Thermodynamics of Accuracy

Luca Peliti

Montreal QC, May 5 2016

M. A. and H. Chooljan Member
Simons Center for Systems Biology
Institute for Advanced Study
Princeton NJ (USA)

Outline

Thermodynamics and Information

Generalized Second Law

Dissipation-Speed-Accuracy Trade-off

Summary

In collaboration with Riccardo Rao (Naples and Luxembourg)

Thermodynamics and Information

Maxwell's demon:

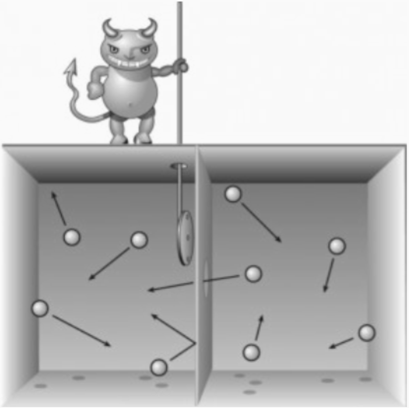
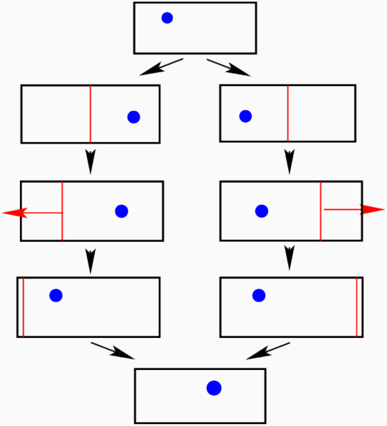


Image credit: J. Torchinsky

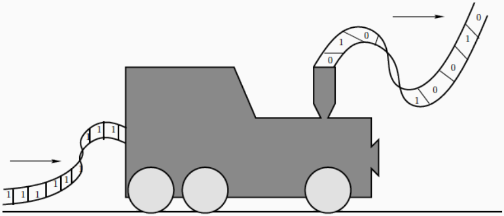
From Maxwell's demon to Szilard's engine

Szilard's engine:



$W = k_{\mathrm{B}}T \log 2$ per cycle

Feynman's engine:

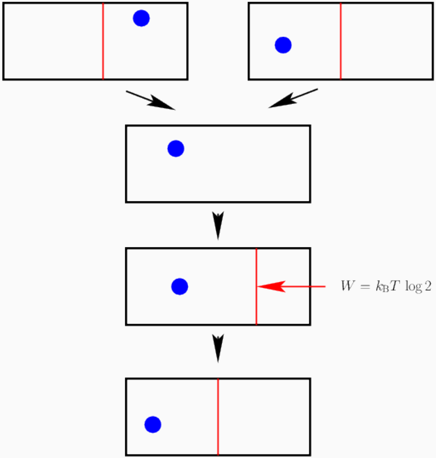


$H = -\sum_i p_i \log p_i$: Shannon entropy

$$W \leq N\, k_{\mathrm{B}} T\ (H_{\mathrm{out}} - H_{\mathrm{in}})$$

Landauer’s Principle

Reconciling Szilard’s demon with the Second Law:



Landauer's Principle

> *Any logically irreversible manipulation of information, such as the erasure of a bit or the merging of two computation paths, must be accompanied by a corresponding entropy increase in non-information bearing degrees of freedom of the information processing apparatus or its environment.*

Bennett, 2003

In particular, error correction is logically irreversible, thus implies dissipation

Kelly's Horse Races

Kelly, 1953

Kelly's horse races:

- There are n horses in a race, the i-th horse can win with probability p_i and yields o_i times the bet
- What is the best betting strategy $\left(b^* = (b_i^*)\right)$ if the race is indefinitely repeated?

Kelly's Horse Races

Kelly, 1953

Kelly's horse races:

- There are n horses in a race, the i-th horse can win with probability p_i and yields o_i times the bet
- What is the best betting strategy $(b^* = (b_i^*))$ if the race is indefinitely repeated?

Results:

1. Maximize the expected growth rate of the capital: $\Lambda(b) = \lim_{N\to\infty} \langle \log(S_N/S_0) \rangle / N = \sum_{i=1}^{n} p_i \log(o_i b_i)$
2. If the bet is "fair", $o_i = (p_i)^{-1}$, $\forall i$, then $\Lambda_{\max} = 0$
3. If the "true" probabilities are $p_i(y)$, the optimal strategy is $b_i^* = p_i(y)$
4. Then $\Lambda(b^*) = \sum_i p_i(y) \log(p_i(y)/p_i) = D_{\mathrm{KL}}(p(y) \| p) \geq 0$
5. Thus $D_{\mathrm{KL}}(p(y) \| p)$ measures the value of the extra information y

Kelly vs. Szilard

Vinkler, Permuter and Merhav, 2014

Horse races	Szilard engine
$X_k \in \{1,\dots,n\}$: k-th res.	$X_k \in \{\mathrm{L},\mathrm{R}\}$: k-th cycle location
y: extra info	y_k: (noisy) measure result
p_X: prob. vector for X	p_X: prob. vector of location
$p_X(y)$: prob. with extra info	$p_X(y)$: prob. after measure
o_X: odds vector	o_X: $v^{\mathrm{tot}}/v_0(x)$, $x \in \{\mathrm{L},\mathrm{R}\}$
$b_X(y)$: bet on X, given y	$v_{\mathrm{f}}(x)/v^{\mathrm{tot}}$: normalized final volume
$\log(o_{X_k} b_{X_k})$: log capital incr.	$W_k = k_{\mathrm{B}}T \sum_x p_x(y) \log(v_{\mathrm{f}}(x)/v_0(x))$

N.B.: We take the liberty to choose the initial and final locations of the barrier $v_0(x), v_{\mathrm{f}}(x)$

$$\max \langle W_N \rangle = N\, k_{\mathrm{B}}T \left\langle \log \frac{p_X(Y)}{p_X} \right\rangle = N\, k_{\mathrm{B}}T\, I(X;Y)$$

Generalized Second Law

A generalized Clausius inequality

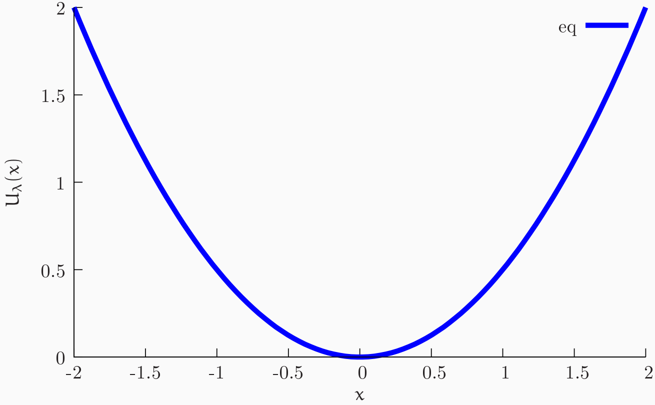
- System described by a hamiltonian $H_x(\lambda)$, $p_x^{\mathrm{eq}}(\lambda) := \mathrm{e}^{-(H_x(\lambda)-F(\lambda))/T}$
- Information content: $I(p|\lambda) := D_{\mathrm{KL}}(p\|p^{\mathrm{eq}}) := \sum_x p_x \log(p_x/p_x^{\mathrm{eq}})$
- Manipulation: $\lambda = \lambda(t)$, $\lambda(0) = \lambda_0$, $\lambda(t_{\mathrm{f}}) = \lambda_{\mathrm{f}}$
- Work: $W := \int_0^{t_{\mathrm{f}}} \mathrm{d}t\, \dot{\lambda}(t)\, \partial_\lambda H_{x(t)}$
- $W_{\mathrm{irr}} := W - (F_{\lambda_{\mathrm{f}}} - F_{\lambda_0})$

$$\boxed{\langle W_{\mathrm{irr}} \rangle \geq T\left[I(p(t_{\mathrm{f}})|\lambda_{\mathrm{f}}) - I(p(0)|\lambda_0)\right]}$$

Esposito and van den Broeck, 2011

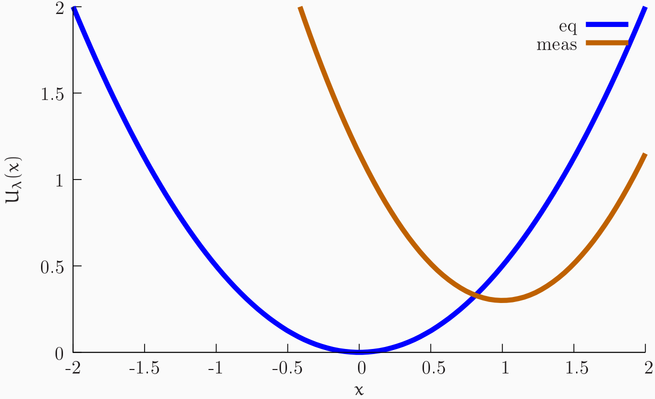
Optimal Protocol for Work Extraction

Equilibrium: $U = U_0$



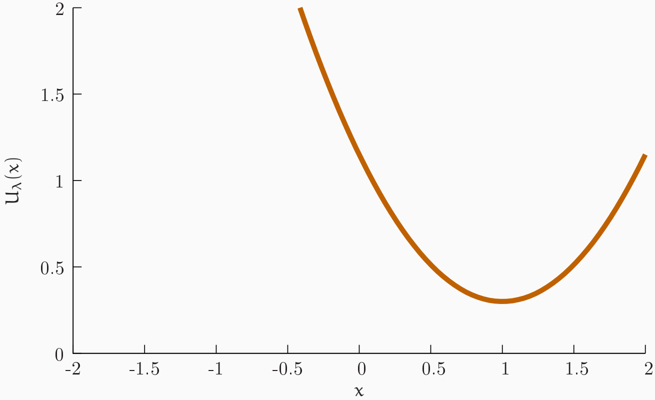
Optimal Protocol for Work Extraction

Measurement: $U = U_\lambda = -T \log p^{\text{meas}}(x|\lambda)$



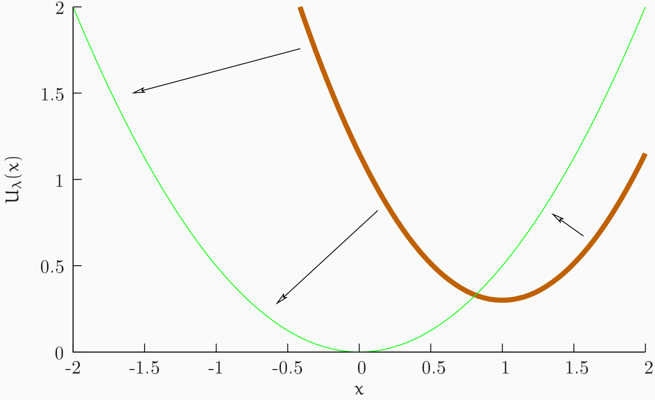
Optimal Protocol for Work Extraction

Quench: $U \longrightarrow U_\lambda, W_{\text{irr}} = \langle (U_\lambda - F_\lambda) - (U_0 - F_0) \rangle$



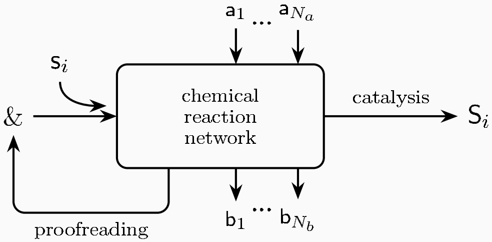
Optimal Protocol for Work Extraction

Slow relaxation: $U_\lambda \longrightarrow U_0$



Dissipation-Speed-Accuracy Trade-off

Enzyme-assisted assembly process



$$\mathsf{s} \in \{\mathsf{r}\text{ “right”}, \mathsf{w}\text{ “wrong”}\}$$

Examples:

- tRNA aminoacylation: tRNA + aa $\longrightarrow$ activated tRNA
- DNA transcription: ssDNA + nucleotide $\longrightarrow$ DNA + RNA

Error rate:

$$\xi := \frac{\text{rate of wrong catalysis: } J_\mathsf{w}}{\text{total rate of catalysis: } J_\mathsf{r} + J_\mathsf{w}}$$

The problem

- Physiological error rates are much smaller than thermodynamically expected
- Kinetic (non-equilibrium) mechanisms have been suggested to explain this fact (Ninio 1974, Hopfield 1975, Bennett 1979)
- Correction entails thermodynamic expense
- Can we characterize the thermodynamic efficiency of proofreading?
- Can we characterize how different proofreading mechanisms fare in efficiency, speed and accuracy?

Description

- Enzyme-substrate complexes identify states i
- Dynamics described by master equation:

$$\frac{\mathrm{d}p_i}{\mathrm{d}t} = \sum_{j\,(\neq i)}{}' \,(k_{ij}p_j - k_{ji}p_i)$$

- Irreversible catalysis rate: F
- Kramers' form for the reaction rates ($k_\mathrm{B}T = 1$):

$$k = \Omega\,\mathrm{e}^{-\Delta}$$

- Entropy production $\dot{S}_\mathrm{i}$ and entropy flow $\dot{S}_\mathrm{e}$ (steady state: $\bar{p}_i$):

$$\begin{aligned} \dot{S}_\mathrm{i} \quad &:= \tfrac{1}{2}\textstyle\sum_{i\neq j}{}' \,(k_{ij}\bar{p}_j - k_{ji}\bar{p}_i)\log\frac{k_{ij}\bar{p}_j}{k_{ji}\bar{p}_i} \\ \dot{S}_\mathrm{e} \quad &:= -\tfrac{1}{2}\textstyle\sum_{i\neq j}{}' \,(k_{ij}\bar{p}_j - k_{ji}\bar{p}_i)\log\frac{k_{ij}}{k_{ji}} \end{aligned}$$

Observables

Entropy balance in the steady state:

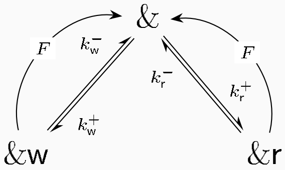
$$-\frac{\mathrm{d}}{\mathrm{d}t}\sum_k p_k \log p_k = \dot{S}_\mathrm{i} + \dot{S}_\mathrm{e} \underbrace{-\dot{S}_F}_{\text{catalysis}} = 0$$

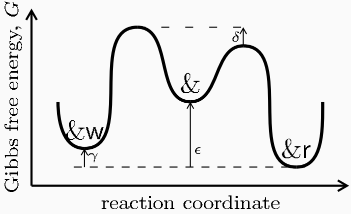
- Mean step duration:

$$\tau := (\text{total catalysis rate: } J_\mathrm{r} + J_\mathrm{w})^{-1}$$

- Entropy production per step: $\Delta_\mathrm{i} S := \tau\,\dot{S}_\mathrm{i} \geq 0$
- Entropy flow per step: $\Delta_\mathrm{e} S := \tau\,\dot{S}_\mathrm{e} \leq 0$
- Free-energy dissipation in the final catalysis:
  $\Delta S_F := \tau\,\dot{S}_F = \tau F \sum_\mathsf{s} \bar{p}_{\text{final state}(\mathsf{s})}\,\Delta\mu_{\text{final step}}$
- Efficiency: $\eta := \Delta S_F/\Delta_\mathrm{e} S = 1 + \Delta_\mathrm{i} S/\Delta_\mathrm{e} S,\ \ 0 \leq \eta \leq 1$

Michaelis-Menten model





$$k_r^+ = \omega e^{\delta+\epsilon}, \qquad k_r^- = \omega e^{\delta}$$

$$k_w^+ = \omega e^{\epsilon}, \qquad k_w^- = \omega e^{\gamma}$$

After Sartori & Pigolotti, 2013

Michaelis-Menten model

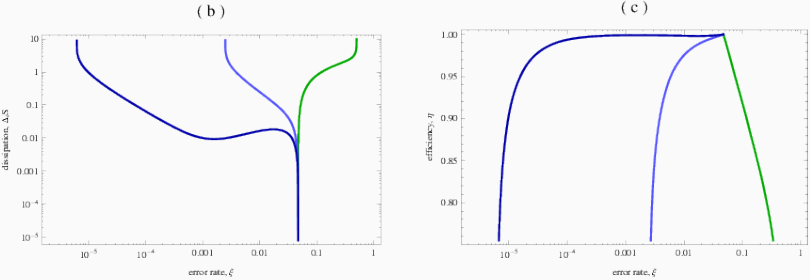
$$\xi = \frac{F\bar{p}_{\mathsf{w}}}{F\bar{p}_{\mathsf{w}} + F\bar{p}_{\mathsf{r}}} = \frac{e^{\delta}\omega + F}{\left(e^{\gamma}+1\right)e^{\delta}\omega + \left(e^{\delta}+1\right)F}$$
$$\geq \frac{1}{e^{\max\{\delta,\gamma\}}+1} \simeq e^{-\max\{\delta,\gamma\}}$$

Two regimes (Sartori & Pigolotti, 2013):

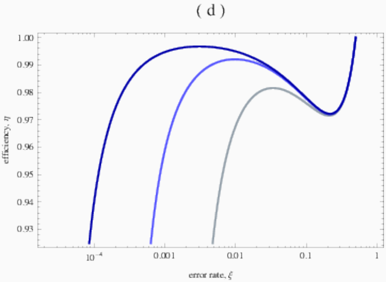
Energetic discrimination: $\gamma > \delta$; $\xi_{\min}$ is reached for $F \to 0$

Kinetic discrimination: $\gamma < \delta$; $\xi_{\min}$ is reached for $F \to \infty$

Michaelis-Menten model



$\gamma = 3$, $\epsilon = 10$, $\omega = 1$ and
$\delta = 0$ (green), $\delta = 6$ (light blue), $\delta = 12$ (dark blue)

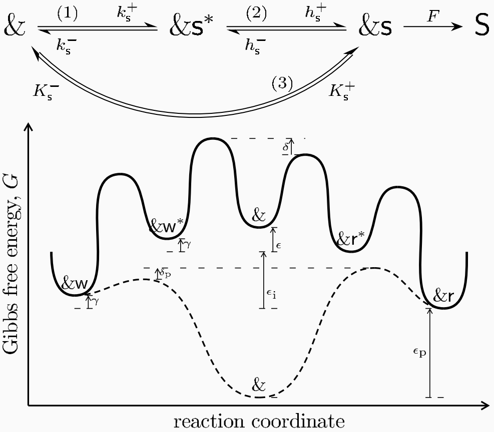


Efficiency-error trade-off in the purely kinetic regime of discrimination (scale change!)

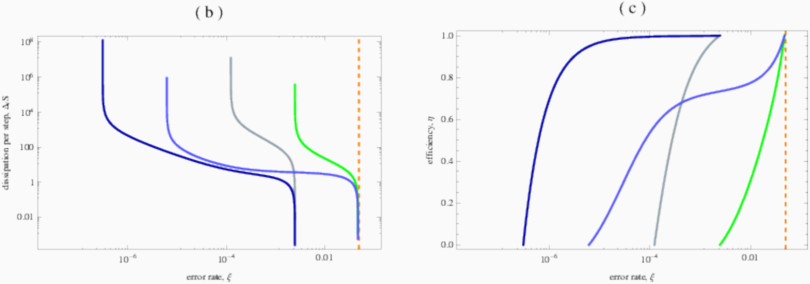
$\gamma = 3$, $\epsilon = 10$, $\omega = 1$ and

$\delta = 6$ (grey), $\delta = 8$ (light blue), $\delta = 10$ (dark blue)

The Ninio-Hopfield model



The Ninio-Hopfield model



$\epsilon = 10$, $\omega = 1$, $\gamma = 3$ and

$(\delta, \delta_{\mathrm{p}}) = (0, 0)$ (green: energetic-energetic)

$(\delta, \delta_{\mathrm{p}}) = (6, 0)$ (grey: kinetic-energetic)

$(\delta, \delta_{\mathrm{p}}) = (0, 6)$ (light blue: energetic-kinetic)

$(\delta, \delta_{\mathrm{p}}) = (6, 6)$ (dark blue: kinetic-kinetic)

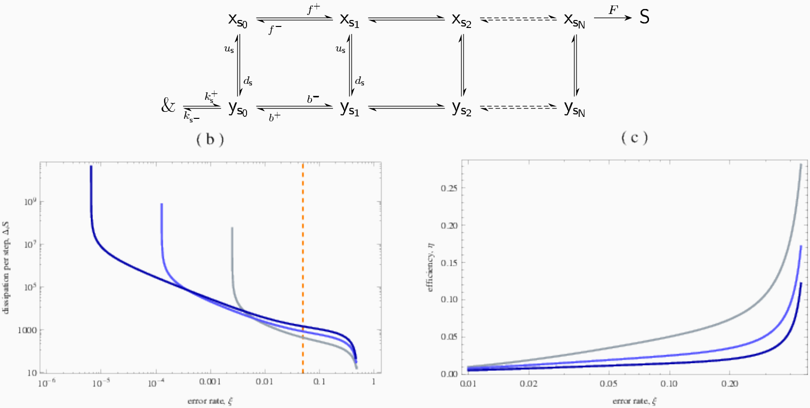
The Ninio-Hopfield model

- Kinetic and energetic discrimination regimes can cooperate in the proofreading pathway reducing the error rate
- faster, more dissipative and more efficient process obtains when the kinetic discrimination predominates on the first pathway
- Minimum error rate (Hopfield 1975: $\xi_{\mathrm{min}} = \mathrm{e}^{-2\gamma}$):

$$\xi_{\mathrm{min}} \simeq \mathrm{e}^{-(\max(\gamma,\delta)+\gamma+\delta_{\mathrm{p}})}$$

- ξ_{min} is reached in the $F \to 0$ limit

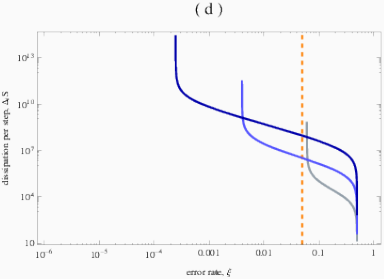
The Murugan-Huse-Leibler model



Energetic discrimination: $\delta = 0$, $\gamma = 3$, $\epsilon_{\mathrm{u}} = 8$, $\epsilon_{\mathrm{f}} = 8$, $\epsilon_{\mathrm{b}} = 8$
grey: $N = 1$; light blue: $N = 2$; dark blue: $N = 3$

The Murugan-Huse-Leibler model

Dissipation per step in the kinetic discrimination regime:



$\gamma = 0$, $\omega = 1$, $\epsilon = 10$, $\delta = 3$, $N = 1, 2, 3$

Summary

Summary

- We analyzed accuracy vs. speed trade-off for several proposed models of kinetic proofreading
- The kinetic vs. energetic discrimination concept plays an essential role
- We introduced and evaluated an efficiency measure for the process

- Outlook
  - We have also considered processes with short-time memory: the results are very similar
  - The analysis can be extended to other kinds of information processing (e.g., sensing)