1. Delays play an important role in a number of modeling areas. In the early 1960s, B. C. Goodwin developed mathematical models using biochemical and enzymatic kinetics approximations for repression of a gene by its end product. He noted that the delays of transcription and translation could have a destabilizing effect on his model. One form of the repression model with delays (rescaled to minimize parameters) is given by:

$$\begin{aligned} \frac{dm(t)}{dt} &= \frac{1}{1+r(t-k)^4} - b_1 m(t), \\ \frac{dp(t)}{dt} &= m(t) - b_2 p(t), \\ \frac{dr(t)}{dt} &= p(t) - b_3 r(t), \end{aligned}$$

where b_1, b_2, and b_3 are decay constants, k is the delay for transcription and translation, and the Hill coefficient is 4 representing a tetramer repressor binding the gene in repression. The variable m represents the concentration of mRNA, p is the protein formed from the mRNA, and r is endproduct repressor created by the protein.

a. Give a brief discussion of genetic repression in bacteria, list at least one specific example, then show how the above model could relate to this process. Explain each of the equations in the model. You do not need to give detailed kinetic explanations for how the nonlinear term arises. (Note that the delay is completely contained in the nonlinear term, which is from combining the transcription and translation. This is done by a simple change of variables or can be interpreted by letting m be the initiation of mRNA production and p be the completed protein.)

b. Consider the undelayed case, where $k = 0$. Let $b_1 = 1$, $b_2 = 0.1$, and $b_3 = 0.5$. Find all equilibria. Linearize the above system of ordinary differential equations about each of the equilibria. Find the eigenvalues at each equilibrium and discuss the stability for this model.

c. Again, let $b_1 = 1$, $b_2 = 0.1$, and $b_3 = 0.5$. The equilibria are the same for the delayed model. Linearize the above system of delay differential equations about each of the equilibria. Write the characteristic equation for finding the eigenvalues at each equilibrium. Consider the cases when $k = 1$ and $k = 4$. For each of these cases, create a program to map the perimeter of rectangle in the complex plane bounded by $0 \le x \le 4$ and $-3 \le y \le 3$ in the counterclockwise direction into the complex image space using the characteristic equation. Using the argument principle, determine how many, if any, eigenvalues are contained the the rectangle described above. With this information, discuss the stability of the delay differential equation for each of these delays. (Extra credit: Use MatLab's dde23 subroutine to simulate both of these cases, and discuss the observed solutions for this model with the two delays.)

d. Let $\lambda = i\omega$ in the characteristic equation and use Maple's fsolve to find where the Hopf bifurcation occurs. (You are welcome to use any other nonlinear solver that can solve this characteristic equation.) Give the value of both k and ω at the bifurcation.