**Quantitative Physiology I / Molecular and Cellular Systems, BMEN E4001x**

**Notes 06 – Numerical simulations**

**Keener & Sneyd, section 1.3 Glycolysis and Glycolytic oscillations**

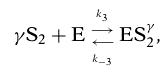
**web-available Runge-Kutta and MATLAB resource**

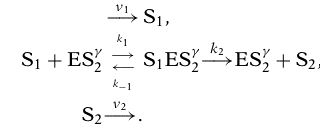
# Sel’kov model



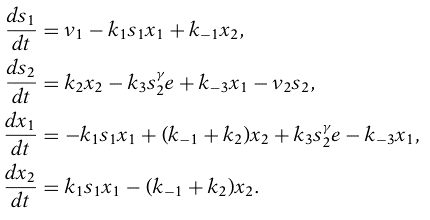
Under certain conditions, this system exhibits oscillations. K&S has a full description of the history and interactions. Earlier, we discussed that PFK1 is inhibited by ATP, and also acts on ATP. In this model, assume that ADP provides a positive regulation on PFK1; need to generate more ATP. Specifically, assume:

* ATP is a substrate and inhibitor to PFK1 (source of phos. for creating F-1,6-P)
* Inhibition is removed by AMP
* Steady state doesn’t capture full behavior
* Oscillations have been observed in yeast models
* Sel’kov model as a simplified explanation
* Goal: find reaction behavior as a function of input ATP
* binding of a certain number of ADPs, γ, (correlated to AMP) activates PFK1
* In the following scenario,
  + PFK1=E, with further substitutions in the next section: [ES2γ]=x1; [S1ES2γ]=x2
  + ATP=S1, ADP=S2,
  + γ= # of ADPs needed to activate PFK1
* scheme, given input rate v1, (ON BOARD)

 (activation of PFK1)

 (input of S1, what is the rate S2)

Gives the differential and conservation equations, using the normal substitutions (along with the one above)



e + x1 + x2 = e0

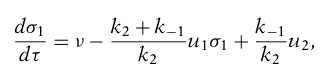
Introduce the following non-dimensional variables (COPY KEY PARTS ONTO BOARD)

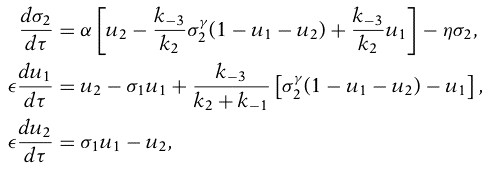
    

along with the following derived parameters

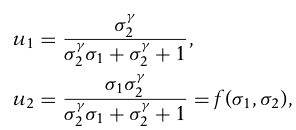
;epsilon ;nu ;eta ;alpha

the system becomes:

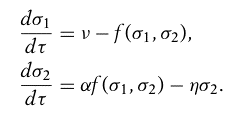




If we assume epsilon is small (following same argument as quasi steady-state, essentially), the lower two equations become:



which allows simplification of the two earlier equations



Following along the steady-state idea, we can set these differential equations to zero, and get the following STABLE SOLUTION



As an example, setting γ=2; ν=0.0285; η=0.1; α=1.0

Stable solution yields σ1= 0.3905; σ2= 0.285

But there are problems. In particular, this link between the two sigmas has no basis, such as a conservation equation. Make a vector plot of the two ODEs for the sigmas, and, indeed, if you solve the ODEs,



More notes:

* You can see on this graph the stability solution
* This stability is not, well, stable. That is, move from this point, you go to the attractors indicated by the curve.
* This path is highly dependent on parameters, including the balance of gamma, eta, nu, alpha. OUR GOAL HERE IS TO EXPLORE THIS BEHAVIOR NUMERICALLY. In solving ODEs, this usually means finding the dependent variables as a function of time, given necessary parameters and initial conditions.

For this, use the MATLAB program. (go to slides for very, very basic tutorial)

The ode45 method:

*(help page from going to* [*www.mathworks.com*](http://www.mathworks.com)*, entering ode45 in the search slot, then going to the first selection)*

<http://www.mathworks.com/access/helpdesk/help/techdoc/index.html?/access/helpdesk/help/techdoc/ref/ode113.html>

See slides for Runge-kutta discussion, and we’ll discuss the implications in class.