# Stochastic thermodynamic analysis of the Michaelis-Menten kinetics

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## 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:

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

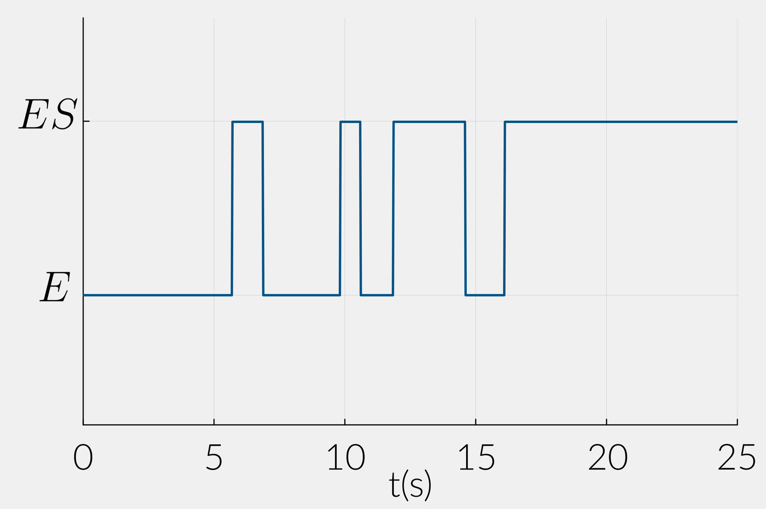



Figure 1

- 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:

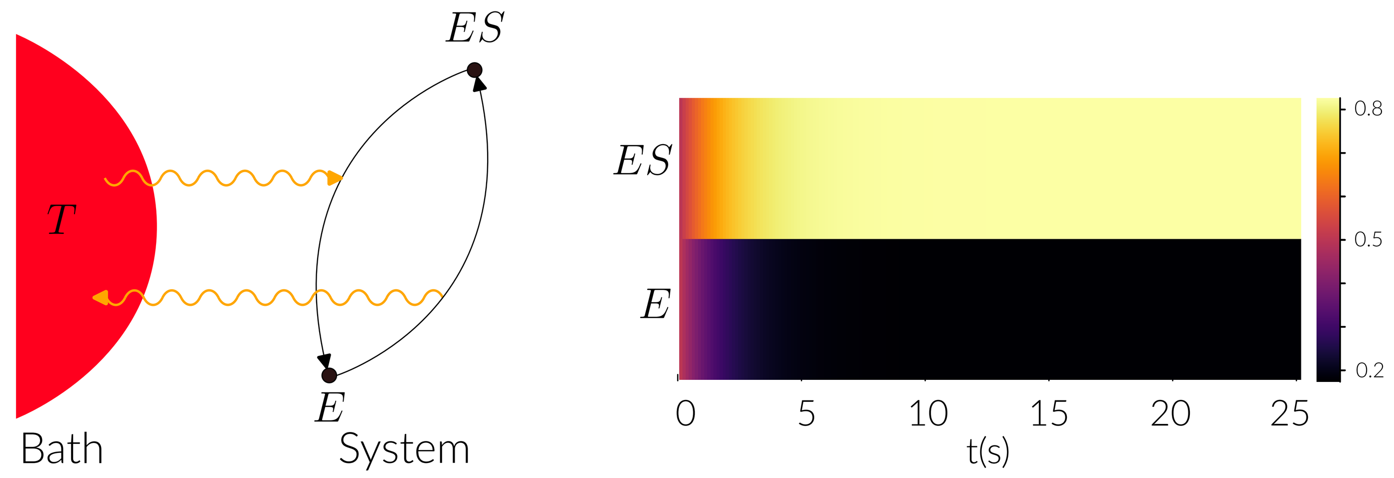
$$\frac{dp_x(t)}{dt} = \sum_x W_{x'x}p_x(t) - W_{xx'}p_{x'}(t) \tag{2}$$

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

## Stochastic Thermodynamics




(a) (b)

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**

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

The difference between the rate of work which is done when we manipulate the system $\dot{w}$ and the one available to be extracted $\dot{F}^{eq}$ is

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

## Analysis

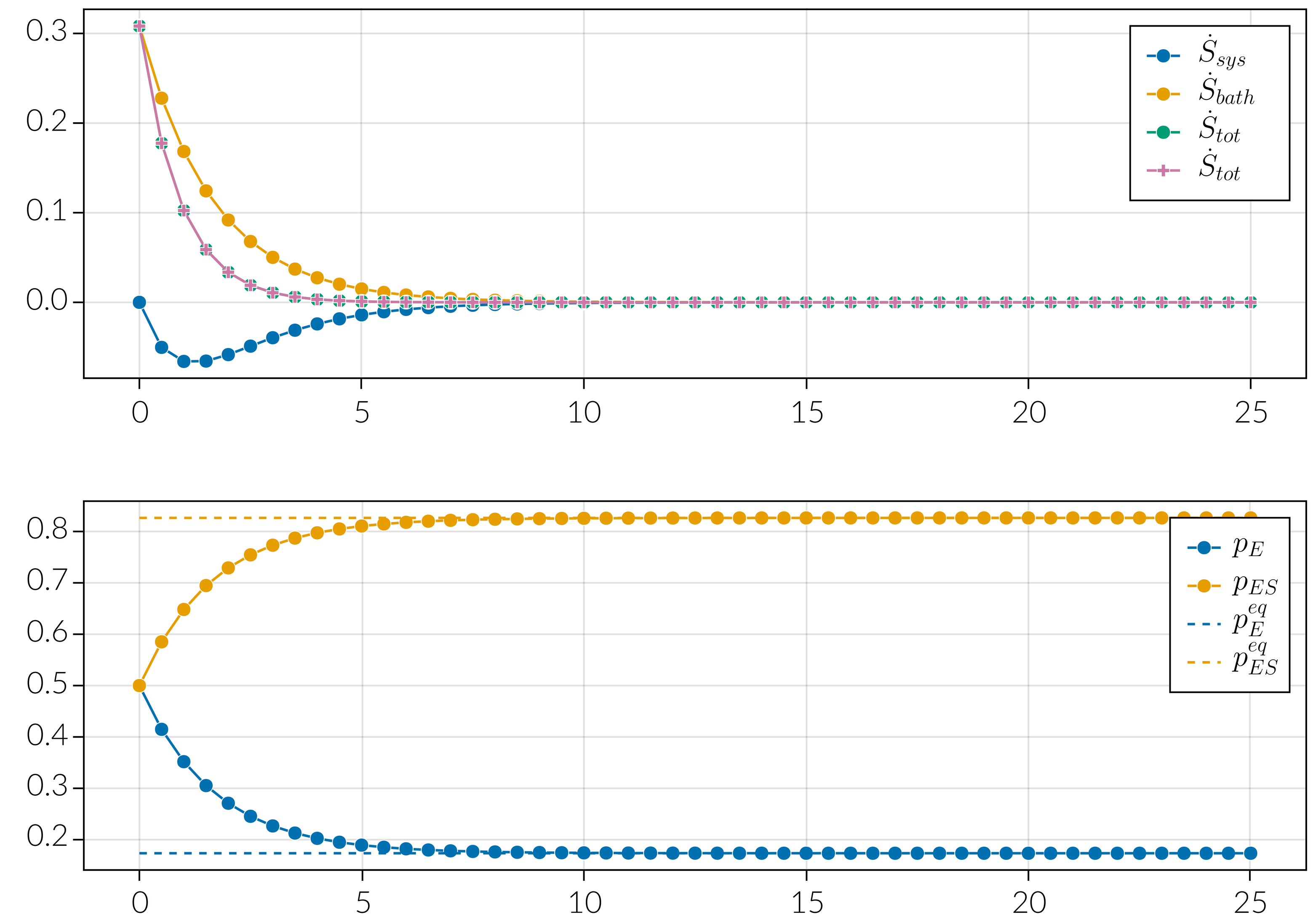



Figure 3. On top the evaluations of equations (4) to (6), to MM system with $k_1 = 0.5$, $k_{-1} = 0.005$, $k_2 = 0.1$ and $k_{-2} = 0.0$. On the bottom, the time evolution of the probability of the system $p_x$ in each state and the respective equilibrium probability $p_x^{eq}$.

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

- By (??) both the thermodynamic force and flux vanish in the steady-state, which is also an equilibrium.
- 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

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