AMATH 422/522
Problem set 6

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.

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

$$\dot{m}_i = -m_i + \frac{\alpha}{1+p_j^n} + \alpha_0 \quad (1)$$

$$\dot{p}_i = -\beta(p_i - m_i) + \gamma(q_i - p_i) \quad (2)$$

$$\dot{n}_i = -n_i + \frac{\alpha}{1+q_j^n} + \alpha_0 \quad (3)$$

$$\dot{q}_i = -\beta(q_i - n_i) + \gamma(p_i - q_i) \quad (4)$$

where most of the terms are exactly as in class / the book, but the γ terms represent the new coupling. Implement a dynamical simulation of this system numerically (in code). **Note: This should involve a total of 12 dynamical variables.** Choose a parameter set which produces clear oscillations for the uncoupled system ($\gamma = 0$). Address the question: 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. Does it matter whether γ is positive or negative? Give some intuition for the effects of γ in two written 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 / 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 function file defining the ode). Then, you have a twelve-variable system, and are ready to couple them via the γ term above and solve the problem!

II **Systems biology and network motifs**. Read the Nature Review Genetics paper by Alon, 2007, on the website. Write down a set of differential equations that can model the phenomenon discussed in Fig. 7a and 7b only, and simulate them in code to produce qualitatively similar figures (i.e., solutions that have roughly the same shape vs time for the full time axis). This will likely take some trial and error, and perhaps some "intuitive" thinking about inputs and equilibria for different portions of the plots 7a and 7b. Write two sentences, for each of 7a and 7b, explaining the form of your differential equations, and why these match the "motif" schematic in the figure. READ THIS: Take a look at the 2002 paper from Shen-Orr et al, also on the website, which has a methods section proposing specific equations that describe the results in that Fig. 2. Your equations should have this same general form (i.e., use a modified form of these equations), involving nonlinear interactions between chemical species and, besides the Z forcing term, no explicit time-dependence (i.e., do not just code in the answer). AMATH 522 ONLY: also do this for the case in Fig. 7c.