

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.⁴ 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:

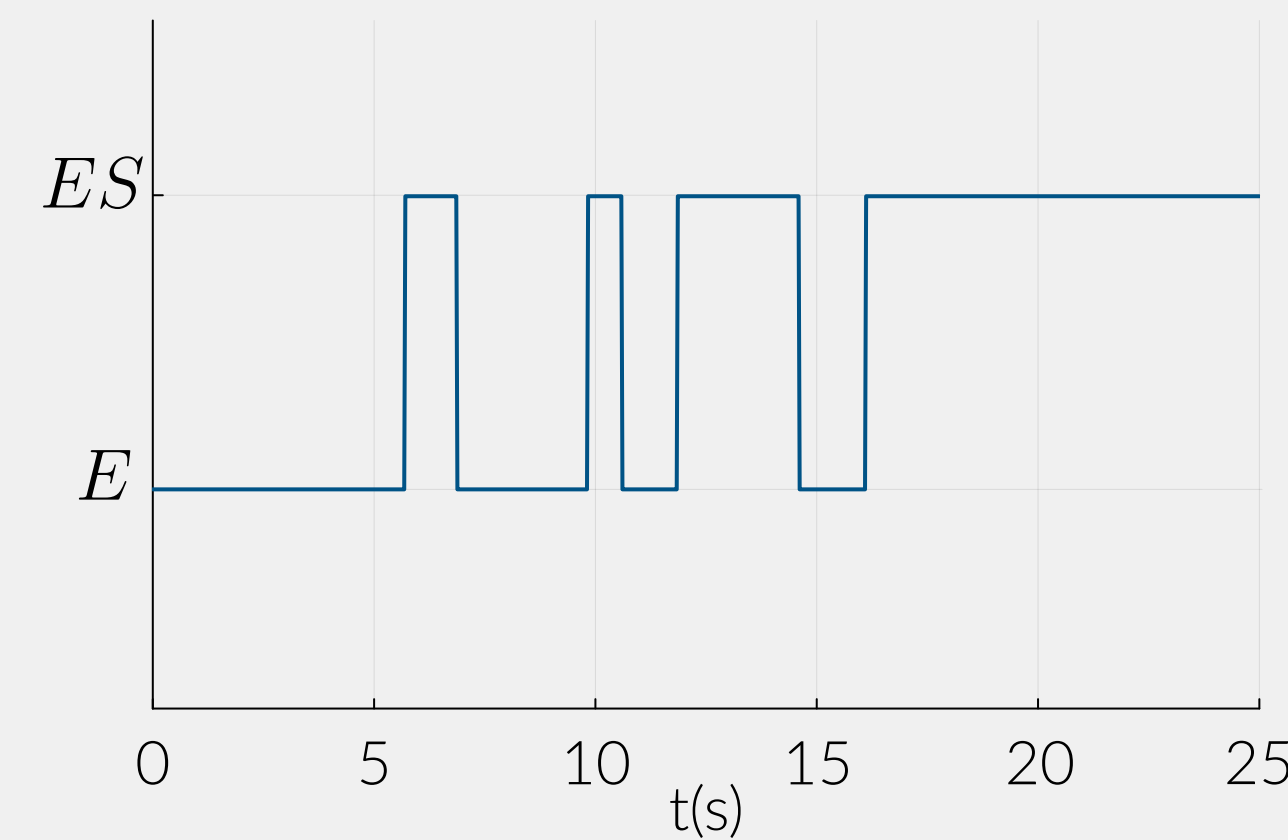


Figure 1

- 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**.⁶ It reads:

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

- 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:³

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

$x_{i,\nu}$ = # 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

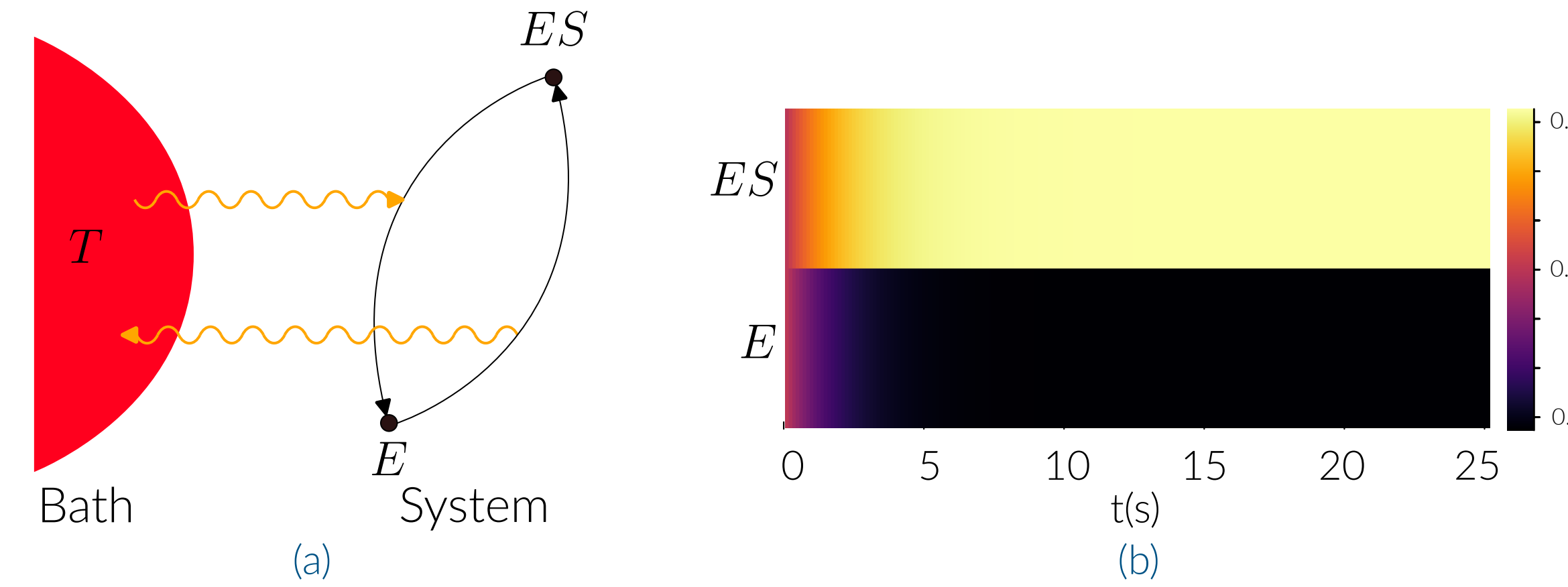


Figure 2. In (a) the representation of MM² and in (b) the evolution of the probability for each state.

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} :

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

This expression can be separated in two parts:

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

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

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 **generalized free energy rate**⁵

$$\dot{F}(t) - \dot{F}^{eq}(t) = \sum_{x \neq x'} [W_{x'x} p_x(t) - W_{xx'} p_{x'}(t)] \ln \frac{p_x(t)}{p_{x'}^{eq}}, \quad (6)$$

where \dot{F}^{eq} is the equilibrium free energy.

- The nonequilibrium free energy rate in (6) is defined as the information I needed to specify the nonequilibrium state,¹ thus

$$F(t) - F^{eq}(t) = TI(t) \equiv TD_{KL}(p_x(t) || p_x^{eq}(t)) \geq 0 \quad (7)$$

where D_{KL} is the Kullback-Leibler divergence measuring the “difference” between the nonequilibrium and the equilibrium probability distributions.

Analysis

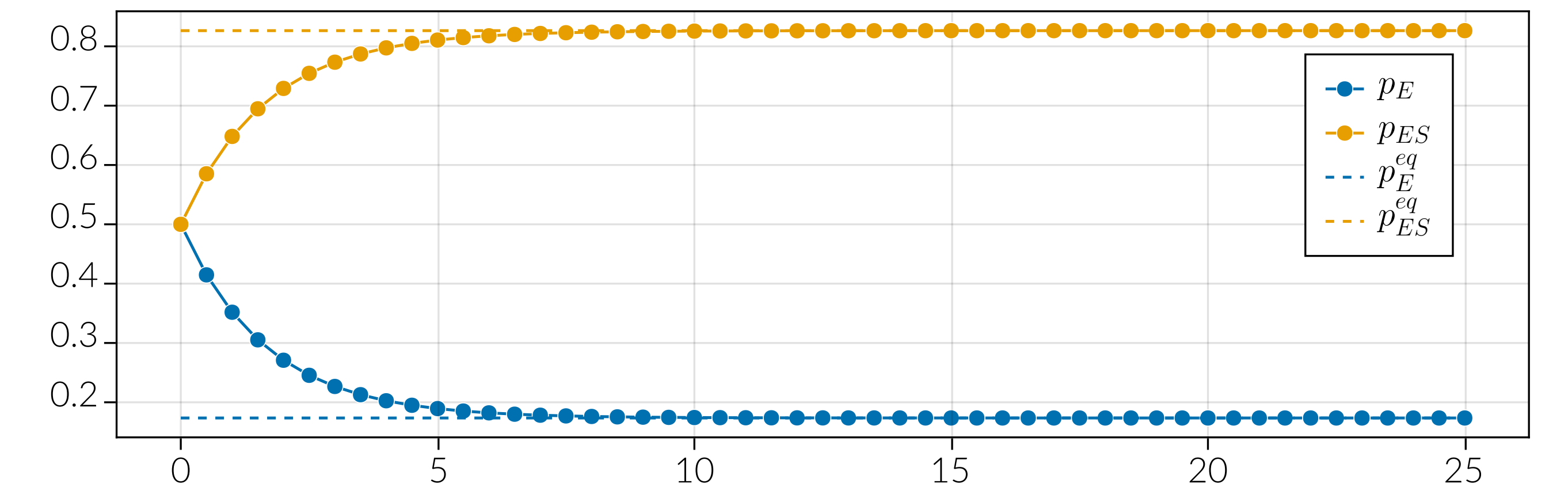
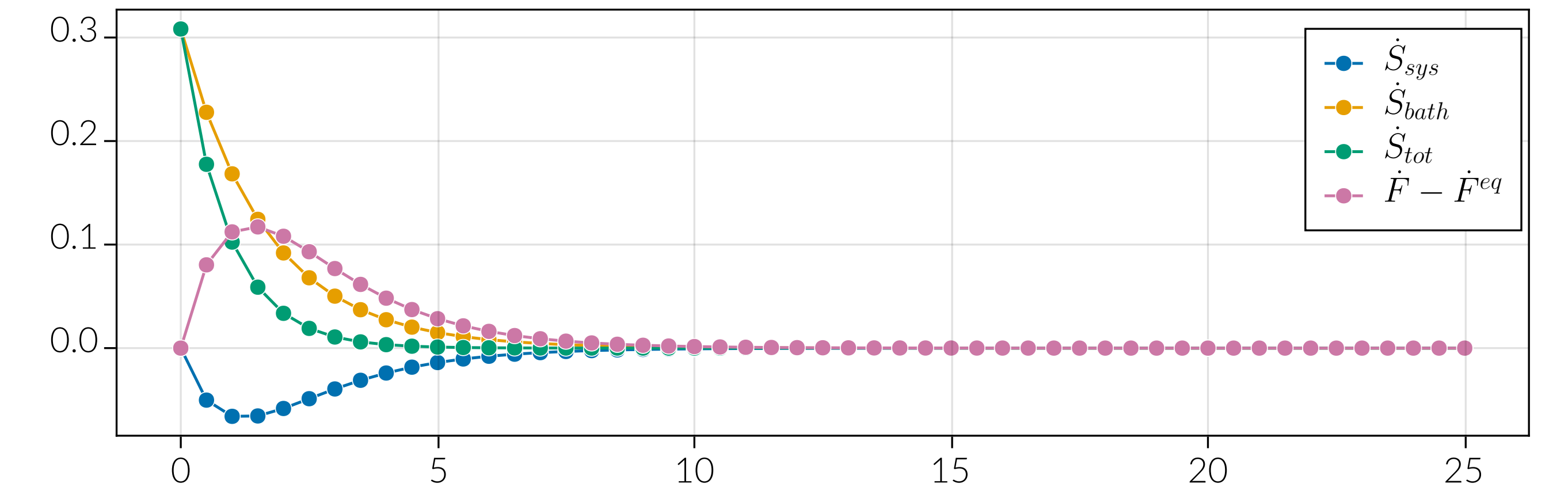


Figure 3. On top the evaluations of equations (4) to (6) in units of $k_B T$, to the MM system with $k_1 = 0.5$, $k_{-1} = 0.005$, $k_2 = 0.1$ and $k_{-2} = 0.0$. On the bottom, the time evolution of the probability of the system p_x in each state and the respective equilibrium probability p_x^{eq} .

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

- Both⁵ 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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