This project deals with Epidemic Models in Continuous time. Some of the problems are related to content presented in [EM-3] (Chapter 3 of, "Epidemic Modelling: an introduction" by Daryl Daley and Joe Gani). We only use parts of sections 3.1 and 3.3 from [EM-3]. Please hand in a single PDF file for your solutions to the questions. The file may involve a combination of scanned hand written results, typed text/formulas, and computer output (and code). In any case, it must have questions answered in order and cannot exceed 8MB in size. Make sure to have your name and student ID on the PDF file, even if you hand in via e-mail.

Throughout this project, time t is continuous and starts at $t = 0$. We deal with a non-lethal epidemic over a population of N individuals (think of N as being around 100, 1000 or perhaps 5000 as is suitable for a small population on an island). In the population, S_t is the number of individuals that are "susceptible" to the disease but not infected at time t. Further, I_t is the number of infected individuals with the disease. Finally, R_t are the number of individuals that are removed from being either susceptible or infected and are assumed to be immune from the disease.

In general, we consider three basic non-negative parameters r_{SI}, r_{IS}, and r_{SR}. Where the first dictates the constant for the rate of infection (moving from S to I). The second dictates the constant for the rate of recovery without gaining immunity (moving from I to S). The third dictates the constant of the rate of removal, also known as recovery with immunity (moving from S to R).

We will with the following models (which we denote via Model 1 – Model 4):

1. SI - this is known as the simple epidemic appearing in [EM-3, Section 3.1]. Here $r_{SI} > 0$, but $r_{IS} = 0$ and $r_{SR} = 0$. In this model $R_t \equiv 0$.
2. SIS. Here $r_{SI} > 0$, $r_{IS} > 0$, but $r_{SR} = 0$. In this model $R_t \equiv 0$.
3. SIR - this is known as the general epidemic appearing in [EM-3, Section 3.3]. Here $r_{SI} > 0$, $r_{IS} = 0$, and $r_{IR} > 0$.
4. $SI(SR)$. Here all constants are strictly positive. After infection an individual is either removed or again susceptible.

These models are described via several Markov chains that you specify in problem 1. In general they are governed by the following transition types:

- $S \to I$: This occurs at rate $r_{SI} c_t(S_t, I_t, R_t) S_t I_t + a$. At its base, this is the "law of mass action" where the product of S_t and I_t drives infections. However, in addition, the value $c_t(S_t, I_t, R_t)$ is a state-dependent time-varying coefficient where if not specified is taken as $c_t \equiv 1$ and otherwise indicates the level of "contact" between individuals. It can be controlled via social distancing or similar measures and is hence dependent on state and time. Also the parameter a, when not 0, dictates external arrival of infection that is not influenced by the state.
- $I \to S$: This occurs at rate $r_{IS} I_t$. Here, recovery without immunity is at a constant rate for each individual.
- $I \to R$: This occurs at rate $r_{IR} I_t$. Here recovery with immunity is at a constant rate for each individual.
- $R \to S$: This occurs at rate $b R_t$. Here the parameter b denotes an external rate of immunity loss.

Consider the parameters a, b, and $c_t(\cdot, \cdot, \cdot)$ as model extensions and initially assume that they are 0, 0 and $\equiv 1$ respectively.

Questions/Tasks, with weighting out of 100 in "( )":

1. Assume $N = 3$ and describe CTMCs for each of the models by specifying the meaning of the state and the generator matrix. For models 1 and 2, let the Markov chain be $\{X_t\}$ with state space $\{0, 1, 2, 3\}$. For models 3 and 4, let the Markov chain be $\{(X_t, Y_t)\}$ with a more complicated state space. Throughout this problem assume $c_t \equiv 1$, $a = 0$, and $b = 0$.

   (a) For Model 1, let X_t represent S_t. What is I_t in terms of X_t? What is the generator matrix? (5)

   (b) Repeat for Model 2. (5)

   (c) For Model 3, let X_t represent S_t and Y_t represent I_t. What is R_t in terms of X_t and Y_t? What is your choice of state space? Specify the generator matrix. (5)

   (d) Repeat for Model 4. (5)

2. Consider pg 58 where it is stated, "Equation (3.1.4) shows that the mean time Et_j until S_t is reduced to $j - 1$ can be approximated by the inverse of the logistic rate". Use our notation r_{SI} instead of β. Continue to assume that $a = 0$ and $c_t \equiv 1$ until stated otherwise.

   (a) Present the expression for this approximation. (5)

   (b) Use Monte Carlo simulations to obtain error estimates on this approximation for different values of r_{SI} and N. (5)

   (c) Take now $r_{SI} = 0.02/N$, $N = 1,000$, $I_0 = 1$ and assume that c_t is regulated as follows: Whenever the number of infected passes a multiple of 100, c_t is dropped from 1 to 0.1 (to enforce social distancing). Then 20 time units later, the value returns to 1. Plot multiple (e.g. 5 or 10) traces of I_t under such a regime. (5)

3. Consider the forward Kolmogorov equations presented in pg 59 where an explicit solution is for $N = 5$ (our notation), $I_0 = 1$, and $r_{SI} = 1$ appears in equation (3.1.11) of pg 60.

   (a) Use numerical evaluation of a matrix exponential to verify (3.1.11) over a sensible grid of t. (5)

   (b) Use Monte Carlo for such an evaluation. (3)

   (c) Repeat the derivation in [EM-3] yielding (3.1.11). (2)

4. Consider now Model 2 (SIS). Assume $c_t \equiv 1$ and initially assume $a = 0$.

   (a) Assume $N = 10$, $I_0 = 5$, and $r_{IS} = 2$. Use Monte Carlo or other means to determine the lowest value for r_{SI} such that $\mathbb{P}(\tau_0 > 15) > 0.9$, where $\tau_0 = \inf\{t > 0 \ : \ I_t = 0\}$ is the duration of the infection. (5)

   (b) Assume now $a > 0$ and explain why the model is an irreducible birth-death CTMC by specifying the birth and death rates. (5)

   (c) Continuing from (b), find the neatest expressions possible for the stationary distribution and present the stationary distribution numerically for the parameters $N = 10$, $r_{SI} = 2$ and $r_{IS} = 0.5$. Do this for a values of a of your choice. (3)

   (d) Continuing from (c), determine $\lim_{t\to\infty} \mathbb{E}[I_t]$ for these parameters. (2)

5. Read pgs. 66-67 introducing "The general stochastic epidemic" (SIR) dealing with Model 3.

   (a) Consider Kolmogorov's forward equations in (3.3.3). Write these equations using our notation of Model 3. (5)

   (b) Consider a system with $N = 100$ (our notation), $I_0 = 5$, $r_{SI} = 2/N$, $r_{IR} = 1/N$, $a = 0$, $b = 0$. Use a numerical solution of the forward equations to determine the $\mathbb{E}I_t$ for $t = 5, 10, 20, 50$. (10)

   (c) Try to verify the above using Monte Carlo Simulations. (5)

   (d) Consider P_n which is the distribution of number of initial susceptibles ultimately infected. Attempt to find a Monte Carlo estimate of P_n for these parameters as well as for its mean. (5)

   (e) Assume now that you are in Model 4, also with $b > 0$ and c_t independent of time. This is an irreducible Markov chain with finite state space and hence has a unique stationary distribution. Still, discuss possible problems with determining this stationary distribution and applying it in practice. (5)

6. Social distancing: Modify the problem above (5b, 5c and 5d) with social distancing rules enforced via $c_t(S_t, I_t, R_t)$. Search for a simple time-independent (but state dependent) rule that you design which will cut the mean of P_n (your 5b) by roughly half. Try to estimate what effect your rule has on the mean duration of the epidemic. (15)