ENZYME KINETICS DRIVEN BY ENTROPY GENERATION

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ABSTRACT

Enzymes are natural machines that act as catalysts increasing the rates of biochemical reactions. They are present in all living beings and play an important role in industrial chemical processes. The performance of enzymes depends on their structure, reactivity and the activation energy. There is a close but non-trivial relationship between the kinetics of a single enzyme and the performance of a system of enzymes which is the origin of some enzyme kinetic principles like the maximal metabolic flux [1] from which the presence of infinite fluxes is possible [2]. A decrease in the activation energy, however, leads to an increase of the enzymatic reaction rates, a decrease in the reaction time and an increase of the entropy production. In that sense, a kinetic principle that predicts infinite rates will also predict and infinite entropy production, which seems to be meaningless. As the dynamics of the enzyme can be characterized by the entropy generation and the reaction time, the total entropy produced is in general a non-trivial function of the activation energy and can give us information about what are the most efficient configurations of the enzyme.

The enzyme activity takes place at the mesoscopic level [3-4]. Enzyme changes can be modelled by a diffusion process through a potential barrier in which its intermediate states are parametrized by a reaction coordinate, and with the shape of the potential barrier related to the enzyme's structure [5]. The rates can be obtained from the entropy production defined in the space of the reaction coordinate [3]. By using a proposed general shape of a potential barrier, with and without local minima that correspond to intermediate states, we calculate the entropy production [6]. From our mesoscopic thermodynamic analysis, we characterize the enzyme evolution by minimizing the total entropy produced. The results show that in an enzymatic reaction without intermediates states, in order to minimize the total entropy produced, the enzyme evolves towards configurations with the lowest activation energy. On the other hand, if intermediates states are present the configuration of the enzyme is such that the total entropy produced corresponds to local or global minima. According to these behaviours, it seems that in a scenario of a space of structure configurations, the enzyme will choose those to allow the enzymatic process without intermediates states.

We study the catalytic process starting from the enzyme-substrate complex state to produce the enzyme-product complex state, in a homogeneous, isothermal and closed system. The entropy production of the enzymatic process at the mesoscale, taking place along the reaction coordinate γ defined from 0 to 1, is given by:

$$\sigma(\gamma,t;E_a)=-\frac{1}{T}J(\gamma,t;E_a)\frac{\partial\mu(\gamma,t;E_a)}{\partial\gamma}$$

Here J is the current along the reaction coordinate, μ the chemical potential and E_a the activation energy. The linear law for the current is then given by

$$J(\gamma,t;E_a)=-\frac{L(\gamma,T)}{k_B}\frac{\partial\mu(\gamma,t;E_a)}{\partial\gamma}$$

where L is an Onsager coefficient which is in general a function of the state of the protein and the time. The chemical potential along the γ-coordinate is given by

$$\mu(\gamma,t;E_a)=k_BT\ln P(\gamma,t;E_a)+\varphi(\gamma;E_a)$$

Here φ is the potential barrier or enthalpic nature through which the diffusion process takes place. It is a function of the activation energy. By inserting the expression of the current into the continuity equation

$$\frac{\partial P(\gamma,t;E_a)}{\partial t}=-\frac{\partial J(\gamma,t;E_a)}{\partial\gamma}$$

One obtains a Fokker-Planck equation of the Fokker-Planck type. By solving this equation, we can compute the entropy production and therefore the total entropy produced, defined as

$$\Delta S(E_a) = \int_0^{t_R} \int_0^1 \sigma(\gamma, t; E_a) d\gamma dt$$

where t_R is the relaxation time of the process.

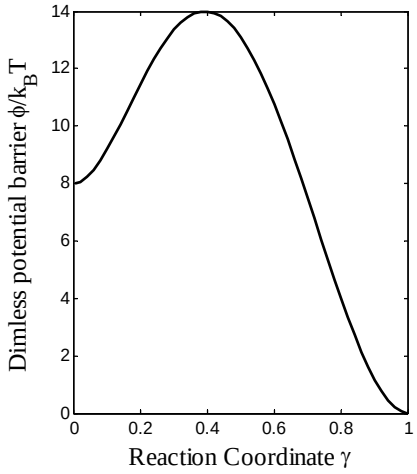

Figure 1: Potential barrier without intermediate states, for a high driving force.

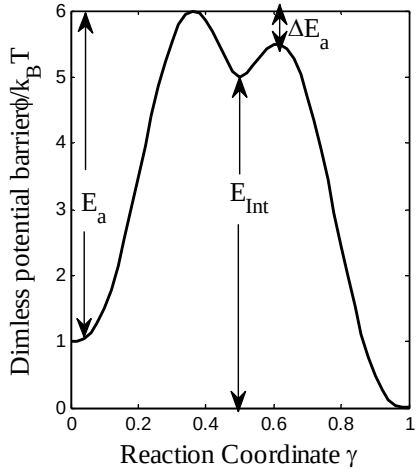

Figure 2: Potential barrier with an intermediate state, for a low driving force.

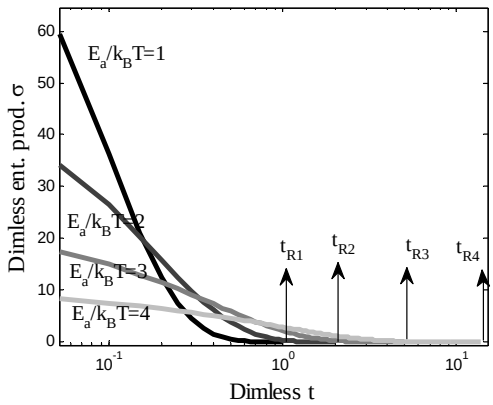

Figure 3: Entropy production against time for different activation energies.

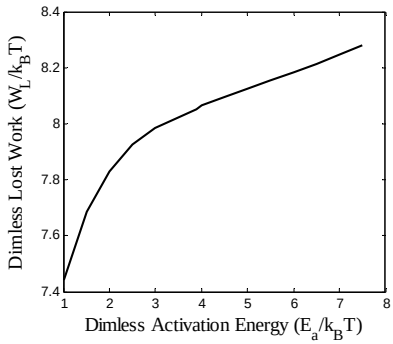

Figure 4: The lost work for the catalysed process without intermediates states, against the activation energy.

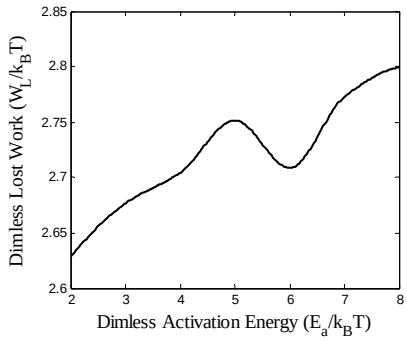

Figure 5: The lost work against the activation energy. The energy of the intermediate state is fixed and close to the stable states energy.

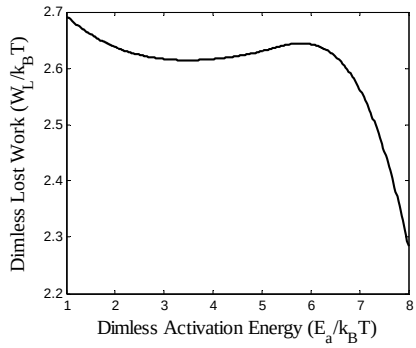

Figure 6: The lost work when the energy of the intermediate state increases proportionally to E_a, for ΔE_a fixed.

The proposed potential barriers are shown in Figs. 1 and 2 and are used in our calculations to study a general scheme in which an enzymatic reaction takes place in a closed system. The entropy production calculated by using the potential barrier without intermediates states, Fig. 1, is showed against time in Fig. 3, where the curves correspond to different values of the activation energy. The relaxation times (t_R) are indicated by arrows. For this case, the lost work always increases when the activation energy increases (Fig. 4). Thus, it is expected that in order to perform the enzymatic process with a minimal in the entropy generated, the enzyme has to evolve to a structural configuration with minimal energy activation.

A more complex behaviour is observed for enzymatic processes with intermediate states, as the one shown in the potential barrier of Fig. 2. The lost work computed as a function of the activation energy presents a local minimum, if the energy of intermediate state is fixed to some value and the gap in the activation energy, ΔE_a, is also fixed (Fig. 5). In this case, an additional result is shown in Fig. 6, where the lost work is computed for a fixed value of the gap ΔE_a. The lost work also exhibits a local minima and, interestingly, for sufficiently high values of activation energy it starts to decrease. One can thus expect that if the enzymatic process necessarily involves an intermediate state, the enzyme could evolve towards a structural configuration with an activation energy that ensures a local minimum in the lost work for the process. There are, however, additional scenarios to evolve towards a more efficient structural configuration. From Fig. 5, at low values of the activation energy and still in presence of the intermediate state, the enzymatic process could take place at the lowest values of the lost work. Moreover, from Fig. 6 at high values of the activation energy, where the energy landscape tends to be similar to the one shown in Fig. 1, the enzymatic process is more efficient. From this behaviour, we can then conclude that the natural evolution of the enzyme to reach an efficient structural configuration is to avoid processes with intermediate states.

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