Math 4335 Homework

Instructions:

- *Staple or bind* all pages together. *DO NOT* dog ear pages as a method to bind. (I do not carry a stapler with me to class.)
- Hand-drawn sketches should be neat, clear, of reasonable size, with axis and tick marks appropriately labeled. All figures should have a short caption explaining what they show and describe.
- Please label each problem and write clearly. If your work cannot be read, or the problem not found, it will not be graded.
- Double check that your scans are readable, with text size of a reasonable size, and decent lighting.
- **.ipynb* refers to python files. **.m* refers to matlab files.

1 Review of ODEs

Solve the following first-order ODEs

1. $$u' = (t^2 + 2), \quad u(3) = 2$$
2. $$u' = \frac{t^2 + 4}{u^2 + 4}$$
3. $$u' = \cos(t)u^2$$
4. $$u' = u(u - 1), \quad u(0) = u_0, \quad \text{(Use partial fractions.)}$$
5. $$u' + 4u = t, \quad u(0) = 1$$
6. $$tu' + u = e^t, \quad u(1) = 1$$
7. The chemical process represented below indicates a reversible reaction with different rates in each direction and is Eqs. (2.6a) and (2.6b) in S & EK.

$$A \underset{k_{-1}}{\overset{k_1}{\Leftrightarrow}} B$$

(a) Suppose the concentration A is fixed (a constant/number) at a value $\bar{A}$. Solve the resulting equation for B shown below

$$\frac{dB}{dt} = k_1\bar{A} - k_{-1}B, \qquad B(0) = B_0$$

(b) Find the asymptotic value of $B(t)$ for long times. In other words, what is the steady-state value of $B(t) = B_s$? ($\lim t \to \infty$)
(c) How long does it take for $B(t)$ to reach the steady state plus ϵ, ie, what is t_c where $B(t_c) = B_s + \epsilon$?
(d) How much longer does it take to get half as close *more*? That is,

- What is t_d where $B(t_c d = B_s + \epsilon/2$?
- What is $t_d - t_c$?

(The resulting formula should match that of the usual 1/2-Life formula you can find in MATH 3313 or a Biology / Chemistry text book.)

2 Graphical Analysis of 1^{st}-order ODEs

1. Sketch the direction field for the following two problems by hand. Do this by drawing short lines of the appropriate slope centered at each of the integer valued coordinates (t, u), where $-2 \leq t \leq 2$ and $-1 \leq u \leq 1$. Add to your sketch some solutions curves (always parallel to the dashes).
   (a) $u' = t - u^2$
   (b) $u' = u^2 + 1$

2. Consider the ODE
$$u' = f(u) = r - u^2$$
   where r is a parameter that can take the values $r = 1, 0.5, 0.1, -0.1$. For each value of r:
   (a) Sketch $f(u) = r - u^2$ and determine the equilibrium points.
   (b) Draw the phase line.
   (d) Determine the stability of the equilibrium points.
   (d) Plot the direction field and some sample solutions,i.e., $u(t)$
   (e) Describe how location of the equilibrium points and their stability change as you increase the parameter r.
   (f) Using the *scalerode.ipynb / phaseline.m* generate a solution for each value of r and the initial condition $u(0) = -0.9$. Print and turn in your result for $r = 1$. Do not forget to add a figure caption.
   (g) In the program *scalerode.ipynb / phaseline.m* set the initial condition to $u(0) = -1.1$ and simulate the ode over the time interval $t = [0, 10]$ for different values of r. What happens? Why? You do not need to turn in a plot for (g), just describe what happens.

3. Consider the ODE
$$u' = f(u) = \cos(u) - r \quad \text{for} \quad r = 1.1, 0.9, 0.$$
   For each value of r
   (a) First sketch the curve $f_1(u) = \cos(u)$. Then, on the same graph, sketch the line $f_2(u) = r$ for the different values of r. Because $f = f_1 - f_2$ is the difference between the two curves. Where the two curves intersect $f = 0$; these are the equilibrium points. Label these points.
   (b) Draw the phase line.
   (c) Determine the stability of the equilibrium points.
   (d) Describe how location of the equilibrium points and their stability change as you increase the parameter r.
   (e) Use *phaseline* to check that your conclusions above are correct. You do not need to print any plots.

3 Single Species Populations

1. Imagine a field with vegetation (grass) being grazed upon by a herd of cows. Let $V(t)$ is the biomass of the vegetation and H be the number of cows. R.M. May (*Stability and Complexity in Model Ecosystems*, Princeton University Press, 1974) proposed the following model:

$$\frac{dV}{dt} = f(V) = g(V) - Hc(V),$$

$$g(V) = rV(1 - \frac{V}{K}) \text{ and } c(V) = \beta \frac{V^2}{V_0^2 + V^2}.$$

$g(V)$ measures the growth of the vegetation and $c(V)$ is the consumption per cow, where r, K, β and V_0 are positive constants.
(a) Describe the biology of $g(V)$. Can you give a physical interpretation of r and K?
(b) Describe the biology of $c(V)$. What happens for V very small or very large?
(c) Verify and $V = 0$ is a steady state and find a formula for non-zero steady states in terms or the parameters.
(d) Let $r = 1/3$, $K = 25$, $\beta = 0.1$ and $V_0 = 3$. Plot* $g(V)$ and $Hc(V)$ for $H = 10,\ 20$ and 30 (three plots). What can you predict for the state of the field in each case.
(e) For the same parameter values and again for the same three values of H plot the phaseline (i.e., plot $f(V)$). Indicate the stability of each steady state. Your result should be consistent with your answer in part (d).
(*) Plot = python, matlab, desmos, some other plotting tool, etc. Something where you can visualize the functions and generate a submittable plot.

2. The standard logistic equation $u' = R(u)u = r(1 - u/K)u$ is said to be *compensatory* or exhibits *compensation*. This refers to the fact that the growth rate $R(u)$ is a decreasing function of u ($R'(u) \leq 0$ for $0 \leq u < K$), which indicates as the population grows the growth rate decreases, presumably due to resource competition.

   However, some populations are *depensatory* (exhibits *depensation*, also known as the *Allee effect*), where the growth rate actually increases with increasing population size ($R'(u) > 0$ for $0 \leq u < K^* < K$. For example, a flock of birds is better able to defend against predators as the flock size increases and, hence, is better able to reproduce.

   There is also the case of *critical depensation* where the growth rate is negative for smaller population sizes ($R'(u) < 0$ for $0 \leq u < K^*$. Thus, if the population is below some critical size, then it can not support itself and will die out. Such populations are sensitive to hunting or harvesting because these may inadvertently drive the population size below the critical value.

   For some organisms finding a suitable mate may cause difficulties at low population levels, and a more realistic equation for population growth than the linear one in the absence of intra-species competition may be $u' = ru^2$, $u(0) = u_0$, $r > 0$.
   (a) Show that this model exhibits depensation.
   (b) Solve this problem and show that the solution becomes infinite in finite time.
   (c) The model above is improved to

$$u' = ru^2(1 - \frac{u}{K}).$$

   Find the steady states and determine their stability from the phase line.

4 Linear Stability

1. Consider the function $y = f(x) = \cos(x)$.
   (a) Find the four term Taylor series (out to $(x - x_0)^4$) for $x_0 = 0$.
   (b) All on the same graph, sketch $y = f(x)$ and the the linear and quadratic approximations to $f(x)$ based on the Taylor series in (a).
   (c) Repeat steps (a) and (b) using $x_0 = \pi/2$. You probably want to start a new graph to keep things legible.

2. Consider the Logistic equation $u' = ru(1 - u/K)$.
   (a) For $r = 1$ and $K = 1$, determine the steady states and analyze their linear stability.
   (b) Now keep r and K as *positive* parameters. Recompute the steady states and determine their linear stability as a function of the parameters.
   (c) Suppose that r is allowed to be negative, how does that change the stability of the steady states?
   (*) Note that your results should be consistent with the graphical analysis of the Logistic equation done in class.

3. Compute the linear stability for the steady states of $u' = \sin(u) - ru$ for general r.

4. (S & EK 5.23 and 4.14). *Another single-species problem.* Consider the Model of Ludwig, Jones and Holling for the spruce budworm, $B(t)$. It uses a logistic equation for the self-dynamics of the budworm (growth rate r_B and carrying capacity of K_B) and also includes a predation term due to birds (parameters α and β that reduces the population. (See also S & EK 4.14)

$$\frac{dB}{dt} = r_B B(1 - \frac{B}{K_B}) - \beta \frac{B^2}{\alpha^2 + B^2}$$

   r_B, K_B, α, $\beta > 0$ are constants.
   (a) Before analyzing these equations we will *non-dimensionalize* them (See S & EK, Sec. 4.1.1). Make the following change of variables:

$$B = K_B b, \quad T = r_B t$$

   Thus, everywhere there is a B, substitute $K_B b$. The only place there is a t is in the derivative. We have that $\frac{d}{dt} = (\frac{dT}{dt})\frac{d}{dT} = r_B \frac{d}{dT}$. After symplifying, the non-dimensionalized DE is

$$\frac{db}{dT} = b(1 - b) - R\frac{b^2}{Q^2 + b^2}, \quad R = \frac{\beta}{r_B K_B}, \quad Q = \frac{\alpha}{K_B}$$

   The advantage of these new equations is that there are only two parameters, R and Q. The intrinsic growth rate is 1 because we have scaled time with r_B and the carrying capacity is 1 because we have scaled the budworm population by K_B.
   (b) Show that $b = 0$ is a steady state and determine it's linear stability.
   (c) Sketch the phase line by sketching the two functions $y_1 = b(1 - b)$ and $y_2 = R\frac{b^2}{Q^2+b^2}$ on the same axis choosing $Q = 0.1$ and $R = 0.1$.
   (d) Indicate the steady-states and determine their *nonlinear* stability from the phase line
   (e) Slowly increase R from 0.1 to 0.3. This corresponds to increasing β, which is the predation rate of the birds on the budworms. What happends to the steady states (values, number of, stability)?

5 Models for Multiple Species

1. The following is a three species predator-prey model for v = vegetation that is the food source for r = rabbits who are the food source for w = wolves:

$$\begin{aligned} v' &= v(\alpha - v) - rv \\ r' &= -r + \beta rv - rw \\ w' &= -w + rw \end{aligned}$$

(a) Identify the coupling term between the vegetation and rabbits, and the couple term between the rabbits and wolves. You should understand how this models predator-prey interactions.
(b) Assume there are no rabbits and no wolves. What are the stead states for the vegetation?
(c) Assume there are no wolves. What are the steady states for vegetation and rabbits?
(d) What are the steady states when all three species are present?
(e) What restriction(s) are needed on α and β for the steady states to be physically realistic. You need to consider what one would expect when each new predator is introduced.
(f) Examine the linear stability of the extinction steady state $(v, r, w) = (0, 0, 0)$. This requires finding the eigenvalues of a Jacobian that is 3×3.

2. Suppose instead of competing populations there is mutualism. That is, each population supports the other. In this case, the mutual competition term must be positive.

$$\begin{aligned} u_1' &= r_1 u_1(1 - u_1 + b_1 u_2) \\ u_2' &= u_2(1 - u_2 + b_2 u_1) \end{aligned}$$

where the b_j must be positive. Simulate this case using the program *twoodes.ipynb / competing.m*. Find parameter values such that the coexistence state is attracting (stable). Generate a plot of the phase plane demonstrating your result. Hints: You may need to compute a condition like in problem (1) to serve as a guide to picking new values for the b_j. You will likely have to adjust tmax and umax. I suggest you experiment by testing different initial conditions to see that they all go to the coexistence steady state.

3. is on the next page.

3. (Based on S & EK example 4.5 and exercise 4.10. See also example 7.3). Below is a model for the process whereby active macrophages (active-MP), $m(t)$, remove dead red blood cells (dead-RBC), $a(t)$. Thus, the macrophages are the predators and the dead RBCs are the prey.

$$\frac{dm}{dt} = g(K_m - m)a - \gamma_m m,$$
$$\frac{da}{dt} = \kappa K_a m - fma - \gamma_a a.$$

- t is measured in hours.
- $m(t)$ is the density (M-cells/cm^3) of active-MP ready to attack dead-RBCs.
- K_m is the density of both active and dead macrophages (M-cells/cm^3).
- $K_m - m$, is the density of dormant macrophages.
- $a(t)$ is the density of dead-RBCs (B-cells/cm^3).
- $+g(K_m - m)a$ is the contact between a dead RBC and a dormant macrophage, activating the later to generate new m (MP), with rate constant g.
- $-\gamma_m m$ is the loss of active MP due to natural deactivation.
- K_a is the density alive RBCs (B-cells/cm^3).
- $+\kappa K_a m$ is contact between an alive RBC and an active-MP that causes the alive RBC to become an dead-RBC. κ is the rate constant for this "bystander" killing of cells.
- $-fma$ is contact between an active-MP and a dead-RBC causing a removal of the RBC with rate constant f. This term represents the main job of the MP.
- $-\gamma_a a$ represents all other mechanisms that remove dead-RBCs, e.g., the spleen.

(a) The units on the left hand side of the equations are active-MP/(cm^3 h) and dead-RBC/(cm^3 h). What are the units of g, κ, f, γ_m and γa?
(b) Non-dimensionalize by making the following change of variables:

$$t = \tau T \text{ so that } \frac{d}{dt} = \frac{1}{\tau}\frac{d}{dT}, \quad m = c_m M \quad a = c_a A.$$

Substitute and determine τ, c_a and c_m such that the new non-dimensionalized equations are as shown below.

$$\frac{dM}{dT} = \alpha(1 - M)A - \delta M,$$
$$\frac{dA}{dT} = M - \eta MA - A.$$

(c) What are α, δ and η in terms of the original parameters?
(d) What are the units of α, δ and η?
Again, the goal of non-dimensionalization is to reduce the number of parameters. More importantly however, what we see is that it is not the actual parameters that are most important, rather, it is specific **ratios of parameters** that are important. It is changes in these ratios that cause changes in the system's behavior. The analysis of these new equations is taken up in S & EK, example 7.3.

6 Phase Plane Analysis

For each of the following problems:

1.

$$\begin{aligned} u' &= u^2 - 1 \\ v' &= uv \end{aligned}$$

2.

$$\begin{aligned} u' &= v + u - u^3 \\ v' &= -v \end{aligned}$$

3.

$$\begin{aligned} u' &= uv - 1 \\ v' &= v - u^3 \end{aligned}$$

(a) Determine the nullclines.

(b) Determine the equilibrium points.

(c) Use the program *PyPlane / PhasePlane.mlapp* to plot (and PRINT) the phase plane. Identify the nullclines and equilibrium points on the phase-plane and plot some important trajectories. Be sure to adjust the axis limits so that the important detail is prominently display in the plot.

Make sure that your results from parts (a) and (b)) are consistent with what is shown by *PyPlane / PhasePlane.mlapp*. Remember that the nullclines indicate where the trajectories are either strictly horizontal or strictly vertical. Your figures should be consistent with that requirement.

(d) For each equilibrium point analyze the linear stability. That is, determine the eigenvalues of the linear system associated with each equilibrium point. State the *type of* and the *stability of* each equilibrium point Verify that your results are consistent with the results of PyPlane / PhasePlane.mlapp.

7 Research paper review - 1

7.1 Select and article:

- Select an article from either
  Bulletin of Mathematical Biology (http://link.springer.com/journal/11538), abbreviation "B. Math. Biol."
  Ecology (http://www.esajournals.org/loi/ecol)
  - Double check that your article is from one of the above journals. Some publishers search engines will pull results from other journals. Often, there is an advanced search option to restrict where it searches from.
  - Double check that your article contains models that are ODEs. Other DE type models are ok (PDE, DDE, IDE, etc) but ODEs are easiest to work with and easiest to compare to our work in class.
- At the journal website search on one of the following: predator-prey, competing species, mutualism, allee effect, harvesting, logistic, mass-action, or other relevant term.
- Select your favorite article.
  The article most contain differential equations (ordinary, partial, delay, stochastics, etc).
- **Is your article from one of the journals above and does it have a model using differential equations?** If the answer to both questions is yes, proceed. If either is a no, try again?

7.2 Review of the article and formatting:

The body of review must begin with the following header information:
your last-name, your first-name
Research Paper Review # 1
Article:
A.B. Authorone and C.D. Authortwo. Title of article. Journal (Year) vol#:firstpage-lastpage. DOI:#
http://www.web-link-to-article *Selecting this should take me to the article. Double check that it works.*

Abstract:
Paste a copy of the abstract.

Review:

1. What is the problem being discussed?
2. What do these authors do that is new? Summarize the main results.
3. What are the open questions and/or what is their plan for the future?
4. Compare the mathematical model to one that we have studied in class. What terms are the same? What terms are new/different? For the terms that are different, why have they been added to this model? What process are they trying to describe?
5. What behavior, result, output is observed in this study and how does it compare to what we have discussed in class? There may be similarities but there is most probably differences. Reference as appropriate.

Length: The review length should be between 1 and 2 pages where a page is defined as follows: standard letter size page with dimensions 8.5 x 11, maximum 1in margins, single spacing between lines, and 11pt font. Make sure you adequately answer the questions; erring on the side of terseness is risky. At the same time, nonsense, filler or redundancy is also risky (see below).

Composition:

- You must write in complete and properly composed sentences. Bulleted lists are not acceptable. You must express yourself in proper sentences that fit together in proper paragraphs. If I have to struggle to parse incomplete, poorly composed, or run-on sentences, it will cost points.
- Proper spelling, grammar, punctuation are expected.
- Nonsense, filler or redundancy will cost points.
- Assume that your writing will be double checked by an instructor from ENGL 1302: First-Year Seminar in Rhetoric.

7.3 Do your own work

I understand that students consult each other on difficult mathematical assignments. Indeed, I support this collaboration and discussion if it leads to increased understanding such that ultimately each student is able to turn in their own work. However, this assignment must be a completely solo effort. Find your own paper and compose your own review. You may come to me for questions but do not discuss your work with fellow students. Do not plagerize from the article or any other resource. If you are not sure what constitutes plagerism, review the information at

- http://www.plagiarism.org/
- `https://smu.edu/studentlife/studenthandbook/PCL_05_HC.asp`

If there is even a hint of inappropriate collaboration, plagerism or dishonest work, at minimum the grade on the assignment will be a zero, at maximum the course grade will be zero, and honor code violation proceedings may be initiated. *Submissions may be submitted to SafeAssign on BlackBoard.*

7.4 How to submit the assignment

- Upload to Canvas/Gradescope as usual.

7.5 Pep talk

Note that it is possible to understand many (most) articles without checking every calculation and reproducing every step. You are not expected to verify the authors work beyond typical scientific criticism and reasonableness. However, you are expected to understand what are problem, goals and results.

7.6 THE Example

...meaning it should look like this (see next page). Please note that in previous semesters, and by previous I mean pre-generative AI, the questions were slightly different. So by *exactly* I am referring to layout, margins, font size and general quality of answers. However, the questions are slightly different and so the answers will be slightly different.

Carr, Thomas
Research Paper Review # 1

Article:
J.L. Mitchell and T.W. Carr, "Oscillations in an Intra-host Model of Plasmodium Falciparum Malaria Due to Cross-reactive Immune Response," B. Math. Biol. (2010) 72: 590-610. DOI:10.1007/s11538-009-9462-2. http://link.springer.com/article/10.1007/s11538-009-9462-2

Abstract:
We consider an intra-host model of malaria that allows for antigenic variation within a single species. More specifically, the host's immune response is compartmentalized into reactions to major and minor epitopes. We investigate the conditions that lead to transient oscillations, which correspond to recurrent clinical episodes of the diseases, and how a small delay in the activation of the immune response can lead to persistent oscillations. We find that the efficacies of the immune responses to the major and minor epitopes, defined in terms of rate constants, play a crucial role in determining when there will be transient oscillations. The delay necessary to excite persistent oscillations, the time duration between disease episodes and their severity are also expressed in terms of the immune response efficacies. In addition, we describe how the severity and duration of the oscillations depend upon the parasite propagation rates and the immune response efficacies.

Review:
1. What is the problem being discussed?
The authors consider an inhost model for malaria and, in particular, the interaction of the pathogen with the immune system. The immune system is modeled to account for both specific and non-specific responses to genetic variants determined by epitopes displayed on the parisitized red-blood cells.

2. What has been done before by this and/or other others?
The model consider was first proposed by Recker and Gupta in 2006 to account for antigenic variation of the malaria website. Antigenic variation is proposed to account for Malaria's ability to continually evade the immune system. The model does not consider the molecular details of the disease but takes a systems level approach by considering the interaction of the immune system with the genetic variants. Previous authors studied the transient oscillations that the model displays, which correspond to recurrent episodes of the disease by an infected individual.

3. What do these authors do that is new? Summarize the main results.
The authors introduce a delay from the time of infection with a new variant to the initiation of the immune response. Delays are well known to cause oscillations, which in this case correspond to recurrent episodes of the disease. The model is rescale to reduce the number of parameters and to identify the important non-dimensionalized parameters. A linear stability analysis determines parameter regimes where oscillations will occur. The authors define cross-reactive and variant specific efficacy terms that well describe how the immune system responds. The authors analyze the oscillations that can occur and determine how the amplitude and period depend on the parameters. An important result is that reducing the number of shared minor epitopes can make the host less susceptible to oscillations of the disease. On the other hand,a large generation rate and a strong cross-reactive immune response favor oscillations.

4. What tools do they use to address the problem, e.g., field studies, lab experiments, data analysis, mathematical model development, computer simulation, mathematical analysis? How do they use these tools?
This was a mathematical analysis. The main tools were nondimensionalization, linear stability analysis, the weakly-nonlinear perturbation method call multiple scales, and numerical simulations. The analysis techniques were used to determine how the parameters generate and determine the properties of oscillations. Numerical simulations were used to check the accuracy of the analysis as well as to study the system in

parameter regimes where the analysis does not apply.

5. Select one important figure and summarize what it describes and what is its significance.
Figure 4 shows the amplitude and the period of the oscillations as a function of the delay. As the delay is increase, the endemic steady state becomes unstable and both the amplitude and period increase monotonically with the delay. There are two different analytical approximations given by Eqs. (36) and (37) and then (38) and (39). The figure shows that the latter simpler approximation fits better for large n, where n is the number of shared variants.

6. What are the open questions and/or what is their plan for the future?
The authors made a number of assumptions that could be relaxed in future studies, e.g., they assumed large n and $\mu \neq 0$. Future work could investigate oscillations of the variants that are asynchronous.

8 Epidemiology

1. Consider the SIS-model where the birth rate is not equal to the death rate.

$$\begin{aligned} \frac{dS}{dt} &= bN - \frac{\beta}{N}SI + \gamma I - \mu S. \\ \frac{dI}{dt} &= \frac{\beta}{N}SI - (\gamma + \mu)I \end{aligned}$$

(a) Add the equations to obtain a differential equation for $N(t) = S(t) + I(t)$. Solve for $N(t)$. When does $N(t)$ increase/decrease?
(b) Follow the steps below to derive a logistic equation for the rescaled infectives $v(t)$.

- Given u and v below substitute for S and I. Note that N is a function of time so that when you substitute for S' and I' you need to use the product rule (or quotient rule depending upon your approach).

$$u(t) = \frac{S(t)}{N(t)} \ \ (S = Nu), \quad v(t) = \frac{I(t)}{N(t)}, (I = Nv)$$

- Use your answer in (a) to substitute for N' but do not substitute your solution for N. Keep the Ns in the equation and they should all cancel in the end.
- Your equations for u and v should be the following:

$$\begin{aligned} \frac{du}{dt} &= b(1-u) - \beta uv + \gamma v, \\ \frac{dv}{dt} &= \beta uv - (\gamma + b)v. \end{aligned}$$

- Note that by definition $u(t) + v(t) = 1$ or $u = 1 - v$. Substitute this into the equation for v, simplify, and you should have a logistic equation for v.

(c) Find a solution for $v(t)$. *We've done this before both in homework and notes.*
(d) Follow the steps below to define and analyze a definition for the basic reproduction number R_0.

- Find the steady states of the logistic equation for v.
- Determine the linear stability of the steady states for v, again using the logistic equation.
- Using the results of the linear stability analysis, define an R_0. Specifically, the non-zero steady state for v should be stable for $R_0 > 1$.
- You will find that R_0 is a function of β, γ and b. How do changes in the values of these constants affect the number of infectious individuals?

(e) As $t \to \infty$, $v(t) \to 0$ or v_∞ (disease free or endemic). Interpret these steady states in terms of the original variables S and I.

2. For the SIR model w/o births and deaths written in terms of *fractions* we found

$$\begin{aligned} \frac{du}{dt} &= -\beta uv, \qquad u(0) = u_0, \\ \frac{dv}{dt} &= \beta uv - \gamma v, \qquad v(0) = v_0, \end{aligned}$$

Note that we haven't written the rescaled equation for the removed class w because $w = 1 - u - v$. (a) Use twoodes.ipynb or PyPlane (or phaseplane.m or PhasePlane.mlapp) to sketch the phase portrait restricted for the positive quadrant for the case $R_0 > 1$ and $R_0 < 1$. Chose initial conditions in the

interval $u_0 = [0, 1]$ with $v_0 = 0$. Note, if for example you choose ICs $(u_0, v_0) = (0.8, 0)$ that implies $w_0 = 0.2$. But we don't care about w_0 so don't worry about it. The point being that $u_0 + v_0$ does not necessarily equal to 1 because w_0 absorbs the difference.
(b) When $R_0 > 1$ the trajectory reaches a maximum such that there is a peak value of v, the fraction who are infectious. By examining the equation $dv/du = g/f$, determine the value of u where the epidemic reaches its peak? Relate your answer to the definition of R_0.
(c) To have a maximum in v, what condition is required for the initial value of $u = u_0$?
(d) Based on the phase portrait sketches observe that that $u_\infty = \lim_{t\to\infty} u(t)$ *decreases* as u_0 increases. Can you explain why this is so from a epidemiological point of view?

3. The model below considers the effect of vaccination where $V(t)$ represents the number of vaccinated or removed individuals.

$$\begin{aligned} \frac{dS}{dt} &= \mu N - \frac{\beta}{N} SI - (\mu + \nu)S, \qquad S(0) = S_0, \\ \frac{dI}{dt} &= \frac{\beta}{N} SI - (\mu + \gamma)I, \qquad I(0) = I_0, \\ \frac{dV}{dt} &= \gamma I + \nu S - \mu V, \qquad V(0) = V_0, \end{aligned} \tag{1}$$

where $S + I + V = N$ and all variables are class *numbers*. Notice that $dN/dt = 0$ and so it suffices to consider the equations for only S and I.
(a) Describe how this model of vaccination differs from that considered in class. "Physically" how is the vaccination process different in each case?
(b) Rescale to consider equations for the class fractions $u = S/N$, $v = I/N$ and $w = V/N$.
(c) Determine the endemic equilibrium and and suggest a probable definition for R_0 (it will depend on ν). If you like (but not required), you can do the linear stability of the system of 3 equations to confirm.
(d) Identify an R_0 and discuss how it depends on the vaccination. rate.

9 Cubic nullclines

1. A variation of the Van der Pol equation that we considered in class is

$$\begin{aligned} u' &= v - a, \qquad a > 0, \\ v' &= -2(v^3 - 3v) - u, \end{aligned}$$

where the most important change is the introduction of the parameter a. The other constants and numbers have been chosen for convenience.
(a) Find the steady state and evaluate it's linear stability. Confirm the following:

- For $2/\sqrt{3} < a$, the steady state is a *stable node*.
- For $1 < a < 2/\sqrt{3}$, the steady state is a *stable focus*.
- For $\sqrt{2/3} < a < 1$, the steady state is an *unstable focus*.
- For $0 \leq a < \sqrt{2/3}$, the steady state is an *unstable node*.

Note that the *bifurcation point* is the value of a where there is a change in stability. Here, the bifurcation point is $a = 1$ when the system changes between a stable and unstable focus. When the change in stability is for a focus, it is called *Hopf bifurcation* because the new stable object is typically a limit cycle.
(b) Use *vanderpo.ipynb / vanderpolhmwk.m* to plot the phase plane for $a < 1$ and $a > 1$. What is the limit set (steady state vs. limit cycle) for each case? *You do not have to make print your results for (b). Just answer the questions above.*
(c) Plot one trajectory in the phase plane for the following specific values of a:
$a = 0.99640000$, $a = 0.99645000$, $a = 0.99645151$, $a = 0.99645152$, $a = 0.99650000$.
Make a sketch of what you observe in each case and describe the results. *You do not have to make a print of your results for (c). Some sketches will do.*

2. Consider the Fitzhumo-Nagumo equations for the case $c = 1$. In class we used the injected current z as a parameter and observed the change in type of the steady-state and the dynamics of the system. Here we will consider the case of $z = 0$, but change the other two parameters a and b. Use *fitzhugh.ipynb / fitzhugh.m* to numerically determine the solutions and, in particular, the steady states as a function of the changing parameter.
(a) First resketch the cubic and linear nullcline and examine what happens to the intersections (steady states) as you vary a and b. This will guide you in when using matlab in parts (b) and (c).
(b) For $c = 1$, $z = 0$ and $b = 0.5$, vary a from 1 to -1. What happens to the steady state (type and stability)? If the steady state is unstable, where do trajectories go, i.e., what is the stable limit set of the system? Sketch a bifurcation diagram; it doesn't have to be quantitatively correct but, rather, qualitatively represent what is observed.
(c) For $c = 1$, $z = 0$ and $a = 1$, vary b from 0.5 to 4. What happens to the number of steady states? What are the types of steady states? Sketch a bifurcation diagram.

3. The model below is a simplification of respiration in bacterial cultures (Fairen and Velarde, J. Math. Bio. 8 (1979) p147). u represents the concentration of oxygen and v represents the concentration of nutrient. The bacteria use oxygen to burn the nutrient for energy.

$$\begin{aligned} u' &= B - u - \frac{uv}{1 + qu^2} \\ v' &= A - \frac{uv}{1 + qu^2} \end{aligned}$$

Each has a constant source term given by B and A. Oxygen can decay out of the system, while it is assumed that the only way the nutrient is removed is by consumption. The mass-action term represents

the consumption process that uses oxygen to burn the nutrient, hence, reducing the amount of each. The denominator acts to reduce the burn rate at high concentrations of oxygen. The effect is referred to as "inhibition by excess of oxygen" and was investigated as a source for experimentally observed oscillations in the oxygen and nutrient concentrations. (The paper is quite old by biological standards and I have not investigated whether the biological mechanisms built into this model are still relevant. Nevertheless, we will use it as an example).

(a) Find the steady state. What condition must be imposed on A and B for the state state to be physically valid, which in this case means both u and v must be positive.

(b) Program these equations into *vanderpol.ipynb / vanderpolhmwk.m.* For $A = 11$ and $q = 0.5$, increase B from 11 to 23. Describe how the behavior of the system changes commenting both on the phase plane and the solutions as a function of time. Note, you will have to continually readjust the window size so that all significant trajectories can be observe.

(c) Change the value of q to investigate the effect of the inhibition term. Can q control whether or not oscillations occur in the system (discuss)?

10 Research paper review - 2

- Select an article from either
  Bulletin of Mathematical Biology (http://link.springer.com/journal/11538), abbreviation "Bulletin Math. Biol."
  Journal of Mathematical Biology (http://link.springer.com/journal/285), abbreviation "J. Math. Biol."
  Mathematical Biosciences (http://www.journals.elsevier.com/mathematical-biosciences/), abbreviation "Mathematical Biosciences."
- At the journal website, select a paper dealing with disease dynamics either epidemiology (population level), immunology (within the host) (either could be Covid related), or neuron dynamics/oscillations/spiking.
- Repeat the assignment of rpr-1 with this new paper.

11 Biochemical Oscillations

The Goodwin Oscillator requires a large degree of cooperativity ($p > 8$) to exhibit oscillations. In 1982, Bliss et al (R. Bliss, P. Painter and A. Marr, " Role of feedback inhibition in stabilizing the classical operon,", J. Theor. Biol. 97:177-193, 2002) proposed the following modified oscillator with a $p = 1$.

$$\frac{dx_1}{dt} = \frac{a}{1 + x_3} - b_1 x_1, \tag{2}$$

$$\frac{dx_2}{dt} = b_1 x_1 - b_2 x_2, \tag{3}$$

$$\frac{dx_3}{dt} = b_2 x_2 - \frac{c x_3}{K + x_3}. \tag{4}$$

(a) Describe both mathematically and physically what is different about this set of equations compared to the Goodwin oscillator.
(b) A completely general analysis of these equations is difficult so we will make the following simplifying assumptions: $K = 1$. $b_1 = b_2 = b$. First solve for the steady state.
(We are going to also make the assumption that $a = c\left(\sqrt{\frac{c}{b}} - 1\right)$ but don't make that substitution now.)
(c) Perform a linear stability analysis:

- Derive the characteristic equation for λ.
- Make the substitution for $x_3 = a/c$ (from part (b)).
- Also make the simplifying assumption that $a = c\left(\sqrt{\frac{c}{b}} - 1\right)$. Why? Because it makes the algebra nice, that's why.
- You will get the characteristic equation:

$$(\lambda + stuff)^3 + morestuff = 0$$

- Show that a Hopf bifurcation occurs when $a = 8c$ (and $b = c/81$). You will get to enjoy using what you learned about the roots of unity.

(d) Create a python / matlab code to simulate these equations and choose parameter values to demonstrate a stable steady state before the Hopf bifurcation and stable oscillations after the Hopf bifurcation. Note, a template code is not provided so you will have to modify one of the other pythong.ipynb / matlab.m files. Also, you are going to have to experiment to find parameter values for "before" and "after." Use the conditions above to guide you.