Stochastic thermodynamic analysis of the Michaelis-Menten kinetics

Filipe P. de Farias[1] Francesco Corona[1] Michela Mulas[1]

[1]Dept.

Universidade Federal do Ceará

Introduction

Stochastic thermodynamics (ST) deals with the interaction of mesoscopic, nonequilibrium physical systems with heat reservoirs in equilibrium.[3] Such interactions are assumed to be the source of the randomness in the dynamics of the system, assigning to it a probability $p_x(t)$ of being in the state x at time t.

- We will use the Michaelis-Menten kinetics as case of study for the ST.

Michaelis-Menten kinetics (MM)

The system (MM) is composed by a single molecule of enzyme E. We assume the enzyme processes a single molecule of substrate S per time. Then the system can be in two states: free enzyme E and enzyme-substrate complex ES.

- The reaction network that models the kinetics is:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} E + P \tag{1}$$

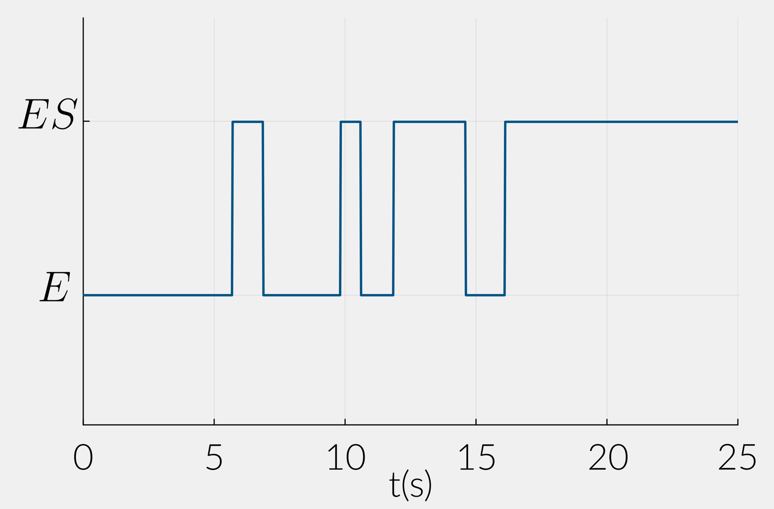

Figure 1

- The observation of a single realization of this system is given in Figure 1. The system fluctuates between the two states until reaches a stationary configuration.

Master Equation

The probability $p_x(t)$ of the system being in $x \in \{E, ES\}$ and how it changes with time, is given by a **master equation**.[4] It reads:

$$\frac{dp_x(t)}{dt} = \sum_x W_{x'x}p_x(t) - W_{xx'}p_{x'}(t) \tag{2}$$

- The $W_{x'x}$ is the **probability transition rate** from the state x' to x, it forms a **stochastic matrix** W dependent on the kinetics of the chemical reactions:[2]

$$W_{x'x} = \sum_\nu \prod_i k_\nu \frac{x_{i,\nu}!}{(x_{i,\nu} - s_{i,\nu})!} \tag{3}$$

$x_{i,\nu}$ = # of molecules in the system of the i-th reactant in the ν-th reaction.
$s_{i,\nu}$ = # of molecules of the i-th reactant participating in the ν-th reaction.

Stochastic Thermodynamics

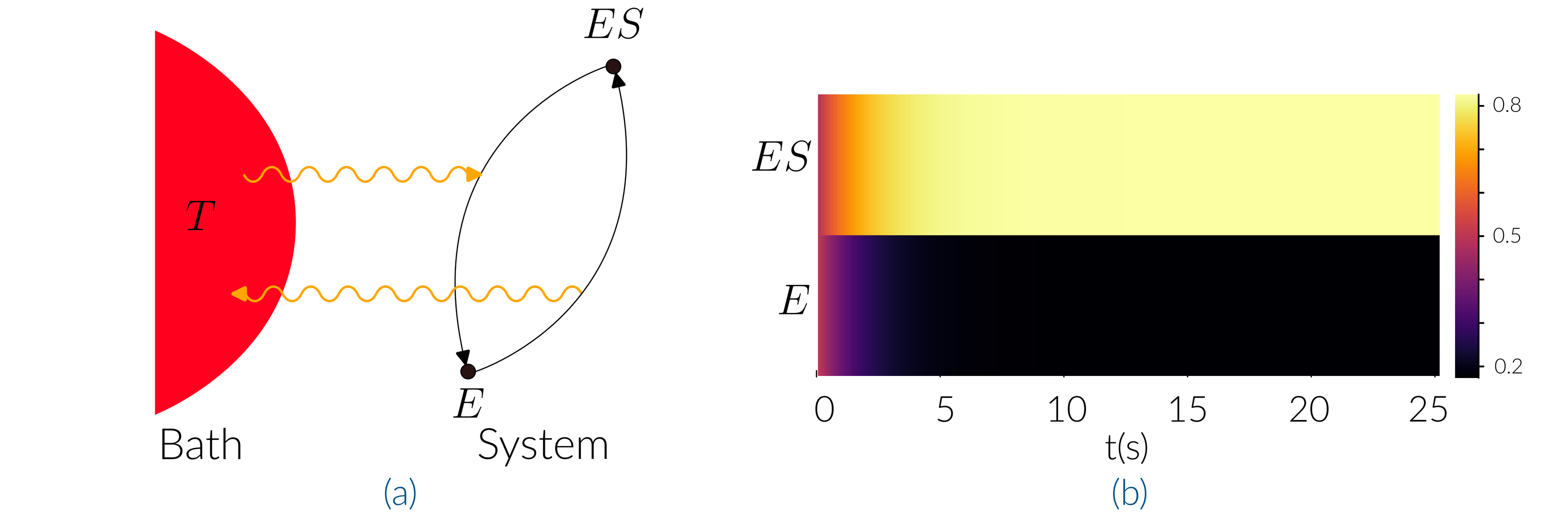

Figure 2. In (a) the representation of MM[1] and in (b) the evolution of the probability for each state.

The classical thermodynamics is defined assumed an **equilibrium** situation of the system.

- In the ST, the equilibrium is held by the bath, the system is allowed to be in **nonequilibrium**.
- In such case, ST gives that the system has nonnegative **average entropy production rate** $\dot{S}^{sys}$:

$$\dot{S}^{sys} = k_B T \frac{1}{2} \sum_{x \neq x'} [W_{x'x}p_x(t) - W_{xx'}p_{x'}] \ln \frac{p_x(t)}{p_{x'}(t)}. \tag{4}$$

This expression can be separated in two parts:

$$\dot{S}^{tot} = k_B T \frac{1}{2} \sum_{x \neq x'} [W_{x'x}p_x(t) - W_{xx'}p_{x'}] \ln \frac{W_{x'x}p_x(t)}{W_{xx'}p_{x'}(t)} \tag{5a}$$

$$\dot{S}^{bath} = k_B T \frac{1}{2} \sum_{x \neq x'} [W_{x'x}p_x(t) - W_{xx'}p_{x'}(t)] \ln \frac{W_{x'x}}{W_{xx'}} \tag{5b}$$

The term $\dot{S}^{bath}$ is the average heat absorbed by the bath when the system jumps between the states, while $\dot{S}^{tot}$ is the total entropy change (or balance) of the universe (system plus bath).

- If p_x^{eq} is the probability of the system when in equilibrium, ST gives us the **free energy**

$$\frac{\dot{F}(t)}{k_B T} = \sum_{x \neq x'} [W_{x'x}p_x(t) - W_{xx'}p_{x'}] \ln \frac{p_x(t)}{p_x^{eq}} = \dot{w} - T\dot{S}^{tot}. \tag{6}$$

The average work w that can be done in the system is then defined in terms of p_x^{eq}

$$w(t) = \frac{1}{2} \sum_{x \neq x'} [W_{x'x}p_x(t) - W_{xx'}p_{x'}] \ln \frac{W_{x'x}p_x^{eq}}{W_{xx'}p_{x'}^{eq}}. \tag{7}$$

- The thermodynamic flux and force are defined as, respectively

$$J_{xx'} = W_{x'x}p_x(t) - W_{xx'}p_{x'}(t) \qquad A_{xx'} = \ln \frac{W_{x'x}p_x(t)}{W_{xx'}p_{x'}(t)} \tag{8}$$

Analysis

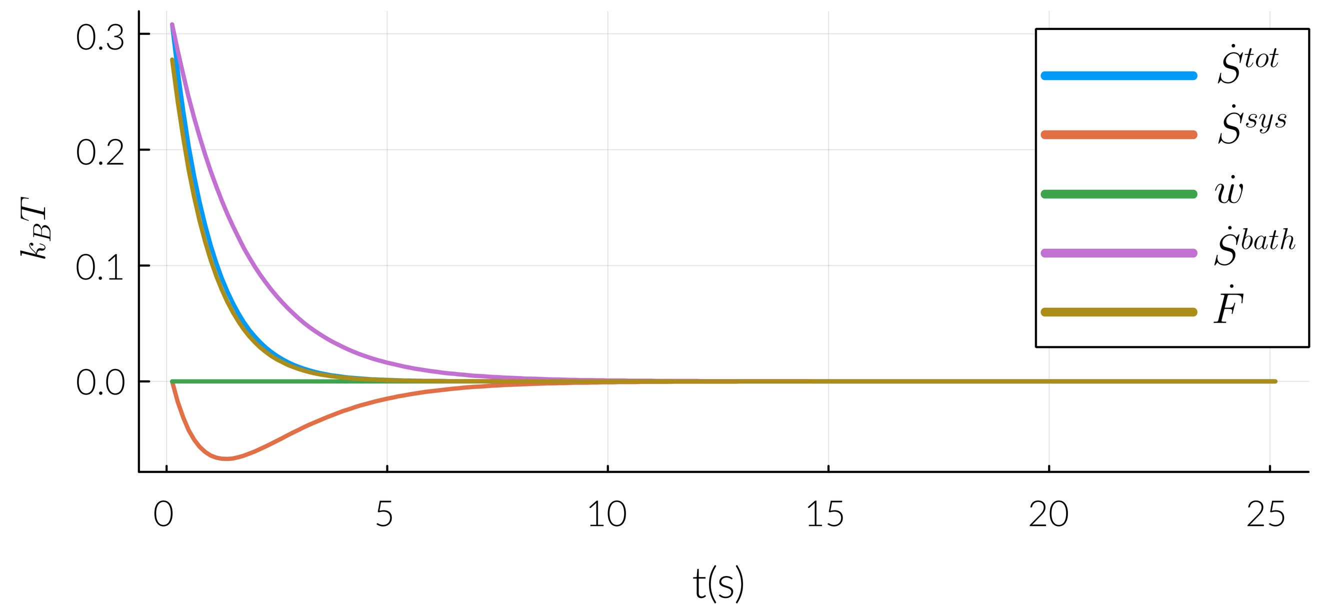

Figure 3

The system reaches the steady-state, which for the case of study happens to be also the equilibrium in about 10 seconds:

- By (8) both the thermodynamic force and flux vanish in the steady-state.
- If $W_{x'x}p_x^{eq} = W_{xx'}p_{x'}^{eq}$ we have detailed balance, which connects the math and the physics by recovering the Boltzmann distribution.
- It can be noticed also that all the free energy is used to produce entropy.
- This could be different if one realize work on the system, and it's subject of further research.

References

[1] Massimiliano Esposito.
Introduction to stochastic thermodynamics.
https://enabla.com/set/144, 2023. Nordita Winter School 2023.

[2] Daniel T Gillespie.
A general method for numerically simulating the stochastic time evolution of coupled chemical reactions.
Journal of Computational Physics, 22(4):403–434, 1976.

[3] Luca Peliti and Simone Pigolotti.
Stochastic Thermodynamics: An Introduction.
Princeton University Press, 2021.

[4] N.G. Van Kampen.
Stochastic processes in physics and chemistry.
North-Holland personal library. Elsevier, 2007.