Project 3 : Molecular biology

Reading: Some papers (to be downloaded)[1], Britton, Essential Mathematical Biology, §6

Glycolysis is a phenomenon of the greatest importance for the energetics of living cells. The glycolytic pathway converts sugar glucose to an energy-rich compound known as Adenosine Tri-Phosphate (**ATP**). As part of this pathway, an enzyme known as Phospho-Fructo Kinase (**PFK**) catalyses cooperatively the quasi irreversible reaction in which ATP releases one of its phosphate bonds to become Adenosine Di-Phosphate ((**ADP**) (see first frame of fig. 1).The cooperativity is reflected here by the fact that the PFK activity increases with the presence of the product ADP.

At the molecular level, this is achieved by a conformational change of the molecule occurring beyond some critical concentration of ADP and revealing more active sites in which ADP and ATP can be fixed.

Detailed analysis leads one to model these effects by an enzyme activity function in the form of a Hill function

$$f(\alpha,\gamma) = q\frac{\alpha(1+\alpha)(1+\gamma)^2}{L+(1+\alpha)^2(1+\gamma)^2} \qquad (1)$$

where α and γ are the normalised concentrations of ATP and ADP.

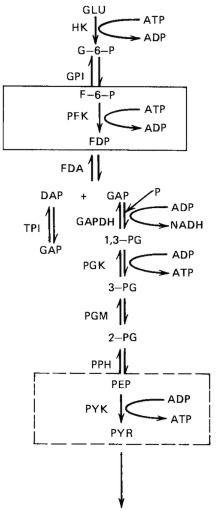

Figure 1: Glycolytic pathway. Upper frame represents steps involving enzyme **PKF**.

1. (*4/20*) Assuming α is supplied at a constant rate σ and γ has a finite lifetime k_{-1}, write out the rate equations of α and γ.

2. (*4/20*) Compute the steady states.

3. (*6/20*) Carry out linear stability analysis around these states and write down the Jacobian matrix.Without doing all the calculations, what type of eigenvalues should you expect to have at the transition to an oscillatory behaviour?

4. (*4/20*) Integrate numerically[2], the rate equations and represent graphically a few phase space trajectories. Explore the parameters (in particular, σ).

5. (*2/20*) With the help of the papers you downloaded, briefly discuss the biological relevance of such oscillations in this context.

[1] `http://www2.math.uu.se/~snicolis/teaching003.html`

[2] use the following parameter values : $\sigma = 2$, $k_{-1} = 1$, $q = 20$, $L = 7.5 \times 10^6$