Math 5515 Lab 1

Christie Burris

The Goodwin Model:

1a. Draw a diagram for this system.

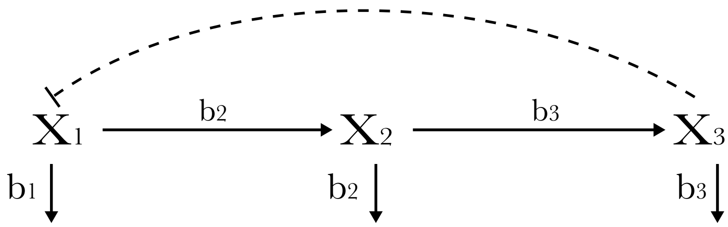
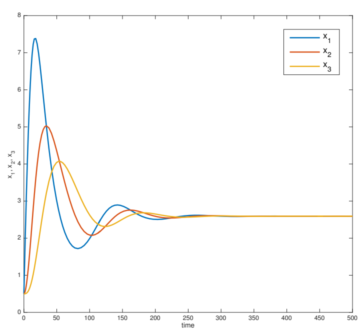


Figure 1: Goodwin model schema.

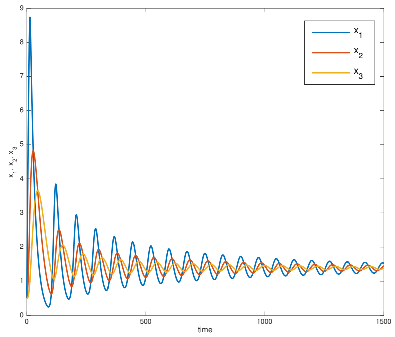
1b. Find the dynamics of x_1, x_2 and x_3 over time for $b_1 = b_2 = b_3 = 0.05, p = 2, x_1(0) = x_2(0) = x_3(0) = .5$. What do you observe?



Simulations of x_1, x_2, x_3 over time with $p = 2$. Each x_i has oscillations as seen in the figures below, however the oscillations quickly dampen to a stable steady state.

Figure 2

1c. Find the dynamics of x_1, x_2 and x_3 over time for $b_1 = b_2 = b_3 = 0.05, p = 8, x_1(0) = x_2(0) = x_3(0) = .5$. What do you observe?



Simulations of x_1, x_2, x_3 over time with $p = 8$. Oscillations are sustained for $p = 8$ as shown by the limit cycle in the plot of x_1 versus x_3.

Figure 3

1d. Draw $x_1(t)$ versus $x_3(t)$ for the parameters in part (c).

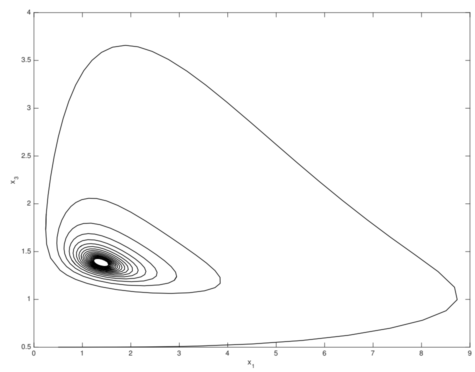


Figure 4: x_1 versus x_3.

The Bliss Model:

2a. Draw a diagram for the system.

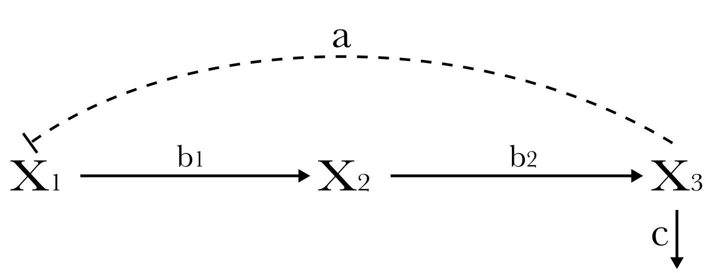
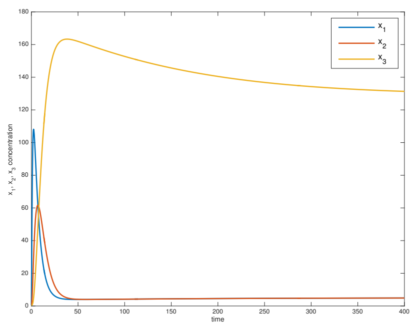


Figure 5

2b. Find the dynamics of x_1, x_2 and x_3 over time for $b_1 = b_2 = b_3 = 0.2, a = 129, c = 1, x_1(0) = x_2(0) = x_3(0) = .5$. What do you observe?

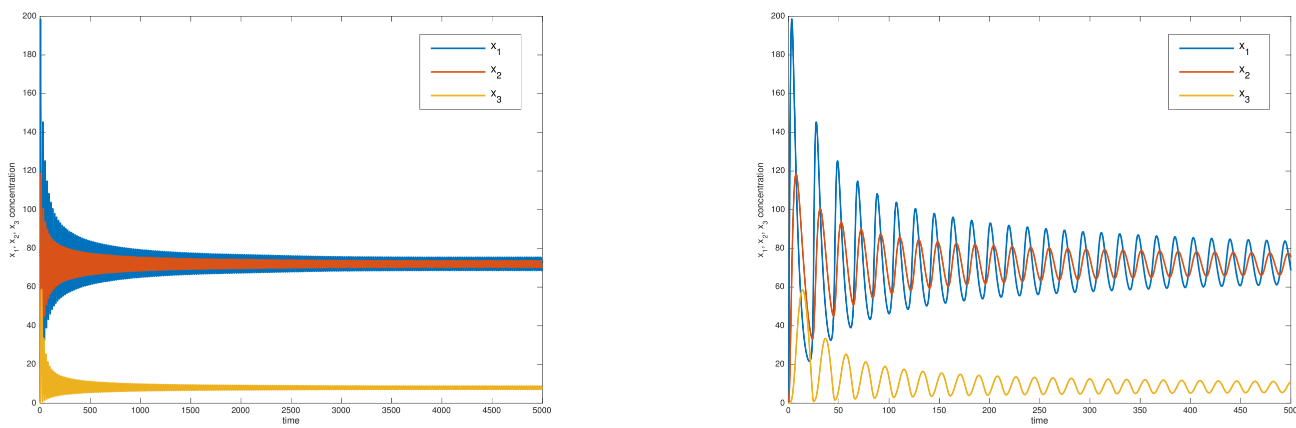


Simulations of x_1, x_2, x_3 over time with $c = 1$. We do not see oscillations. One possible explanation is that the value of c is too high, causing too much dampening in the concentration of x_1 from x_3.

Figure 6

2c. Find the dynamics of x_1, x_2 and x_3 over time for $b_1 = b_2 = b_3 = 0.2, a = 129, c = 16.2, x_1(0) = x_2(0) = x_3(0) = .5$. What do you observe?

Here we have sustained, smooth oscillations. To confirm they are sustained we extended the time and found the amplitude to be unchanging as $t \to 5000$ (Fig. 7a).



(a) Time: 0 to 5000

(b) Time: 0 to 500

Figure 7: Simulations of x_1, x_2, x_3 over time with $c = 16.2$.

2d. Draw $x_1(t)$ versus $x_3(t)$ for the parameters in part (c).

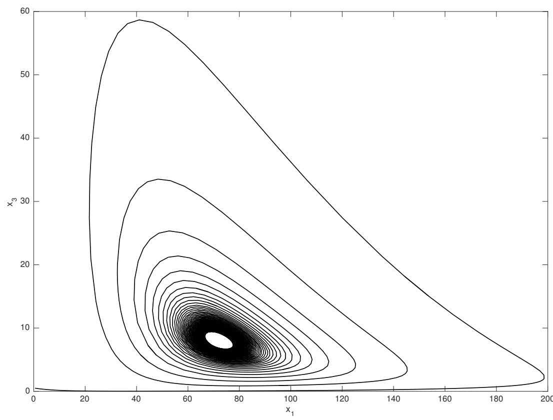


Figure 8: x_1 versus x_3. Notice the stable limit cycle.

The Goldbeter model of circadian rhythms:

3a. Draw a diagram of the system and explain each term.

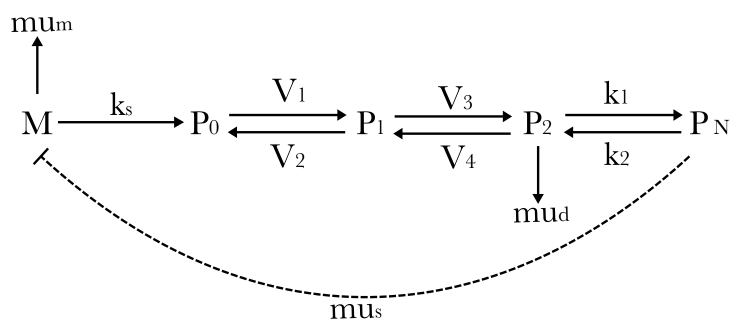


Figure 9

This is the model that describes the dynamics of a protein (*per*).
Variables:

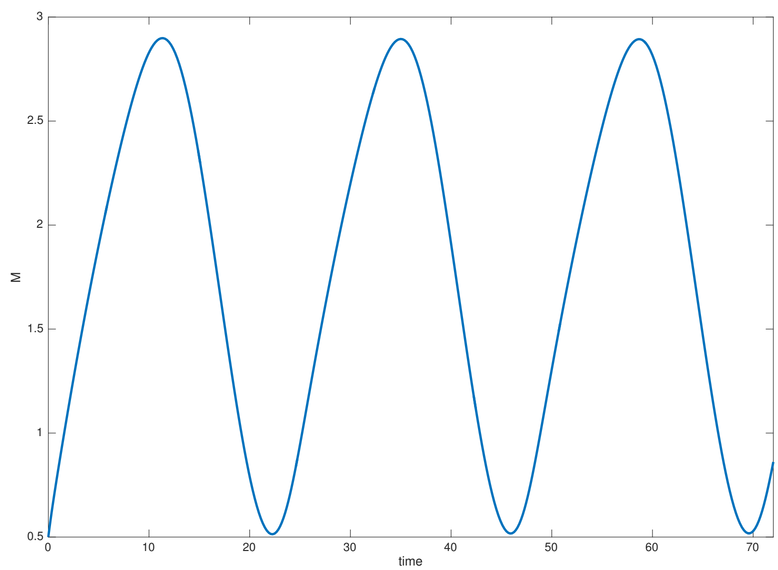
- M: *per* protein mRNA
- P_0: unphosphorylated *per* protein coded by *per* mRNA
- P_1: mono-phosphorylated *per* protein
- P_2: double-unphosphorylated *per* protein
- P_N: *per* protein in the nucleus

Terms:

- $\frac{\mu_s}{1+(P_N/K_I)^n}$: Hill term, inhibition of M by *per* protein in the nucleus.
- $\frac{\mu_m M}{K_{m1}+M}$: natural degradation rate of M.
- $k_s M$: Rate of protein synthesis dependant on M.

- $\frac{V_1 P_0}{K_1 + P_0}$: phosphorylation of *per* protein.
- $\frac{V_2 P_1}{K_2 + P_1}$: dephosphorylation of phosphorylated *per* protein.
- $\frac{V_3 P_1}{K_3 + P_1}$: double phosphorylation of *per* protein.
- $\frac{V_4 P_2}{K_4 + P_2}$: dephosphorylation of double phosphorylated *per* protein.
- $\frac{\mu_d P_2}{k_d + P_2}$: degradation rate of P_2.
- $k_1 P_2$: double phosphorylated *per* protein sent to the nucleus.
- $k_2 P_N$: double phosphorylated *per* protein coming out of the nucleus.

3b. For $n = 4, \mu_s = .76, \mu_m = .65, \mu_d = .95, k_s = .38, k_1 = 1.9, k_2 = 1.3, V_1 = 3.2, V_2 = 1.58, V_3 = 5, V_4 = 2.5, K_1 = K_2 = K_3 = K_I = 1, K_{m1} = .5, K_d = .2$, plot M over time.



3c. Modify the result in (b) to show that the period of M's oscillation depends on μ_d. Choose two values for μ_d and interpret your results.

For $\mu_d = .75$, P_2 degrades slower which means more *per* protein in the nucleus inhibiting M. Therefore M cannot sustain oscillations and drops off. For $\mu_d = .8$, the period of oscillation is smaller than 24 hours, but still sustained.

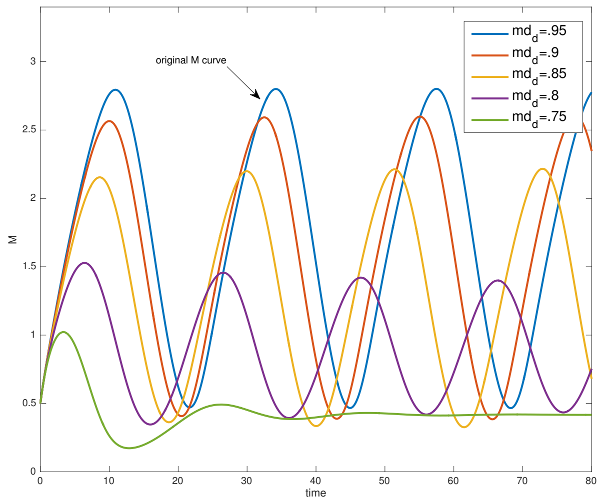


Figure 10

Substrate-depletion model: with $a = .5, b = 1, \epsilon = .05$.

4a. Use pplane8 to determine and classify the steady states.

Using pplane8, the steady state for the given system is a spiral source at $(\overline{x}, \overline{y}) = (1.6529, 0.55)$. $(\overline{x}, \overline{y})$ is therefore unstable and has a limit cycle as seen in Fig. 11 below.

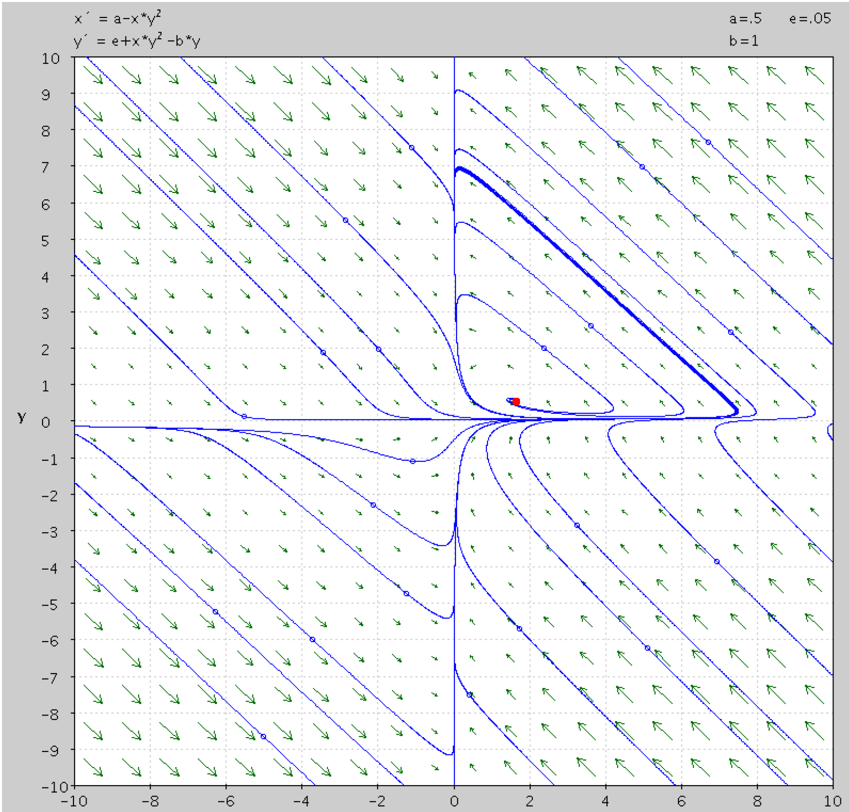


Figure 11: $x(t)$ versus $y(t)$. Blue curves represent solutions for various initial conditions and the red point represents the steady state $(\overline{x}, \overline{y})$

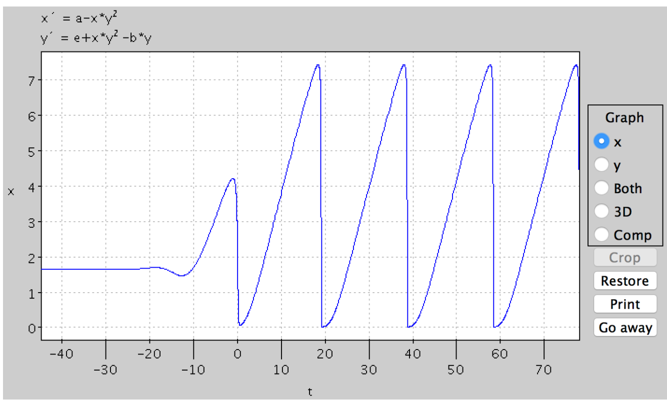


Figure 12: $x(t)$ versus t

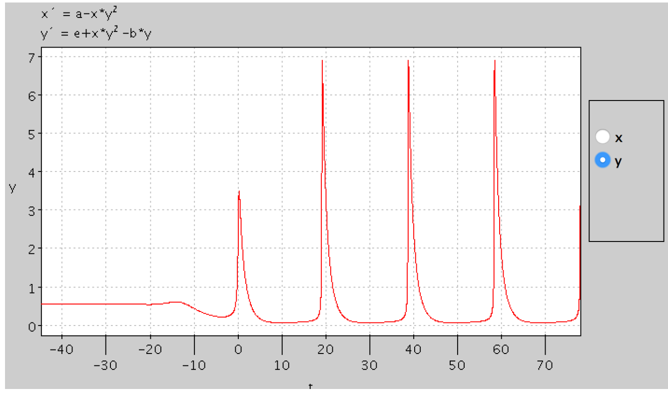


Figure 13: $y(t)$ versus t