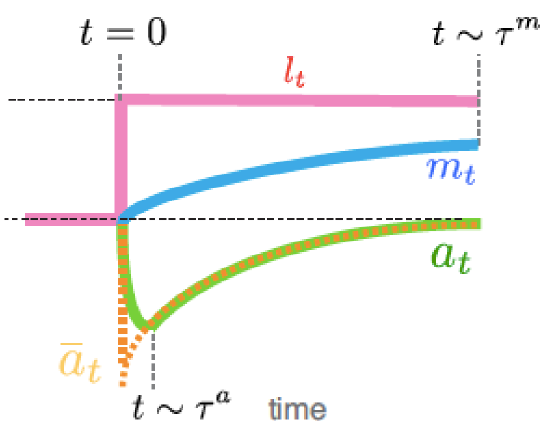
$$\dot{m}_t = -\frac{1}{\tau^m} a_t + \xi_t^m$$

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

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

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

(Weaker version with transfer entropy)

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

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

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:

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

Signal-to-noise ratio

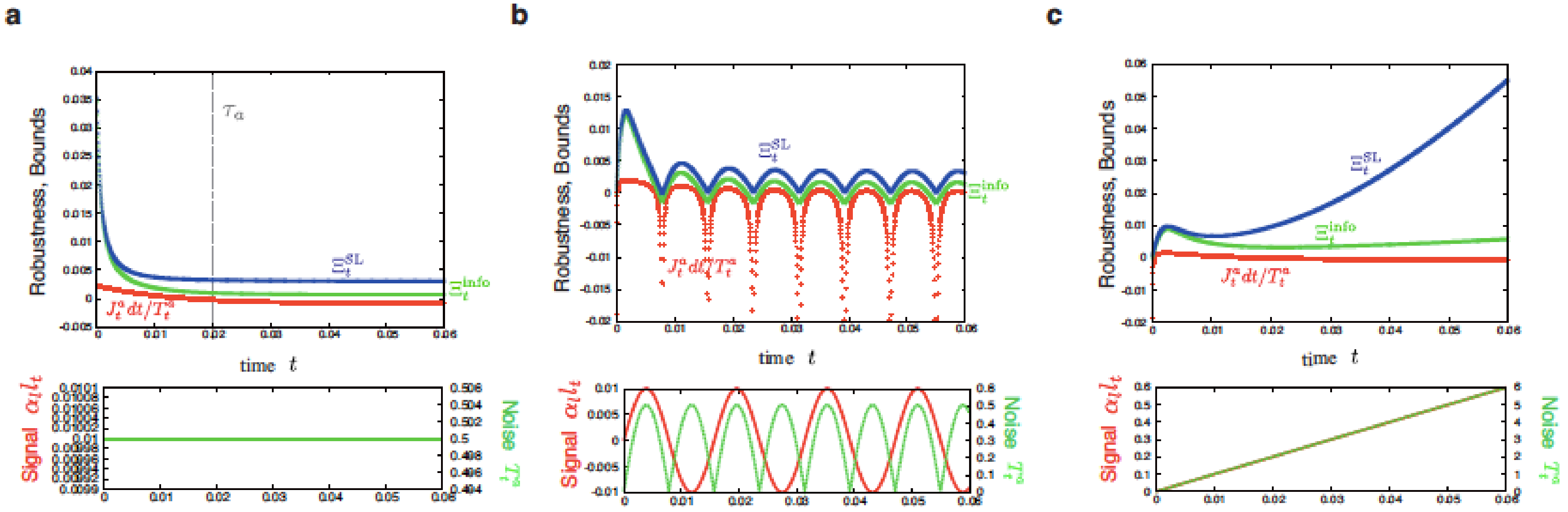
$$dP_t := \frac{(\rho_t^{am})^2 V_t^a}{(\tau^m)^2} dt$$ **: power of the signal from *a* to *m***

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

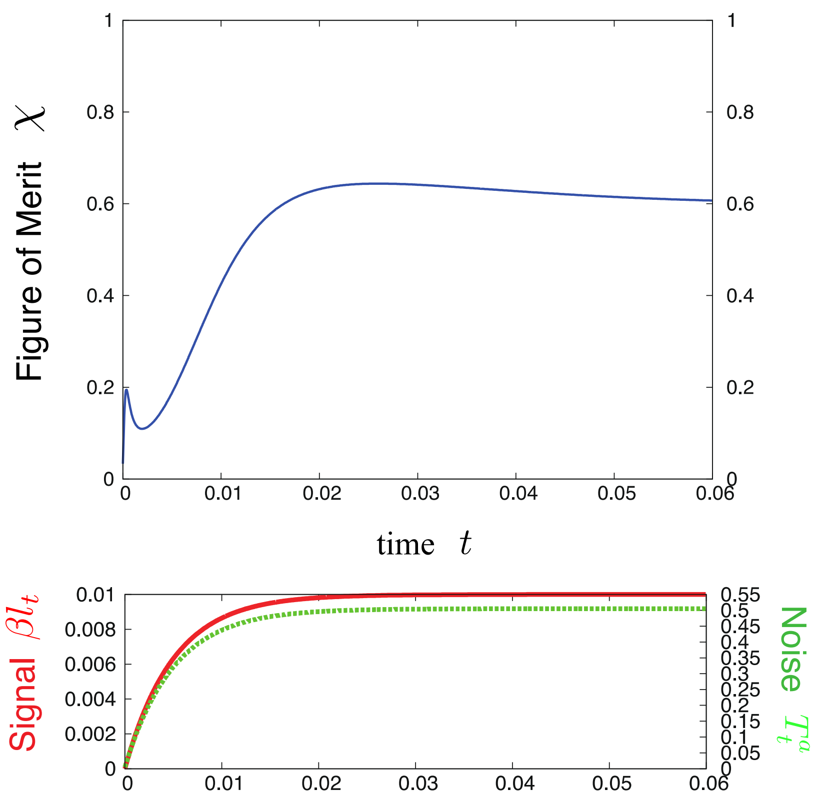
Green: information-thermodynamic bound Ξ_t^{info}

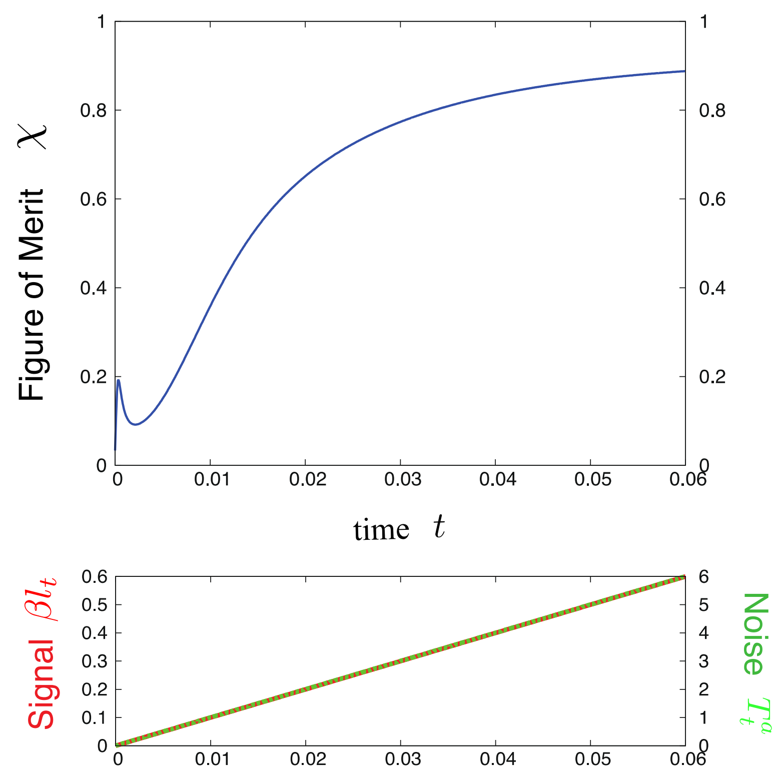
Blue: conventional thermodynamic bound Ξ_t^{SL}

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

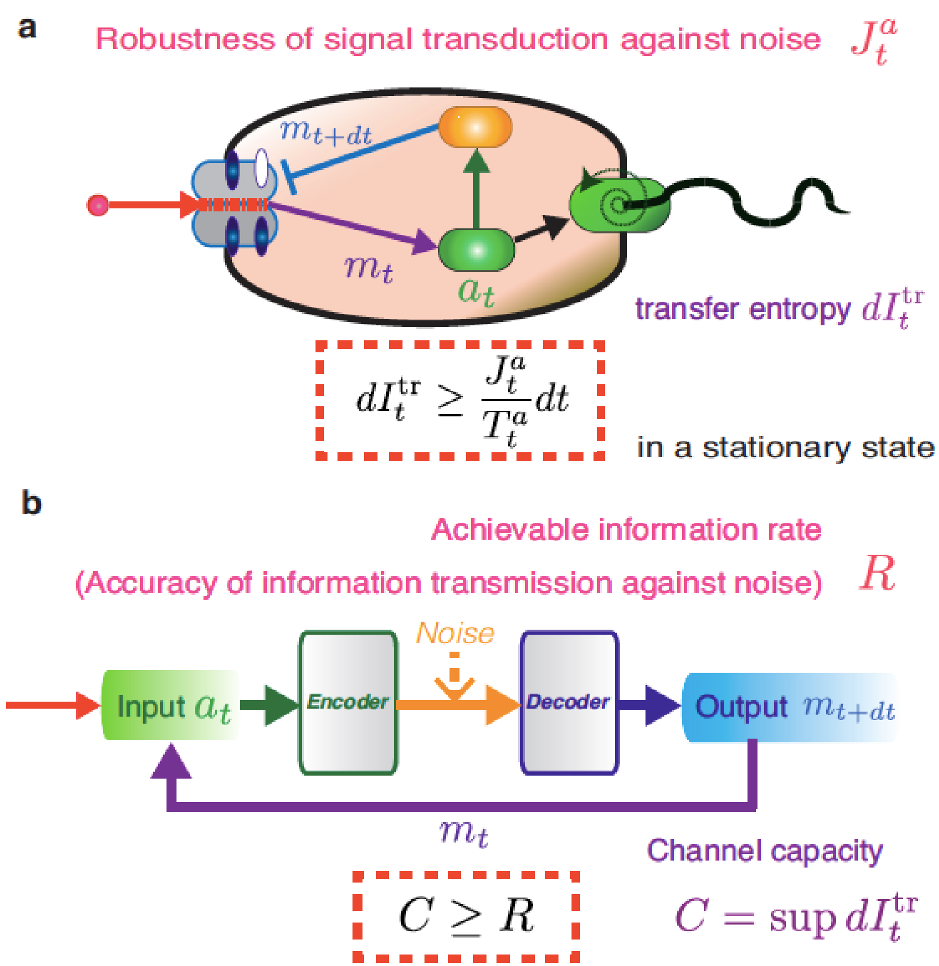
Information-Thermodynamic Figure of Merit

$$\chi := 1 - \frac{\Xi_t^{\rm info} - J_t^a {\rm d}t \,/\, T_t^a}{\Xi_t^{\rm SL} - J_t^a {\rm d}t \,/\, T_t^a}$$





Comparison with Shannon's Information Theory



Second law of information thermodynamics

Information $dI^{tr}{}_t$
gives the bound of robustness $J^a{}_t$

Well-defined in living cells

Shannon's second theorem

Information (channel capacity) C
gives the bound of achievable rate R

How to define in living cells??

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Summary

- Unified framework of information thermodynamics

T. Sagawa & M. Ueda, *Phys. Rev. Lett.* **109**, 180602 (2012).
T. Sagawa & M. Ueda, *New J. Phys.* **15**, 125012 (2013).

- Fluctuation theorem for autonomous information processing

S. Ito & T. Sagawa, *Phys. Rev. Lett.* **111**, 180603 (2013).
Review: S. Ito & T. Sagawa, arXiv:1506.08519 (2015).
N. Shiraishi & T. Sagawa, *Phys. Rev. E* **91**, 012130 (2015).

- Information thermodynamics of biochemical signal transduction

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

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

Thank you for your attention!