AMATH 422/522
Problem set 3

Working together is absolutely encouraged. Please do not refer to previous years' solutions.

For each problem: together with any analysis or explanations, turn in both all code and all relevant plots, labeled and with all line styles, marker sizes etc. adjusted for readability. All materials for each problem should be presented together, then move on to the next problem, etc (as opposed to putting all code stapled on at the end, etc).

Please note: E+G stands for our book, by Ellner and Guckenheimer.

I **Coupled oscillators.** Consider a model for *two* repressilators, coupled via their protein concentrations (as if protein can diffuse between the two cells). That is, let the mRNA and protein concentrations for the first repressilator be m_i and p_i, and for the second repressilator be n_i and q_i. Let the dynamics be

$$\begin{aligned}
\dot{m_i} &= -m_i + \frac{\alpha}{1+p_j^n} + \alpha_0 &(1)\\
\dot{p_i} &= -\beta(p_i - m_i) + \gamma(q_i - p_i) &(2)\\
\dot{n_i} &= -n_i + \frac{\alpha}{1+q_j^n} + \alpha_0 &(3)\\
\dot{q_i} &= -\beta(q_i - n_i) + \gamma(p_i - q_i) &(4)
\end{aligned}$$

where most of the terms are exactly as in class and the book, but the γ terms represent the new coupling. Implement a dynamical simulation of this system using `ode45` in MATLAB. Note: This should involve a total of 12 dynamical variables. Choose a parameter set which produces clear oscillations for the uncoupled system ($\gamma = 0$).

Answer the following questions, and support your answer with plots from your simulation:

(a) Draw the interactions among the variables, as an interaction graph. Have a node for each variable and edges indicating interactions. Indicate which interactions are activating versus repressing.

(b) Do nonzero values of γ serve to synchronize the two oscillators, in that when you start each oscillator with different initial conditions, the trajectories eventually converge over time? Illustrate this with appropriate plots.

(c) Does it matter whether γ is positive or negative?

(d) Give some intuition for the effects of γ in a few sentences.

Hint: The first point is to make sure that you really have two coupled repressilators represented by your equations. You could start with the code for ONE repressilator, from class and on our website. With the right parameters from class, that should produce a single oscillator. That's a six-variable system. Then, you could add code, so you have a second repressilator that you are also simulating (i.e., within the same ode .m file). Then, you have a twelve-variable system, and are ready to couple them via the γ term above and solve the problem!

II **SIR model with births, part 1.** Read Chapter 6 about models of infectious disease. We are going to study Equation 6.9:

$$\dot{S} = \mu N - \beta SI - \mu S$$
$$\dot{I} = \beta SI - (\gamma + \mu)I$$
$$\dot{R} = \gamma I - \mu R,$$

where $N = S + I + R$.

(a) Draw the interaction graph for this model.

(b) Explain what the variables in the model measure.

(c) Explain what each of the parameters measures and why they must be all be positive.

(d) Show, without MATLAB, that $\dot{N} = 0$. Explain what this means and why you can use this to reduce the system to 2 equations.

III **SIR model with births, part 2.** Read Chapter 6 about models of infectious disease. Now, we are going to study Equation 6.10, which as the book explains is equivalent to Equation 6.9.

$$\dot{X} = \mu(1 - X) - LX$$
$$\dot{L} = (\gamma + \mu)L(R_0 X - 1).$$

This has fewer variables and fewer parameters, always a good thing. Implement the model in MATLAB and write a script to simulate it for arbitrary initial conditions and parameters. Again, use `ode45`. When you describe the behavior of the ODE, explain what it means for the disease. If you find an equilibrium, explain if it is disease-free or there remain a non-zero population of infectives (endemic state). Note that, with the parameters given, time can be measured in "years."

(a) Let $X(0) = 0.99, L(0) = 0.2$. This corresponds to 99% of the population susceptible initially. For the parameters, set $\gamma = 28$, $\mu = 1$, and $R_0 = 0.4$. Simulate the system from time 0 to time 20 and explain what you find.

(b) Now, change just the R_0 parameter to 1.4. What changes and what is different?

(c) Do the same thing for $R_0 = 1.05$.

(d) Same thing for $R_0 = 3$. Note that Ebola, which is extremely infective, has $R_0 \approx 2$, so this is getting beyond the reasonable range of this parameter.

(e) Measure the frequency of any oscillations observed for the previous parameter values in (a–d). You do not have to do anything fancy, just find the average distance between the peaks you observe. Compare this value to the frequency predicted in Equation 6.18:

$$T \approx \frac{2\pi}{\sqrt{\gamma\mu(R_0 - 1)}}.$$

Summarize your results in a table or figure for different R_0.

IV **Vaccination at birth. Grad student problem or undergrad extra credit.** This is Exercise 6.5 in E+G. Starting with the constant population SIR model, Equation 6.9 (the equation in problem II), suppose that newborns are vaccinatied so that a fraction $p \leq 1$ of all newborns are born as removed rather than susceptible.

(a) Write down the resulting system of differential equations. Note that the population size should still be constant, and that when $p = 0$ your model reduces to (E+G) Equation 6.9.

(b) Show that as p is increased from 0, the number of infectives at the endemic steady state decreases until it reaches 0 at some value $p < 1$. This is sometimes called *herd immunity*: even though some individuals have not been immunized by vaccination, the disease cannot sustain itself in the population as a whole.

(c) Let p^* be the value of p at which the endemic state reaches zero. Find this as a function of the other variables. If only 50% of the children are vaccinated, can there be herd immunity, for reasonable values of the other variables?

Note: the endemic steady state is a point in the phase space $(S, I, R) = (S^*, I^*, R^*)$ for which $\dot{S} = \dot{I} = \dot{R} = 0$, and $I^* \neq 0$. You may need to work through the rescaling/non-dimensionalizing that is carried out in the book to more easily tackle this problem.