1.6 Homework # 5 (Due Monday, Nov. 21)

1. Consider the following biochemical reaction system:

$$DNA + 2\,TF \underset{f}{\overset{h}{\rightleftharpoons}} DNA \cdot (TF)_2, \tag{1.39a}$$

$$DNA + AA \xrightarrow{g_0} DNA + TF, \tag{1.39b}$$

$$DNA \cdot (TF)_2 + AA \xrightarrow{g_1} DNA \cdot (TF)_2 + TF, \tag{1.39c}$$

$$TF \xrightarrow{k} \text{ degradated.} \tag{1.39d}$$

Let $x(t)$ be the fraction of the DNA which has the trascription factors (TF) bound, and $y(t)$ be the concentration of the TF, at time t. Let the concentration of AA (amino acids) be a constant. We further assume that the $g_1 > g_0$, so the TF is an "activator" for its own gene expression. We also assume that the amount of DNA is much smaller than that of TF.

(a) Show with non-dimensionalization, the pair of ordinary differential equations can be written as

$$\begin{aligned} \frac{dx}{d\tau} &= \omega\left[\theta z^2(1-x) - x\right], \\ \frac{dz}{d\tau} &= g + (1-g)x - z. \end{aligned} \tag{1.40}$$

Give the expressions for z, τ, ω, θ, and g in terms of the original variables and parameters of the problem.

(b) Consider the ODE systems in (1.40). Plot the null-clines (also called iso-clines) for the two equations, and show the system can have 1 or 3 steady states, depending on the parameter values of g and θ.

(c) Fixed $g = 0.03$, obtain the steady state value z^* as a function of θ. What do you observe if you change the value of g?

2. Now let us assume that in Eq. (1.40) the $\omega \ll 1$.

(a) Justify that since $\omega \ll 1$, we can approximately "solve" the second equation to obtain $z = g + (1-g)x$.

(b) Substituting th relation $z = g + (1-g)x$ into the first equation, discuss the solution to the differential equation for $x(t)$.

(c) What can you do if $\omega \gg 1$?

3. A self-regulating gene system is represented by the system of ODEs:

$$\begin{aligned} \frac{\mathrm{d}u_1}{\mathrm{d}t} &= f(u_n) - k_1 u_1, \\ \frac{\mathrm{d}u_k}{\mathrm{d}t} &= u_{k-1} - \gamma_k u_k, \quad k = 2, 3, \cdots, n. \end{aligned}$$

The feedback function $f(u)$ is given by

$$(i)\ f(u) = \frac{a + u^m}{1 + u^m}, \quad (ii)\ f(u) = \frac{1}{1 + u^m},$$

in which a and m are positive constants.

(a) Which of the feedbacks is positive, and which is negative control?

(b) Find the steady states; show that with positive feedback multi-stability is posible.

(c) Show that for any $f(u)$ that represents a negative feedback there is only a unique steady state.

<u>I wish you all a good Thanksgiving holiday!</u>