Diffusion Controls Reaction Rates and Steady States

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***Short Abstract* — We analyze the dependence of effective macroscopic reaction rates on diffusion in discrete biochemical models on a hexagonal lattice. Substrates are subject to phosphorylation and dephosphorylation by respective enzymes. We demonstrated that effective (de)phosphorylation rates decrease with decreasing diffusion, and this dependence is stronger for the less abundant enzyme. As a result, the fraction of phosphorylated substrate may increase or decrease with diffusion, depending on relative concentrations of the enzymes.**

***Keywords* — kinetic Monte Carlo, macroscopic reaction rates**

I. Model and Methods

We analyzed a model of reversible phosphorylation/ dephosphorylation cycle on a hexagonal lattice serving as a model of plasma membrane. In the model, reacting molecules (substrates, kinases, phosphatases) are allowed to diffuse with a given motility m and may react with specified propensities while in contact (i.e. in adjacent lattice sites). Our aim was to determine effective macroscopic reaction rates and the steady state fraction of phosphorylated substrate. The reaction rules for the model are:

$$\mathrm{K} + \mathrm{S_u} \xrightarrow{c} \mathrm{K} + \mathrm{S_p}$$
$$\mathrm{P} + \mathrm{S_p} \xrightarrow{d} \mathrm{P} + \mathrm{S_u}$$

where $\mathrm{S_u}$ and $\mathrm{S_p}$ stand for unphosphorylated and phosphorylated substrates, respectively, K is the kinase and P - the phosphatase. Coefficients c and d are the propensities of phosphorylation and dephosphorylation reactions catalyzed by the adjacent enzyme. The above model is analyzed analytically and by means of kinetic Monte Carlo simulations.

II. Results

We demonstrated that the effective reaction rates decrease with decreasing motility, see Fig.1, where $c_{\mathrm{eff}}(m)$ is shown. We also show $c_{\mathrm{eff}}(m)$ for the First Order Dephosphorylation model (FOD), with the dephosphorylation rate $d_{\mathrm{eff}}^{\infty} = 6d\rho_{\mathrm{P}}$.

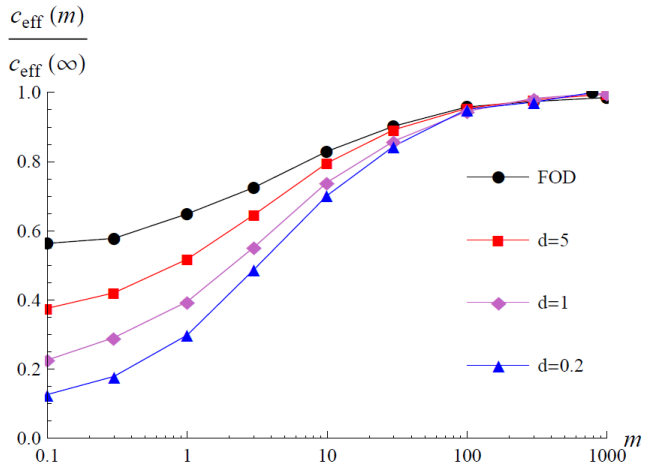

Fig.1. Effective phosphorylation rate as a function of motility, m.

It turns out that the dependence of effective reaction rates on motility is stronger for the less abundant enzyme. As a result, the fraction of phosphorylated substrate may increase or decrease with diffusion, depending on relative concentrations of the enzymes, see Fig. 2. Here, the change in phosphatase concentration is compensated by the change in the dephosphorylation propensity so that $d_{\mathrm{eff}}^{\infty}$ is kept constant. As a result, for growing motility the fraction of phosphorylated substrate tends to 0.5, regardless of phosphatase concentration. For high ρ_{P} (equal to 0.3), the dephosphorylation is effectively of first order and the $\rho_{\mathrm{P}} = 0.3$ line closely matches the FOD line.

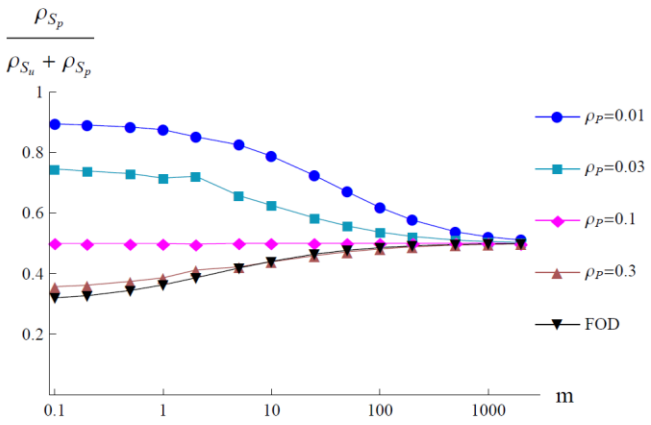

Fig. 2. Steady state fraction of phosphorylated substrate as a function of motility, m.

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