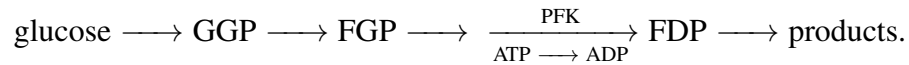Math 5110

Homework 5
Due: Thursday Dec. 10 (By 5pm)

1. Read Chapter 8 in the textbook.

2. A biochemical reaction that is ubiquitous in metabolic systems is the following sequence:

$$\text{glucose} \longrightarrow \text{GGP} \longrightarrow \text{FGP} \longrightarrow \xrightarrow[\text{ATP} \longrightarrow \text{ADP}]{\text{PFK}} \text{FDP} \longrightarrow \text{products}.$$

Here, FGP is the abbreviation for fructose-6-phosphate and FDP is fructose-1,6-diphosphate, two important metabolites. The conversion of FGP to FDP requires energy (via the dephosphorylation of ATP to ADP), and is also catalyzed by the enzyme PFK. It is generally known that PFK can have two states, one of which is more "active" and thus increases the rate of conversion of FGP to FDP. It is also known that ADP can promote the conversion of PFK to its active state. Thus, the products of the FGP/FDP reaction increase the rate at which the reaction occurs. This small part of the reaction chain can be represented schematically as

$$\text{substrates} \longrightarrow \text{FGP} \xrightarrow{+} \text{ADP} \longrightarrow \text{products}.$$
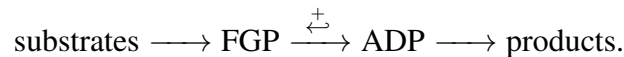
Here, the symbol ($\xrightarrow{+}$) indicates the positive feedback of ADP on the consumption of FGP. If we let x be the non-dimensional concentration of FGP and y be the concentration of ADP, then the equations which have been derived to describe this reaction are

$$\frac{dx}{dt} = \delta - kx - xy^2$$
$$\frac{dy}{dt} = kx + xy^2 - y. \tag{1}$$

(a) Find the single positive steady state of ADP and FGP.

(b) For what parameter values does the system behave as a positive feedback system (as discussed in class) *near the steady state*?

(c) When is the steady state stable? What behavior does the system exhibit when it is unstable?

3. In 1977, Goldbeter and Segel proposed the following equations to model AMP signaling within the cell. cAMP (cyclic adenosine monophosphate) is derived from ATP and is an important "second messenger" involved in signaling many biological processes. The original equations are

$$\frac{da}{dt} = v - \sigma\Phi(a, c)$$
$$\frac{db}{dt} = q\sigma\Phi(a, c) - k_b b$$
$$\frac{dc}{dt} = \frac{k_b}{h}b - k_c c. \tag{2}$$

Here, a, b, and c are the non-dimensional concentrations of intracellular ATP, intracellular cAMP, and extracellular cAMP respectively. The other parameters are dimensional. The function Φ is given by

$$\Phi = \frac{a\,(1+a)\,(1+c)^2}{L + (1+a)^2\,(1+c)^2},$$

and represents the allosteric kinetics of adenylate cyclase (BIG WORDS!). For the original analysis of this model and realistic parameter values, see "Unified mechanism for relay and oscillation of cyclic AMP in *Dictyostelium discoideum*", Goldbeter, A., and L. A. Segel, *PNAS*, 74(4), 1977.

(a) Assume that the reaction for intracellular cAMP proceeds quickly to equilibrium and reduce the system to two equations.

(b) Choose a value of L is *very* large, and a value of k_c that is small. Show that for moderate values of a, the system exhibits an "n-shaped" null-cline like we've seen in class.

(c) The parameter v represents the input of ATP (energy) into the system. What is the behavior of the system for small values of v? Does the system behaves like an excitable system?

(d) What happens as more energy is put into the system?