All answers need to be written in a clear, succinct manner. Write a brief paragraph summarizing the answers to the problems with each answer clearly stated in a sentence. Supporting graphs should be provided when asked for, but you should not include printouts of spreadsheets. You can create an appendix to a problem, but that should only include significant material to back up your answers.

1. a. In this problem, you will repeat many of the calculations that we did in class and write summary paragraphs about the modeling. Consider the Center for Disease Control (CDC) data for the Type A strain in the 2006-2007 flu season. For this year, the CDC analyzed 179,268 specimens. The majority of the flu cases were influenza A with the subtypes H1 or H3.

The mathematical model that we shall fit to the CDC data is the classic SIR model with constant population $N = S_n + I_n + R_n = 179,268$, which in this case assumes no births or deaths into the population. The model is given by the equations:

$$\begin{aligned} S_{n+1} &= S_n - \frac{\beta}{N} S_n I_n, \\ I_{n+1} &= I_n(1-\gamma) + \frac{\beta}{N} S_n I_n, \end{aligned}$$

where you fit the best parameters β and γ to the CDC data below.

n (wk)	Infected	n (wk)	Infected	n (wk)	Infected
0	13	17	760	34	34
1	26	18	1172	35	12
2	37	19	1491	36	10
3	37	20	1544	37	13
4	46	21	1388	38	2
5	75	22	1006	39	10
6	93	23	751	40	8
7	74	24	569	41	9
8	110	25	491	42	8
9	111	26	322	43	14
10	145	27	228	44	14
11	306	28	158	45	14
12	392	29	138	46	10
13	366	30	86	47	21
14	240	31	51	48	13
15	293	32	43	-	-
16	420	33	39	-	-

Assuming that $I_0 = 13$ (and $R_0 = 0$), find the best fitting (LSSE) parameters, β and γ, to the data. Also, report the sum of square errors between the model fit of the infecteds, I_n, and the data from the table above. Give the model prediction for people infected with influenza at $n = 20$ and find the percent error at that time from the actual CDC data. (Assume that the CDC value is the best value for the percent error, as we are testing the model.) Find when the

maximum number of infecteds occur and what value I_n obtains at that time. Create a graph showing the CDC data and your best fitting model. Describe how well the model fits the actual data.

b. The parameter γ is the probability that an infected person recovers (enters class R of the SIR model). Thus, the ratio $\frac{1}{\gamma}$ is the average length of the infectious period of the disease. Find this period in units of days.

Epidemiologists often examine what is called the *basic reproduction ratio* given by

$$R_0 = \frac{\beta}{\gamma},$$

which provides a measure of how rapidly a disease will spread and how much of the population will be affected by a particular disease. Use your values of β and γ to find R_0.

To determine the impact of a particular flu season, we want to know the total number of individuals who were infected by the influenza virus. Based on the model, estimate the number of Influenza A cases for the 2006-2007 flu season. What percent of the original population ultimately got this strain of influenza?

c. In class we discussed three methods of controlling the flu: vaccines, isolation or education, and tamiflu. Suppose that we vaccinate 5% of the population before the beginning of the flu season (and assume that the vaccination is 100% effective). Describe how you would do this in the model. Simulate the model. Give the model prediction for people infected with influenza at $n = 20$.

Find when the maximum number of infecteds occur with vaccination and what value I_n obtains at that time. Compare this to your results for the model from Part a. How many fewer individuals end up getting the flu for this flu season based on this simulation? (Give the number and percent infected.)

d. Suppose we isolate or educate the public to better hygienic practices. Assume that this lowers the contact rate by 5%. Describe how you would do this in the model. Simulate the model. Give the model prediction for people infected with influenza at $n = 20$.

Find when the maximum number of infecteds occur with this behavioral modification and what value I_n obtains at that time. Compare this to your results for the model from Part a. How many fewer individuals end up getting the flu for this flu season based on this simulation? (Give the number and percent infected.)

e. Oseltamivir or Tamiflu is a drug that shortens the symptoms of flu for many people. Assume that this drug shortens the length of the period of infectivity of the infected individuals by 5%. Describe how you would do this in the model. Simulate the model. Give the model prediction for people infected with influenza at $n = 20$.

Find when the maximum number of infecteds occur with this behavioral modification and what value I_n obtains at that time. Compare this to your results for the model from Part a. How many fewer individuals end up getting the flu for this flu season based on this simulation? (Give the number and percent infected.)

f. Create a graph overlaying the data, the original model, and the three different treatments simulated in Parts c-e. Describe what you observe in your graphs both quantitatively and qualitatively. Describe which approach (if any) is the best and discuss the advantages and disadvantages of the different approaches. Include a discussion of the practicality and financial burden of each of these approaches.

g. Find the equilibria for these models. Linearize the model about the equilibria and find the eigenvalues. Use this information to determine what changes in each of the three treatments will prevent the outbreak of this strain of flu according to the model. (Bifurcation analysis)

h. Write a paragraph discussing the strengths and weaknesses of this model. (Give at least two advantages and two disadvantages.) Discuss the assumptions that need to be made and how they affect the output of the model. What are some of the most significant changes that you believe should be incorporated into the model, and how would you do this? Use information from the CDC report at http://www.cdc.gov/flu/weekly/weeklyarchives2006-2007/06-07summary.htm How does this analysis extend to other diseases? Briefly give a discussion.

2. a. An alternate SIR Model includes births and deaths. For simplicity, we assume that the birth rate and death rate are the same so that total population stays the same. We also assume that we are analyzing a disease that is not vertically transmitted, so all births go into the susceptible class. The SIR model now satisfies the discrete dynamical system given by:

$$\begin{aligned} S_{n+1} &= S_n - \frac{\beta}{N} S_n I_n + b(I_n + R_n), \\ I_{n+1} &= I_n(1 - \gamma - b) + \frac{\beta}{N} S_n I_n, \\ R_{n+1} &= R_n(1 - b) + \gamma I_n, \end{aligned} \tag{1}$$

where β is the contact rate, γ is the rate of recovery, and b is the birth and death rate. The assumption is that the population is constant, so

$$N = S_n + I_n + R_n.$$

Use this information to reduce the model two difference equations in S_n and I_n. Find all equilibria for this model. Give a condition relating the parameters β, γ, and b that implies all equilibria are non-negative.

b. Linearize the model with the two difference equations that you found above. Give the general Jacobian matrix, then find the eigenvalues for the disease free equilibrium, $I_e = 0$. The *basic reproduction number*, R_0, is given by

$$R_0 = \frac{\beta}{\gamma + b}.$$

How many nonnegative equilibria are there when $R_0 < 1$? How about when $R_0 > 1$? Discuss the local stability of the disease free equilibrium for $R_0 < 1$ and $R_0 > 1$.

c. Assume $N = 100$ is the constant total population. Let $\beta = 0.3$, $\gamma = 0.2$, and $b = 0.2$ with initial populations $S_0 = 70$ and $I_0 = 30$. Simulate the two difference equation model for $n \in [0, 25]$. Show a graph of your simulation (both S_n and I_n) and describe what you observe. Find R_0. What does this simulation say about this particular disease?

d. Find all equilibria for this system (possibly including ones with negative populations). Linearize about the equilibria. Find the eigenvalues for the linearized system at each of the equilibria, and discuss the behavior of the linearized system near those equilibria. Does this analysis support your observations in Part c?

e. Repeat the steps you did in Parts c and d with $\beta = 0.8$, $\gamma = 0.1$, and $b = 0.1$.