CALIFORNIA INSTITUTE OF TECHNOLOGY
BioEngineering

BE 250C

M. Elowitz and R. M. Murray — **Problem Set #3** — Issued: 25 Jan 12
Winter 2011 — Due: 31 Jan 12

1. *Repressilator.* Simulate the following simplified version of the Repressilator:

$$\frac{dm_1}{dt} = \frac{k_p}{1 + (\frac{p_3}{K_M})^n} - k_{mdeg} m_1$$

$$\frac{dm_2}{dt} = \frac{k_p}{1 + (\frac{p_1}{K_M})^n} - k_{mdeg} m_2$$

$$\frac{dm_3}{dt} = \frac{k_p}{1 + (\frac{p_2}{K_M})^n} - k_{mdeg} m_3$$

$$\frac{dp_1}{dt} = k_{trans} m_1 - k_{pdeg} p_1$$

$$\frac{dp_2}{dt} = k_{trans} m_2 - k_{pdeg} p_2$$

$$\frac{dp_3}{dt} = k_{trans} m_3 - k_{pdeg} p_3$$

   a) Simulate the system using the following parameters: $k_p = 0.5, n = 2, K_M = 40, k_{mdeg} = 0.0058, k_{pdeg} = 0.0012, k_{trans} = 0.116$.

   b) Suppose the protein half-life suddenly decreases by half. Which parameter(s) will change and how? Simulate what happens. What if the protein half-life is doubled? How do these two changes affect the oscillatory behavior?

   c) Now assume that there is leakiness in the transcription process. How does the system's ODE change? Simulate the system with a small leakiness (say, 5e-3) and comment on how it affects the oscillatory behavior.

2. *Autoinhibition with Transcriptional Delay. (based on Lewis, J. DOI 10.1016/S0960-9822(03)00534-7).* Consider the following delayed differential equations:

$$\frac{dp(t)}{dt} = am(t - T_p) - bp(t)$$

$$\frac{dm(t)}{dt} = f(p(t - T_m) - cm(t)$$

   with

$$f(p) = \frac{k}{1 + p^2/p_0^2}$$

   f(p) represents the action of the inhibitory protein as a dimer. m, p are mRNA and protein concentrations, T_m is the delay from initiation of transcription and the arrival of mature mRNA into the cytoplasm, T_p is the delay from initiation of translation to the emergence of a complete functional protein. b and c are degradation of protein and mRNA.

(a) Implement the delayed differential equation model above.

(b) Choose parameters to obtain sustained oscillations and plot mRNA and protein concentrations.

(c) Comment on the robustness of sustained oscillations with respect to reduction in protein synthesis rate.

(d) Leave parameters as in a), and change only one parameter to obtain damped oscillations and plot mRNA and protein concentrations. Do not change the protein synthesis rate. Comment on how the change of parameter might affect dampening.