

The following rules apply:

- **This exam is due on November 04 at 3:30.** Except for this first problem, please use separate sheets of paper to write up your solutions and staple them to the exam when you hand it in. Please only include well written finalized answers. I will not look at scrap paper.
- **You cannot use a computer to assist you in this exam.** You cannot use the internet, external software such as Mathematica and Matlab, your phone etc. You can use your notes and textbook.
- **You cannot collaborate.** You cannot work with other students or talk about this exam with other students.
- **If you use a “fundamental theorem” you must indicate this and explain why the theorem may be applied.**
- **Organize your work,** in a reasonably neat and coherent way, in the space provided. Work scattered all over the page without a clear ordering will receive very little credit.
- **Short answer questions:** Questions labeled as “Short Answer” can be answered by simply writing an equation or a sentence or appropriately drawing a figure. No calculations are necessary or expected for these problems.
- **Unless the question is specified as short answer, mysterious or unsupported answers might not receive full credit.** An incorrect answer supported by substantially correct calculations and explanations might still receive partial credit.

Problem	Points	Score
1	15	
2	25	
3	25	
4	35	
Total:	100	

Do not write in the table to the right.

Reference Page

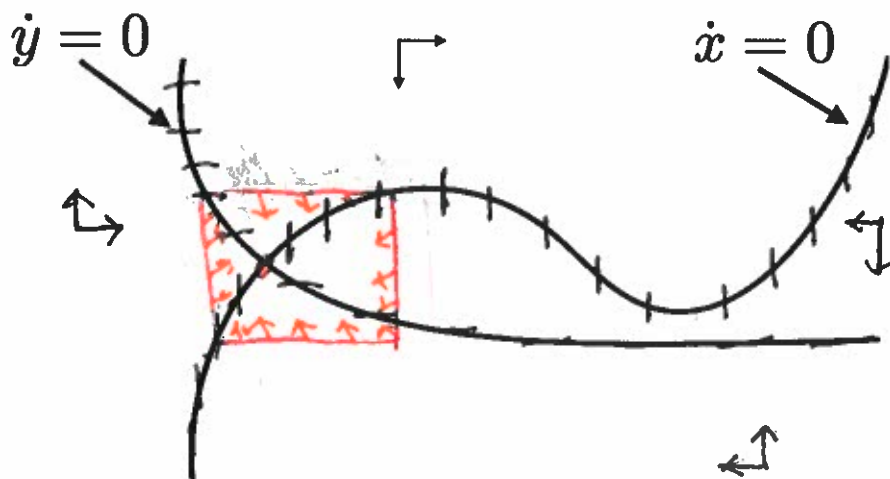


1. (15 points) The figure shown below contains the two nullclines of the system

$$\begin{cases} \dot{x} = f(x, y) \\ \dot{y} = g(x, y) \end{cases}$$

In one of the regions partitioned off by the nullclines, the overall direction of the vector field is indicated by two arrows.

- (2 points) In the figure, label all fixed points.
- (3 points) For each of the regions in the phase plane separated by the nullclines, indicate the overall direction of the vector field.
- (5 points) Construct a trapping region for this system.
- (5 points) What do you need to assume about the fixed point(s) in order to conclude the existence of a limit cycle?



(d) Need to assume that the fixed point is unstable.

2. (25 points) Recall, the differential equations for the dynamics of the nodes and edges for the standard *SIS* model are given by

$$[\dot{S}] = -\beta[SI] + \alpha[I]$$

$$[\dot{I}] = \beta[SI] - \alpha[I]$$

$$[\dot{SS}] = -2\beta[SSI] + 2\alpha[SI]$$

$$[\dot{SI}] = \beta([SSI] - [ISI] - [SI]) + \alpha([II] - [SI])$$

$$[\dot{II}] = 2\beta([ISI] + [IS]) - 2\alpha[II]$$

- (a) (5 points) Suppose susceptible nodes connected to infected individuals can break connections to infected individuals and add a new connection to a random susceptible node at a rate $w > 0$. Modify the above differential equations to account for this reconnection process.
- (b) (5 points) Assuming that $[S] + [I]$ and $[SS] + 2[SI] + [II]$ are constants in time and $[SI] = \langle k \rangle [S] - [SS]$, reduce your model to two differential equations in $[S]$ and $[SS]$.
- (c) (5 points) Using the standard moment closure approximation for triple links, derive a closed system of differential equations for $[S]$ and $[SS]$.
- (d) (10 points) For the system of differential equations you have derived, determine the fixed points, analyze their stability, and sketch phase portraits that illustrate all of the qualitatively different cases that can occur.

Exam #2

#2

$$(a) \quad [\dot{S}] = -\beta [SI] + \alpha [I]$$

$$[\dot{I}] = \beta [SI] - \alpha [I]$$

$$[\dot{SS}] = -2\beta [SSI] + 2(\alpha + w) [SI]$$

$$[\dot{SI}] = \beta ([SSI] - [ISI] - [SEI]) + \alpha ([II] - [SEI]) - w [SEI]$$

$$[\dot{II}] = 2\beta ([ISI] + [IS]) - 2\alpha [II]$$

(b) The equations for $[S]$ and $[SS]$ are given by

$$[\dot{S}] = -\beta (\langle k \rangle [S] - [SS]) + \alpha (N - [S])$$

$$[\dot{SS}] = -2\beta [SSI] + 2(\alpha + w) (\langle k \rangle [S] - [SS])$$

(c) Using the moment closure we have that

$$[\dot{S}] = -\beta (\langle k \rangle [S] - [SS]) + \alpha (N - [S])$$

$$[\dot{SS}] = -2\beta \frac{(\langle k \rangle - 1) [SS][SI]}{\langle k \rangle [S]} + 2(\alpha + w) (\langle k \rangle [S] - [SS])$$

$$\Rightarrow [\dot{S}] = -\beta (\langle k \rangle [S] - [SS]) + \alpha (N - [S])$$

$$[\dot{SS}] = -2\beta \frac{(\langle k \rangle - 1) [SS] (\langle k \rangle [S] - [SS])}{\langle k \rangle [S]} + 2(\alpha + w) (\langle k \rangle [S] - [SS])$$

(d). Letting $x = [S]/N$, $y = [SS]/N\langle k \rangle$, and $\tau = \alpha t$ it follows that

$$\frac{dx}{d\tau} = -\beta \frac{\langle k \rangle}{\alpha} (x - y) + (1 - x)$$

$$\frac{dy}{d\tau} = -2\beta \frac{(\langle k \rangle - 1)}{\alpha} y \frac{(x - y)}{x} + 2(1 + \frac{w}{\alpha})(x - y)$$

Letting $R_0 = \beta \langle k \rangle / \alpha$, $K = \langle k^2 \rangle - 1 / \langle k \rangle$, and $\gamma = \omega / \alpha$ it follows that:

$$\frac{dx}{d\tau} = -R_0(x-y) + 1 - x,$$

$$\frac{dy}{d\tau} = -2R_0 K \frac{y}{x} (x-y) + 2(1+\gamma)(x-y).$$

The nullclines are given by:

$$1. y = \left(1 + \frac{1}{R_0}\right)x - \frac{1}{R_0} \left(\frac{dx}{d\tau} = 0\right) \quad (N1)$$

$$2. y = x \left(\frac{dy}{d\tau} = 0\right) \quad (N2)$$

$$3. y = \frac{(1+\gamma)x}{R_0 K} \left(\frac{dy}{d\tau} = 0\right) \quad (N3)$$

One fixed point is given by

$$(x_1^*, y_1^*) = (1, 1)$$

The other satisfies

$$\frac{(1+\gamma)x}{R_0 K} = \left(1 + \frac{1}{R_0}\right)x - \frac{1}{R_0}$$

$$\Rightarrow (1+\gamma)x = (R_0 K + K)x - K$$

$$\Rightarrow (1+\gamma - K(R_0+1))x = -K$$

$$\Rightarrow x_2^* = \frac{K}{K(R_0+1) - 1 - \gamma}$$

$$y_2^* = \frac{1+\gamma}{R_0(K(R_0+1) - 1 - \gamma)}$$

The Jacobian is given by:

$$J(x, y) = \begin{bmatrix} -R_0 - 1 & R_0 \\ -2R_0 K \frac{y^2}{x^2} + 2(1+\gamma) & -2R_0 K K \left(1 - \frac{3z}{x}\right) - 2(1+\gamma) \end{bmatrix}$$

Therefore,

$$J(1, 1) = \begin{bmatrix} -R_0 - 1 & R_0 \\ -2R_0 K + 2(1+\gamma) & 2R_0 K - 2(1+\gamma) \end{bmatrix}$$

Now,

$$\text{Tr}(J(1, 1)) = -R_0 - 1 + 2R_0 K - 2(1+\gamma)$$

$$\begin{aligned} \text{Det}(J(1, 1)) &= 2(R_0 + 1)(1+\gamma) - R_0 K + 2(R_0 K - (1+\gamma)) \\ &= 2(R_0 K - (1+\gamma))(1 - (1+\gamma)(1+R_0)) \\ &= 2(R_0 K - (1+\gamma))(-\gamma - R_0 - \gamma R_0) \end{aligned}$$

Therefore, $(1, 1)$ is stable if

$$R_0 K - (1+\gamma) < 0$$

$$\Rightarrow R_0 K < (1+\gamma)$$

$$\Rightarrow \frac{R_0 K}{1+\gamma} < 1,$$

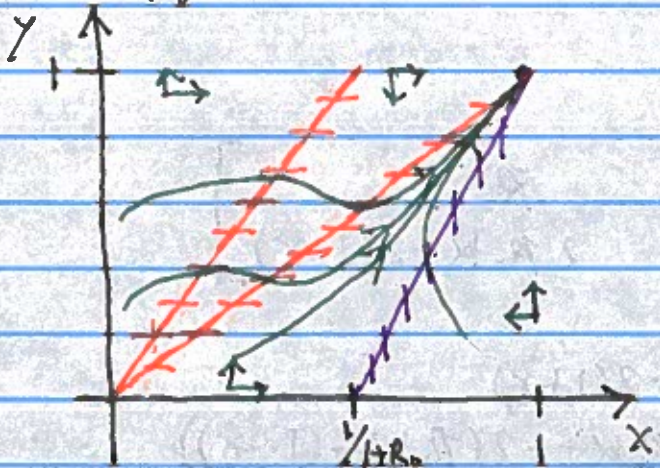
Since this will imply $\text{Tr}(J(1, 1)) < 0$ and $\text{Det}(J(1, 1)) > 0$.

Note, this condition is equivalent to the statement that $(N3)$ lies above $(N4)$.

We now sketch the phase portraits:

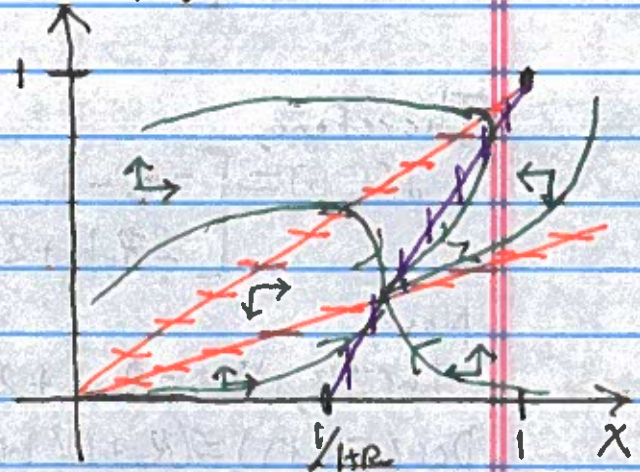
Case 1:

$$\frac{R_0 k}{1+\gamma} < 1$$



Case 2:

$$\frac{R_0 k}{1+\gamma} > 1$$



3. (25 points) Consider the following *SIS* model with two strains:

$$\begin{aligned}\dot{S} &= -\beta_1 I_1 S - \beta_2 I_2 S + \alpha_1 I_1 + \alpha_2 I_2, \\ \dot{I}_1 &= \beta_1 I_1 S - \alpha_1 I_1 + \beta_1 I_1 I_2, \\ \dot{I}_2 &= \beta_2 I_2 S - \alpha_2 I_2 - \beta_1 I_1 I_2,\end{aligned}$$

where S denotes the susceptible population, I_1, I_2 denote infectious individuals with the different strains, and $\beta_1, \beta_2, \alpha_1, \alpha_2$ are positive parameters.

- (10 points) Using the next generation approach, compute the basic reproduction number for this model.
- (5 points) Show that the total population $N = S + I_1 + I_2$ is conserved in this system and use this to reduce the system to differential equations for I_1 and I_2 by eliminating the dependence on S .
- (5 points) For the reduced system determine the fixed points and analyze their stability.
- (5 points) For the reduced system sketch all possible qualitatively different phase portraits that can occur. Interpret your results in practical terms.

#3

The infected compartments are I_1, I_2 and the disease free equilibrium is $(N, 0, 0)$, where N is the total population. The reduced system is therefore

$$\dot{I}_1 = \beta_1 I_1 S - \alpha_1 I_1 + \beta_1 I_1 I_2$$

$$\dot{I}_2 = \beta_2 I_2 S - \alpha_2 I_2 - \beta_1 I_1 I_2$$

With Jacobian:

$$J = \begin{bmatrix} \beta_1 S - \alpha_1 + \beta_1 I_2 & \beta_1 I_1 \\ -\beta_1 I_2 & \beta_2 S - \alpha_2 - \beta_1 I_1 \end{bmatrix}$$

$$\Rightarrow J(N, 0, 0) = \begin{bmatrix} \beta_1 N - \alpha_1 & 0 \\ 0 & \beta_2 N - \alpha_2 \end{bmatrix} = \begin{bmatrix} \beta_1 N & 0 \\ 0 & \beta_2 N \end{bmatrix} - \begin{bmatrix} \alpha_1 & 0 \\ 0 & \alpha_2 \end{bmatrix}$$

Consequently:

$$R_0 = \rho \left(\begin{bmatrix} \beta_1 N / \alpha_1 & 0 \\ 0 & \beta_2 N / \alpha_2 \end{bmatrix} \right)$$
$$= \max \{ \beta_1 N / \alpha_1, \beta_2 N / \alpha_2 \}$$

$\dot{S} + \dot{I}_1 + \dot{I}_2 = 0$ and thus this system is conserved. We therefore can analyze the reduced system:

$$\dot{I}_1 = \beta_1 I_1 (N - I_1 - I_2) - \alpha_1 I_1 + \beta_1 I_1 I_2$$

$$\dot{I}_2 = \beta_2 I_2 (N - I_1 - I_2) - \alpha_2 I_2 - \beta_1 I_1 I_2$$

Letting $x = I_1/N, y = I_2/N, \tau = \alpha_1 t$ it follows that:

$$\frac{dx}{d\tau} = R_1 x(1-x-y) - x + R_1 xy,$$

$$\frac{dy}{d\tau} = R_2 y(1-x-y) - \alpha y - R_1 xy,$$

where

$$R_1 = \frac{\beta_1 N}{\alpha_1}, \quad R_2 = \frac{\beta_2 N}{\alpha_2}, \quad \alpha = \frac{\alpha_2}{\alpha_1}$$

Therefore,

$$\frac{dx}{dt} = x(R_1(1-x) - 1)$$

$$\frac{dy}{dt} = y(R_2(1-x-y) - \alpha - R_1x)$$

The nullclines are therefore,

$$N1: x = 0 \quad \left(\frac{dx}{dt} = 0\right)$$

$$N2: x = 1 - 1/R_1 \quad \left(\frac{dx}{dt} = 0\right)$$

$$N3: y = 0 \quad \left(\frac{dy}{dt} = 0\right)$$

$$N4: y = -(1 + R_1/R_2)x + 1 - \alpha/R_2$$

The fixed points are therefore,

$$FP1: (0, 0)$$

$$FP2: (0, 1 - \alpha/R_2)$$

$$FP3: (1 - 1/R_1, 0)$$

$$FP4: (1 - 1/R_1, 1/R_1 + 1/R_2 - R_1/R_2 - \alpha/R_2)$$
$$= (1 - 1/R_1, R_2 + R_1 - R_1 - \alpha R_1/R_2)$$

The Jacobian for this system is given by!

$$J(x, y) = \begin{bmatrix} R_1 - 2R_1x - 1 & 0 \\ * & -2R_2y + R_2(1-x) - \alpha - R_1x \end{bmatrix}$$

Therefore,

$$J(0, 0) = \begin{bmatrix} R_1 + 1 & 0 \\ * & R_2 - \alpha \end{bmatrix}$$

which is stable if $R_1 - 1 < 0$ and $R_2 - \alpha < 0$.

$$J(0, 1 - \alpha/R_2) = \begin{bmatrix} R_1 - 1 & 0 \\ * & \alpha - R_2 \end{bmatrix}$$

which is stable if $R_1 < 1$ and $R_2 > \alpha$.

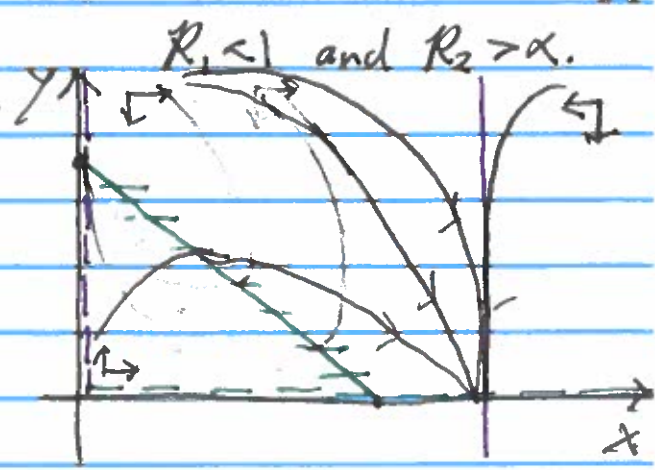
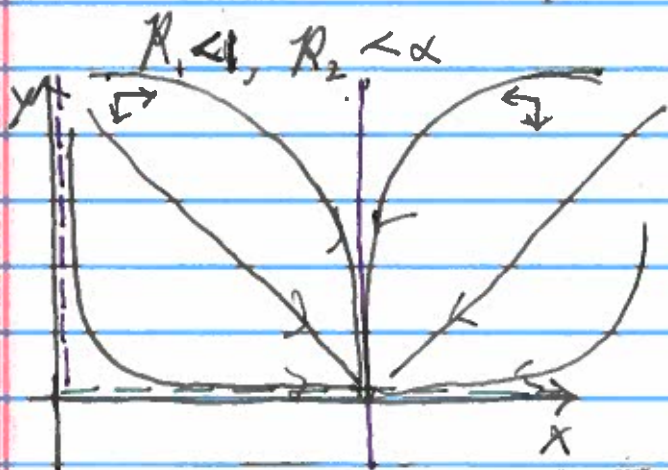
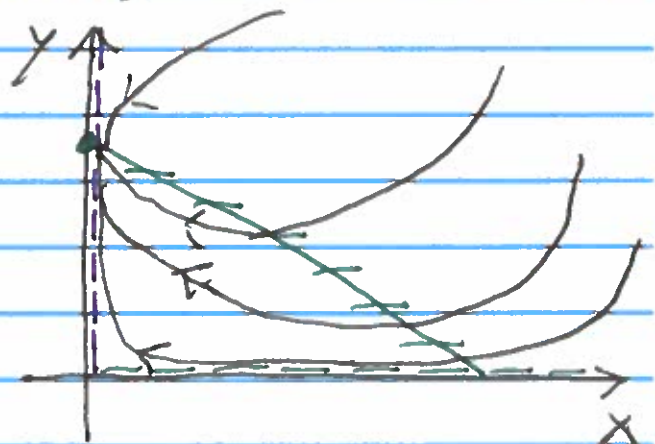
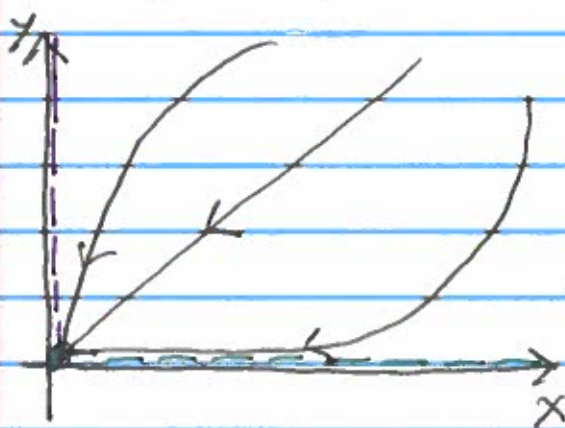
$$J(1 - 1/R_1, 0) = \begin{bmatrix} 1 - R_1 & 0 \\ * & R_2 - \alpha \end{bmatrix}$$

which is stable if $R_1 > 1$ and $R_2 < \alpha$.

$$J(1 - 1/R_1, 1/R_1 + 1/R_2 - R_1/R_2 - \alpha/R_2) = \begin{bmatrix} 1 - R_1 & 0 \\ * & -R_2/R_1 - 1 + R_1 - \alpha \end{bmatrix}$$

which is stable if $1 - R_1 < 0$ and $-R_2/R_1 - \alpha < 1 - R_1$
 $\Rightarrow 1 - R_1 < 0 \quad R_2/R_1 + \alpha > R_1 - 1$

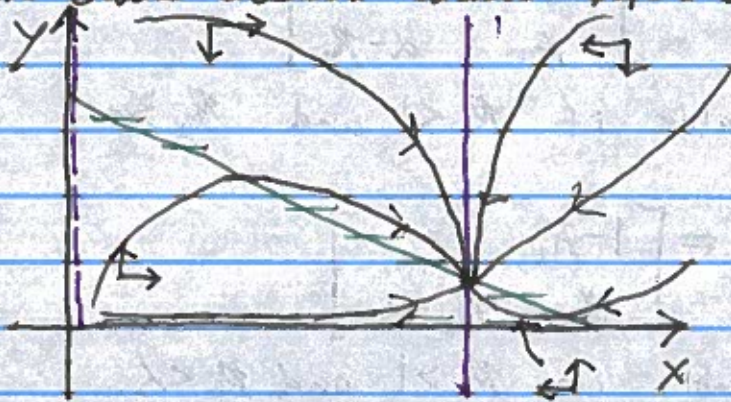
The phase portraits are given by



$R_1 > 1, R_2 < \alpha$

$R_1 > 1, R_1 - R_2/R_1 - \alpha > 1, R_2 > \alpha$

The final case occurs when $R_1 > 1$ and $R_2 / R_1 + \alpha > R_1 - 1$



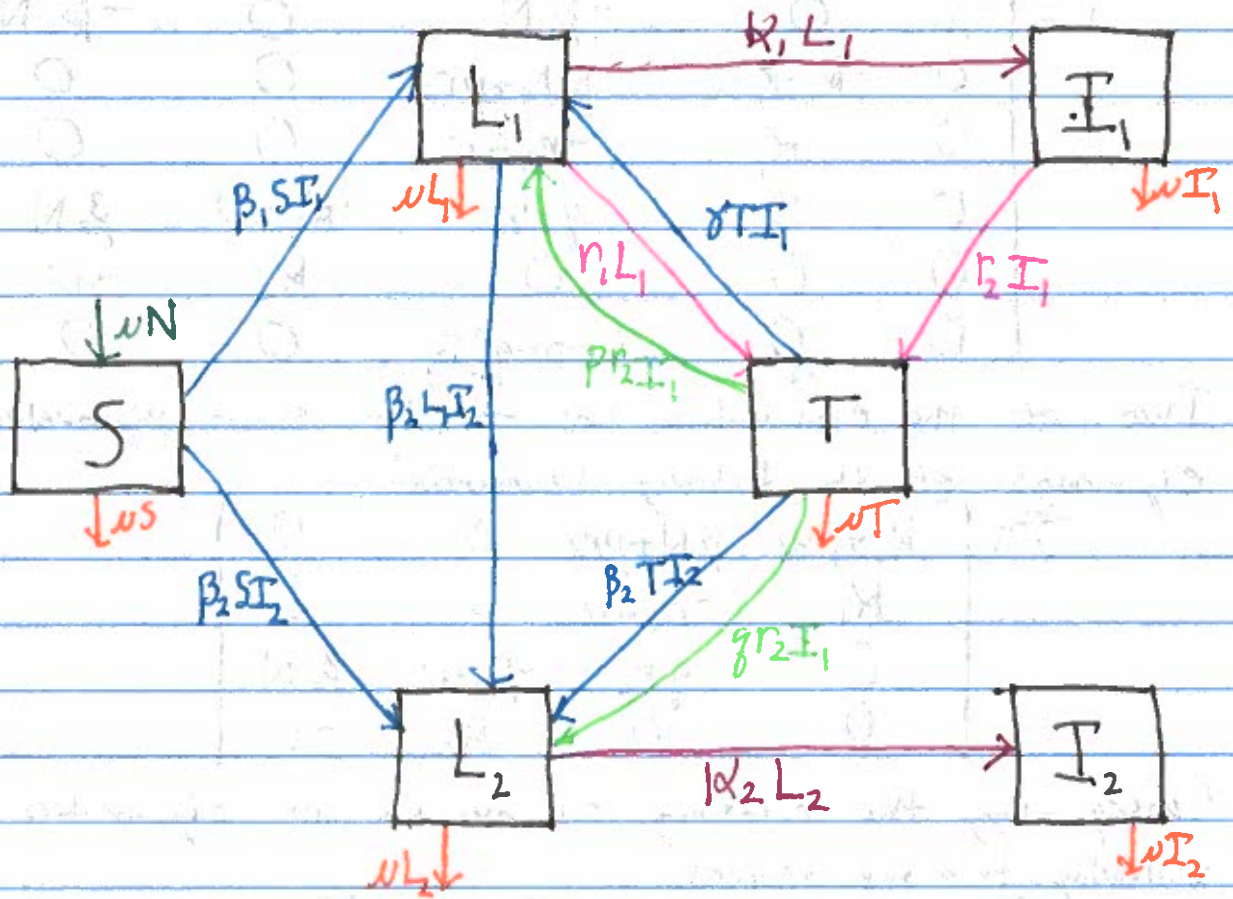
4. (35 points) Treatment of tuberculosis (TB) may take as long as twelve months, and a lack of compliance with these treatments may lead to the development of an antibiotic resistant strain of TB. The following is a model for the spread of tuberculosis with a resistant strain:

$$\begin{aligned}\dot{S} &= \mu N - \beta_1 S I_1 - \beta_2 S I_2 - \mu S, \\ \dot{L}_1 &= \beta_1 S I_1 - \kappa_1 L_1 - r_1 L_1 + p r_2 I_1 + \gamma T I_1 - \beta_2 L_1 I_2 - \mu L_1, \\ \dot{I}_1 &= \kappa_1 L_1 - r_2 I_1 - \mu I_1, \\ \dot{L}_2 &= q r_2 I_1 - \kappa_2 L_2 + \beta_2 (S + L_1 + T) I_2 - \mu L_2, \\ \dot{I}_2 &= \kappa_2 L_2 - \mu I_2, \\ \dot{T} &= r_1 L_1 + (1 - p - q) r_2 I_1 - \gamma T I_1 - \beta_2 T I_2 - \mu T,\end{aligned}$$

where S denotes the susceptible population, L_1, I_1 denote the latent and infectious individuals with the standard strain, L_2, I_2 denote the latent and infectious individuals with the resistant strain, and T denotes the individuals being treated for the disease. The parameters $\mu, \beta_1, \beta_2, \kappa_1, \kappa_2, r_1, r_2, p, q$ and γ are assumed to be positive and $N > 0$ denotes the constant population size.

- (5 points) **Short Answer:** Draw a flow diagram for this model. Carefully indicate all possible flows between compartments.
- (5 points) **Short Answer:** Briefly interpret all of the parameters in this problem in practical terms.
- (5 points) **Short Answer:** Determine the disease free equilibrium for this problem.
- (5 points) Calculate J^* , the Jacobian matrix evaluated at the disease free equilibrium.
- (10 points) Determine the eigenvalues of J^* . **Hint:** Use the structure of this matrix to simplify this calculation.
- (5 points) Determine conditions under which the disease free equilibrium is a stable fixed point.

#4



The parameters can be interpreted as follows!

- $\nu \sim$ birth/death rate
- $\beta_i \sim$ force of infection for i -th strain
- $\kappa_i \sim$ transition rate to being infectious for i -th strain.
- r_1, r_2 - treatment rates from latent and infectious stages for the first strain.
- γ force of infection into strain 1 for patients being treated.
- p, γ rate of relapse in treatment into strain one and two respectively.

The disease free equilibrium is clearly $(N, 0, 0, 0, 0, 0)$.

The Jacobian at the disease free state is given by:

$$J = \begin{bmatrix} -\nu & 0 & -\beta_1 N & 0 & -\beta_2 N & 0 \\ 0 & -k_1 - r_1 - \nu & \beta_1 N + p r_2 & 0 & 0 & 0 \\ 0 & k_1 & -r_2 - \nu & 0 & 0 & 0 \\ 0 & 0 & q r_2 & -k_2 - \nu & \beta_2 N & 0 \\ 0 & 0 & 0 & k_2 & -\nu & 0 \\ 0 & 0 & (1-p-q)r_2 & 0 & 0 & -\nu \end{bmatrix}$$

Two of the eigenvalues are $-\nu$. The other eigenvalues are eigenvalues of the following submatrix:

$$\tilde{J} = \begin{bmatrix} -k_1 - r_1 - \nu & \beta_1 N + p r_2 & 0 & 0 \\ k_1 & -r_2 - \nu & 0 & 0 \\ 0 & q r_2 & -k_2 - \nu & \beta_2 N \\ 0 & 0 & k_2 & -\nu \end{bmatrix}$$

Consequently, the remaining eigenvalues are eigenvalues of the following two submatrices:

$$\tilde{J}_1 = \begin{bmatrix} -k_1 - r_1 - \nu & \beta_1 N + p r_2 \\ k_1 & -r_2 - \nu \end{bmatrix}, \quad \tilde{J}_2 = \begin{bmatrix} -k_2 - \nu & \beta_2 N \\ k_2 & -\nu \end{bmatrix}$$

Therefore, the disease free equilibrium is stable if

$$\begin{cases} (k_1 + r_1 + \nu)(r_2 + \nu) - k_1(\beta_1 N + p r_2) > 0 \\ (k_2 + \nu)\nu - \beta_2 N k_2 > 0 \end{cases}$$