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Markov Chain Epidemic Models and Parameter Estimation

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APPROVAL OF THESIS/DISSERTATION

We, the faculty supervising the work of Oluwatobiloba Ige, affirm that the thesis, *Markov Chain Epidemic Models and Parameter Estimation*, meets the high academic standards for original scholarship and creative work established by the Department of Mathematics and the College of Science. This work also conforms to the formatting guidelines of Marshall University. With our signatures, we approve the manuscript for publication.

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ABSTRACT

Over the years, various parts of the world have experienced disease outbreaks. Mathematical models are used to describe these outbreaks. We study the transmission of disease in simple cases of disease outbreaks by using compartmental models with Markov chains. First, we explore the formulation of compartmental SIS (Susceptible-Infectious-Susceptible) and SIR (Susceptible-Infectious-Recovered) disease models. These models are the basic building blocks of other compartmental disease models. Second, we build SIS and SIR disease models using both discrete and continuous time Markov chains. In discrete time models, transmission occurs at fixed time steps, and in continuous time models, transmission may occur at any time. Third, we simulate examples of SIS and SIR disease models in discrete time and in continuous time to see how the number of infected individuals changes over time. Fourth, we estimate the transmission and recovery rates from simulated data using the method of maximum likelihood. The parameter estimates in discrete time are obtained using computer algorithms and those in continuous time are obtained using both computer algorithms and theoretical formulas. Finally, we compute the bias and mean squared error of the estimators.

CHAPTER 1

INTRODUCTION

Over the years, various parts of the world have experienced infectious disease outbreaks. These outbreaks have lead to the loss of lives and have also caused severe adverse economic effects on the areas affected [27]. Infectious diseases are caused by pathogens such as bacteria and viruses. Transmission of infectious disease can happen through physical contact with an infectious person, use of contaminated objects, ingestion of contaminated food and water, or bites from insects or animals. The spread of infectious diseases is a major concern in densely populated developing countries. A major reason is that infectious diseases can spread rapidly in a very short period of time, especially when they can be transmitted from person to person through physical contact [1]. In developed countries, infectious disease can spread rapidly over a large area due to the advancement in transportation networks in these countries [28].

Epidemics are infectious disease outbreaks that are confined to a certain area (e.g., a country). The cholera epidemic in Nigeria in 2010 had a total of 41,787 cases, including 1,716 deaths [10]. Pandemics are infectious disease outbreaks that spread across a much larger area (e.g., continents or the world). The "Asian" influenza pandemic between 1957 and 1958 affected China, Singapore, Hong Kong and the United States, killing about two million people [19]. An infectious disease is considered endemic to a location if the disease persists in the location. Chickenpox is endemic in the United Kingdom. By age 9, over 60 percent of children in the U.K. will acquire the infection [13].

Past and current disease outbreaks have had great adverse effects. The Spanish influenza pandemic between 1918 and 1920, which was tagged the "mother" of all pandemics, infected over 500 million people, killing about 50 million of them [29]. The number of deaths caused by the Spanish influenza was more than the number of deaths recorded in the First World War [29]. The Severe Acute Respiratory Syndrome (SARS) epidemic of 2003 was truly a global concern [7, 24]. SARS caused high adverse economic effects on Asian countries due to the sharp decline in the travel rate and tourism during the outbreak. The epidemic infected over 8,000 people, killing 774 people [7, 24]. Malaria is one of the leading causes of death in Africa and continues to claim a

large number of lives each year, with children under age 5 making up approximately 80% of the deaths [21]. Recently, over 700 cases of measles were reported in the United States between January and April of 2019. This is the largest number of measles cases reported in one year since 1994 [22]. The report raised some concerns because measles was said to be eradicated from the United States in 2000 [8]. With advancements in the transportation system, disease outbreaks may spread across continents in a matter of days infecting a large number of people even before being detected [28]. The most recent pandemic is the coronavirus disease (COVID-19). Originating from Wuhan, China, in December 2019, the disease has infected over 3,000,000 people in over 200 countries, killing about 200,000 of them as of April 2020. The adverse effects of disease outbreaks have prompted scientists to devise several means of making important predictions about these disease outbreaks [6].

1.1 MATHEMATICAL MODELING OF INFECTIOUS DISEASES

Epidemiology is the study of the cause, spread and control of disease. Mathematical modeling is a vital part of understanding disease outbreaks and making predictions in epidemiology [14]. Models are representations of objects, ideas and scenarios on a small scale. They are used in understanding the behavior of real life problems and making predictions about future occurrence of events. Mathematical modeling is the representation of models using mathematical equations.

Modeling in epidemiology is important because it can be used to predict how a disease outbreak can affect a population. The incidence, prevalence, morbidity and mortality rates of a disease outbreak can be predicted by using models. The incidence rate is the number of newly infected persons over a specific period of time, the prevalence rate is the total number of infected persons over a period of time, the morbidity rate is the rate of infection in a population, and the mortality rate is the number of people who die in a given year and area divided by the population of that area.

Models can be used to make predictions to understand if an outbreak may lead to an epidemic or a pandemic. These predictions help in understanding how fast an infection can spread, the effects of certain measures to contain the disease outbreak and even how long the

infection will persist in a given population. By analysing and making accurate predictions about the outcome of a disease outbreak, the right measures to contain an outbreak can be taken.

When modeling a disease outbreak, various factors may be considered in the formulation of the mathematical model. The type of infection, contact rate, latent period, age, sex, surrounding temperature and other factors may be considered. Infections can be categorized into two types: acute and chronic. Acute infections generally have a shorter life span than chronic infections in humans. Acute infections can be present in humans from a few days to few weeks, while chronic infections can remain in humans for a longer period of time up to an entire lifetime. Examples of acute infections are influenza, measles, SARS and Ebola. Examples of chronic infections are hepatitis C and the Human Immunodeficiency Virus (HIV).

Acute infections may be modeled with fewer equations and variables, since the infection lasts just over a very short period of time in a person. A model for an acute infection may assume a constant population over the period of the outbreak since the infection will last for a short period of time. The population growth of the area of infection can be negligible. Chronic infections are usually more complicated to model since there may be an increase or decrease in population size during the course of the outbreak. It takes a longer time to study and collect data. The assumed population size may be small, as in a household, a little larger, as in students in a school, or even up to an entire country or the globe. Disease modeling has been successfully used in real time to make predictions and understand the dynamics and analysis of the bovine spongiform encephalopathy epidemic in cattle in Great Britain amongst other epidemics [20].

The number of equations and variables considered affect the behavior of the model, and thus describe the disease outbreak characteristics. Different numbers of equations and variables need to be used to accurately describe the behavior of different models. This means that some models are simpler while some are more complex. The complexity of a model is usually determined by the number of variables. Thus, the more equations and variables a model has, the more complex it is to analyze.

Since models are representations of ideas and real life scenarios, it is impossible to consider every single variable involved, so several assumptions need to be made. The more assumptions made, the simpler the model and the easier it is to understand and modify, but this

comes at a cost. We generally try to find a balance between the assumptions and variables to be considered in a model. If a model has too many assumptions, then it may not be helpful in making predictions. Also, if a model has too many variables, it becomes complex and can be very difficult to solve or modify. When making models we try to always use only the most important factors as variables to get a simpler and more meaningful model. Recent models may contain more variables since technological advancements in computing can help solve and analyse the system of equations arriving from such a model.

1.2 COMPARTMENTS IN DISEASE MODELING

When modeling disease transmission, the population is split into different compartments, each of which determines the group an individual in the population belongs to. No person is allowed to be in more than one compartment at a particular point in time. The classical paper by Kermack and McKendrick [17] laid the foundation of compartmental modeling in understanding the spread of disease. These compartments vary depending on the type of infection that is to be modeled. In general cases of acute infections, a member of the population falls into one of three compartments: susceptible, infectious, or recovered.

The susceptible population consists of individuals who are free of infections. They are not infected and are not carriers of the disease but can become infected if all transmission conditions are satisfied. The infectious class consists of people who are carriers of the disease and are infectious. They are able to transmit the disease to the susceptible class. The recovered class consists of people who have been infected and then have recovered from the infection. Depending on the disease, different compartments may be required. It is known that with certain infections, like chickenpox, after recovery from the infection, a person is unlikely to be infected again and thus has permanent immunity. The recovered compartment is required for the case of chickenpox. Infections like influenza may be contacted again and there is no permanent immunity. So influenza can be modeled with no recovered compartment.

The SIS (Susceptible-Infectious-Susceptible) epidemic model describes the transmission of infectious disease when recovered individuals may become infectious again immediately (no permanent immunity). When a disease is introduced into the population, transmission of infection

Figure 1. SIS Epidemic Model

SIS Epidemic Model showing the transmission of infection in a fixed population. Here β and γ are the transmission rate and recovery rate, respectively.

moves members of the susceptible compartment to the infectious compartment. Then later, the infected individual recovers but does not gain immunity thereby becoming susceptible again. The SIS model can be used to model the transmission of acute infections like influenza. Since the infection generally lasts for a short period of time, we assume that the population size is constant over the course of the outbreak, that is, the number of births and deaths are equal during this time or there are no births or deaths during the outbreak period. It is also assumed that infections can not be transmitted vertically, that is, infection cannot be passed from a mother to her unborn child and so no child is born infected. Figure 1 shows a simple example of an SIS epidemic model.

The SIR (Susceptible-Infectious-Recovered) epidemic model describes the transmission of infectious disease where the recovered individuals may no longer become infected again. A susceptible person gets infected with disease and then later recovers from it. There is permanent immunity in this model and the recovered individuals remain permanently in the recovered compartment. Recovery can mean immunity to the disease or even death. Assumptions similar to the SIS model can be used to simplify the model. We assume that the population size is constant at every point in time of the outbreak and that the infection can only be transmitted horizontally, that is, we consider transmission to be from person to person and not parent to child. The SIR model can be used to model the transmission of chickenpox since immunity is gained after recovery. Figure 2 shows a simple example of an SIR Epidemic Model.

The Kermack-McKendrick [17] model of 1927 is one of the simplest SIR models and is still in use to date. It was used to explain the fluctuation in the number of infected people in the Great Plague of London between 1665 and 1666 [5]. A complex SIR model can be obtained from the Kermack-McKendrick model by making fewer assumptions and taking more parameters into
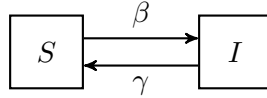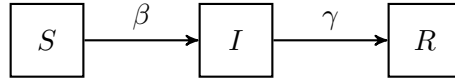
Figure 2. SIR Epidemic Model

SIR Epidemic Model showing the transmission of infection in a fixed population. Here β and γ are the transmission rate and recovery rate, respectively.

consideration.

1.3 INTRODUCTION TO STOCHASTIC PROCESSES

SIS and SIR epidemic models can be interpreted using stochastic processes. A stochastic process is a collection of random variables $\{X(t) : t \in T\}$ where each state X is a function of time t, that is, a number $X(t)$ is observed at each time t. The set T is the set of times when the system can be observed. A stochastic process models how a random variable changes with time. When the set T is countable and evenly spaced, the stochastic process is a discrete time process. A simple example of a discrete time stochastic process is shown in Figure 3. When the set T equals $[0, \infty)$, the stochastic process is a continuous time process. A simple example of a continuous time stochastic process is shown in Figure 4. The state space is defined depending on what values the process can take. The state space tells us the states in which a stochastic process can be observed. In disease modeling, the state spaces are usually countable. In the case of an SIS model, the state space is the number of individuals in each of the two classes, the susceptible class and the infectious class. For SIR models, the state space is the number of individuals in each of the susceptible, infectious and recovered class.

There are basically two types of models: stochastic and deterministic. Stochastic models can handle randomness and thus give different outputs for every input specified. Deterministic models cannot handle randomness and thus give the same output for every input given [25]. Both types of models are useful in disease modeling. Although deterministic models are usually simpler than stochastic models, stochastic models are preferred since the transmission of disease in real life is highly prone to randomness.

Stochastic processes in disease transmission are best modeled using Markov chains. In
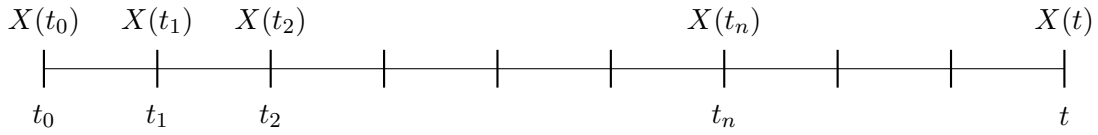
Figure 3. Discrete Time Stochastic Process

A simple figure of a discrete time process. At each time t_n, the observed value of the state is the random variable $X(t_n)$. The time difference between any two consecutive observations is constant.

Figure 4. Continuous Time Stochastic Process

A simple figure of a continuous time process. At each time t, the observed value of the state is the random variable $X(t)$. The times of consecutive observations $(t_0, t_1, \ldots)$ are not evenly spaced.

most naturally occurring processes, the previous outcome may influence the next outcome of an event. A stochastic process describing such an event is a Markov chain. The state space of a Markov chain is usually discrete. The chance of transiting to any state depends on the current state and time. Such events can be seen in disease modeling, where the probability of the number of infectious persons at the nearest future time depends on the number of infectious persons in the present time. That is, we need only information about the current state to be able to predict the future state, and any additional information about the past state does not matter. This fact is called the Markov property or memoryless property. The memoryless property makes Markov chains an important tool in modeling naturally occurring events. For example, we may assume a small population of fifty people with one infectious person. The probability of a new infection is dependent only on the transmission of the infection by the one infectious person at that point in time. It does not matter if the disease may have caused an epidemic in the past. Information about the past has no effect on the future state transitions. The spread of the disease only depends on the current state.

1.4 PARAMETER ESTIMATION

Statistical inference allows us to draw conclusions about a population system based on observed data and parameters [12]. Parameters are numerical quantities that determine the behaviour of a population system. We may take a sample of a population and make general conclusions about the entire population and its parameters based on the observed samples. The transmission rate β, recovery rate γ, and the basic reproduction number R_0 are some parameters of interest when modeling the spread of infectious diseases. The basic reproduction number R_0 is the number of secondary infections that are caused by one infectious person in a completely susceptible population [30]. For the SIR and SIS disease models, the basic reproduction number is

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

where $\frac{1}{\gamma}$ is the duration of infection [15]. For the SIS model, when R_0 is greater than 1, the population will reach an endemic equilibrium, but when when R_0 is less than 1, the infection quickly dies down. Stochastic SIS models with R_0 greater than 1 may have infection die out because of the stochastic nature of the model. For the SIR model, when R_0 is greater than 1, the number of infectious individuals increases and then starts to decrease till the infection dies out. When R_0 is less than 1, the number of infectious individuals decreases until the infection dies out [11].

In disease modeling, it can be difficult to collect all data relating to an outbreak, and so inferential statistics are used to make generalizations about disease outbreaks in a population based on the available observed data. Parameter estimation is one type of inferential statistics and is important in describing the behaviour of a population system. It is the process of using population data to estimate the parameters of a population system. Several methods have been developed over the years. Point estimation is used to estimate a parameter as a single value from a random sample.

Maximum likelihood estimation is a type of point estimation. It is one of the general methods for parameter estimation and has been used in epidemiology [9]. Given a set of data, the method of maximum likelihood estimates a parameter by finding the parameter value that maximizes the likelihood of getting the observed data. The likelihood function is used in

determining the maximum likelihood estimate (MLE) of the parameters. Generally, if $X(0) = x_0$, $X(1) = x_1, \ldots, X(n) = x_n$ are independent random variables and have a joint density function of $p[X(0), X(1), \ldots, X(n) \mid \theta]$, the likelihood function is a function of θ, where θ is now an unknown parameter. The likelihood function is

$$L(\theta) = L(\theta \mid x_0, x_1, \ldots, x_n) = p(x_0, x_1, \ldots, x_n \mid \theta) = \prod_{i=0}^{n} p(x_i \mid \theta).$$

For a Markov process, the transition probabilities are not independent and are also regarded as parameters. For some observed data, $x'_n = (x_0, x_1, \ldots, x_n)$, the likelihood function of the Markov process is the product of the transition conditional probabilities and is given by

$$L(\theta) = L(\theta \mid x'_n) = p(x_n \mid x_{n-1})p(x_{n-1} \mid x_{n-2}) \ldots p(x_1 \mid x_0)p(x_0) = p(x_0)\prod_{i=1}^{n} p(x_i \mid x_{i-1}).$$

The transition probability from state x_{i-1} to x_i is denoted by $p_{x_i \leftarrow x_{i-1}}$, giving

$$p(x_i \mid x_{i-1}) = p_{x_i \leftarrow x_{i-1}}.$$

The likelihood function can be rewritten as

$$L(\theta) = L(\theta \mid x'_n) = p(x_0)\prod_{i=1}^{n} p(x_i \mid x_{i-1}) = p(x_0)\prod_{i=0}^{n}\prod_{j=0}^{n} p_{j \leftarrow i}^{n_{ji}}, \tag{1.1}$$

where n_{ji} is the count of transitions from i to j. It is possible for a process, after leaving state i to j, to return back to state i, and then transition again to state j. For a Markov process, we can estimate the parameter θ by maximizing the logarithm of the likelihood function (1.1) with the result being the maximum likelihood estimator of θ. We may also choose to minimize the negative log likelihood function to estimate the parameter θ. In estimating parameters in a discrete time stochastic process, the times between consecutive events are equal and thus uniformly distributed. In the case of a continuous-time stochastic process, the times between consecutive events are random, and are exponentially distributed. The distribution of the times between consecutive events can affect the likelihood function. More details on parameter estimation using the method of maximum likelihood are given in Chapter 4.

After obtaining the point estimates of the parameters using MLE, it is important to compare our estimates with the actual values of the parameter. A point estimate can overestimate or underestimate a parameter. Bias is the difference between the expected value of our estimates and the actual value of our estimate. If $\hat{\theta}$ is an estimate of a parameter θ, the bias of $\hat{\theta}$ is

$$B(\hat{\theta}) = E(\hat{\theta}) - \theta,$$

where $E(\hat{\theta})$ is the expected value of $\hat{\theta}$ [31]. The bias may be positive or negative. If $B(\hat{\theta}) > 0$, $\hat{\theta}$ is an overestimate of θ and is a biased estimate. If $B(\hat{\theta}) < 0$, $\hat{\theta}$ is an underestimate of θ and is also a biased estimate. If $B(\hat{\theta}) = 0$, $\hat{\theta}$ is an unbiased estimate. The mean squared error (MSE) is simply the mean of the squares of the errors. The MSE measures variation in estimation and is given as

$$\text{MSE}(\hat{\theta}) = E(\hat{\theta} - \theta)^2.$$

The MSE is always non-negative. The smaller the MSE, the better the precision of the estimates.

1.5 AIMS AND OBJECTIVES

The aim of this thesis is to explain the formulations of the simple SIR and SIS epidemic models for the spread of infectious diseases and also to estimate transmission and recovery rates of the models. In Chapter 2, we will see how to build simple SIS and SIR models using discrete time Markov chains. In Chapter 3, we build the same models using continuous time Markov chains. Finally, in Chapter 4, we will use the method of maximum likelihood to estimate transmission and recovery rates using data obtained from simulated outbreaks. For each estimate of the transmission rate and recovery rate, we compute the bias and mean squared error of the estimators.

CHAPTER 2

EPIDEMIC MODELS USING DISCRETE TIME MARKOV CHAINS

In this chapter, we use discrete time Markov chains to formulate SIS and SIR epidemic models.

2.1 DISCRETE TIME MARKOV CHAINS

Let $\{X(t) : t \in T\}$ be random variables denoting the state of a system at time $t \in T = \{0, \Delta t, 2\Delta t, ...\}$ with a discrete state space

$$\{i_0, i_{\Delta t}, i_{2\Delta t}, ..., i_{t-\Delta t}, i, j\} = S \subset \{0, 1, 2, ..., N\}.$$

A stochastic process is a Discrete Time Markov Chain (DTMC) if it satisfies the following equation

$$P[X(t + \Delta t) = j \mid X(t) = i, ..., X(\Delta t) = i_{\Delta t}, X(0) = i_0]$$
$$= P[X(t + \Delta t) = j \mid X(t) = i] = p_{j \leftarrow i}(\Delta t).$$

A discrete time process satisfies the Markov property, that is, the process at any time $t + \Delta t$ depends only on the state of the immediate past process in time t. As time goes on, the process does not require the information from further back for future transitions. The probability that the process will transition from state i at time t to state j at time $t + \Delta t$ is $p_{j \leftarrow i}(\Delta t)$. We assume that the process is time homogeneous, that is, the transition probability does not change with time. The process is independent of t and

$$P[X(t + \Delta t) = j \mid X(t) = i] = P[X(\Delta t) = j \mid X(0) = i] = p_{j \leftarrow i}(\Delta t).$$

The one-step transition probability is the probability of transiting from state i to state j in one step, that is, in a period of Δt. We denote the one-step transition probability as $p_{j \leftarrow i}(\Delta t)$. It is sometimes denoted by $p_{ji}(\Delta t)$. The n-step transition probability is the probability of moving

from state i to state j in n steps, that is, in a period of $n\Delta t$ and is given as

$$P[X(t + n\Delta t) = j \mid X(t) = i] = p^{(n)}_{j\leftarrow i}(n\Delta t).$$

The probability $p_{j\leftarrow i}(\Delta t)$ may sometimes be zero.

A transition matrix $P(\Delta t)$ is used to describe all possible one-step transitions in a discrete time Markov chain. Since the states can take values from 0 to N, $P(\Delta t)$ is an $(N + 1) \times (N + 1)$ matrix. The matrix $P(\Delta t)$ is given as

$$P(\Delta t) = (p_{j\leftarrow i})_{j,i\in S},$$

that is,

$$P(\Delta t) = \begin{pmatrix} p_{0\leftarrow 0} & p_{0\leftarrow 1} & \cdots & p_{0\leftarrow i} & \cdots & p_{0\leftarrow N} \\ p_{1\leftarrow 0} & p_{1\leftarrow 1} & \cdots & p_{1\leftarrow i} & \cdots & p_{1\leftarrow N} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ p_{j\leftarrow 0} & p_{j\leftarrow 1} & \cdots & p_{j\leftarrow i} & \cdots & p_{j\leftarrow N} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ p_{N\leftarrow 0} & p_{N\leftarrow 1} & \cdots & p_{N\leftarrow i} & \cdots & p_{N\leftarrow N} \end{pmatrix}.$$

Each cell in the matrix is the probability of transiting from the state of the column to the state of the row. For example, the element (j, i) corresponds to $p_{j\leftarrow i}$ and is the probability of transiting from state i to state j. The columns of the transition matrix $P(\Delta t)$ form a probability distribution and sum up to 1. We have

$$\sum_{j=0}^{N} p_{j\leftarrow i}(\Delta t) = 1,$$

and the transition matrix is called a left stochastic matrix. If $P(\Delta t)$ is transposed then the rows of the new transition matrix sum to 1. The resulting matrix is called a right stochastic matrix. We will regard $P(\Delta t)$ as a left stochastic matrix.

States of a Markov chain are classified according to their properties. A Markov chain can generally have two types of states: transient and recurrent. A state i of a Markov chain is a

transient state if, after the process leaves to another state j, the probability of returning to i is less than 1. A state j of a Markov chain is a recurrent state if, after the process leaves to another state k, the probability of returning to j is 1. This means that transition back to state j is almost surely guaranteed. For both transient and recurrent states, there is no guarantee of a transition back to the states. An absorbing state is a special kind of recurrent state. A state k is an absorbing state if, after the process reaches k, the process cannot leave state k. No other state is reachable from an absorbing state. A finite Markov chain must have at least one recurrent state.

2.2 SIS EPIDEMIC MODELS USING DISCRETE TIME MARKOV CHAINS

In formulating SIS epidemic models using discrete time Markov chains, we follow Allen's approach [2]. Let $S(t)$ and $I(t)$ denote discrete random variables counting the number susceptible and infectious persons at each time $t \in T = \{0, \Delta t, 2\Delta t, ...\}$ with $S(t), I(t) \in \{0, 1, 2, ..., N\}$. These two random variables count the number of individuals in each of the two compartments needed for an SIS epidemic model, the susceptible and the infectious compartments. We make the assumption that the population is constant throughout the observed time of the disease outbreak. That is, at any time t, $N = S(t) + I(t)$, thus

$$\frac{dN}{dt} = \frac{dS(t)}{dt} + \frac{dI(t)}{dt} = 0. \tag{2.1}$$

The discrete time derivative for the SIS model is given as Equation 2.1. Since there are only two compartments in this model, it is sufficient to use the value of the infectious class to estimate the value of susceptible class, reducing the dimension of the system.

By choosing the time step small enough, we may assume that at most one transition happens during each time step. That is, for $I(t) = i$ and a time step of Δt, only one of the following can occur:

$$i \xrightarrow{\Delta t} i + 1, \quad i \xrightarrow{\Delta t} i - 1 \quad \text{or} \quad i \xrightarrow{\Delta t} i.$$

For every change in time, one new person may get infected, recover from an infection and become susceptible again, or there may be no change in the number of infectious persons in the population. With a new infection in the population, the number of susceptible persons decreases
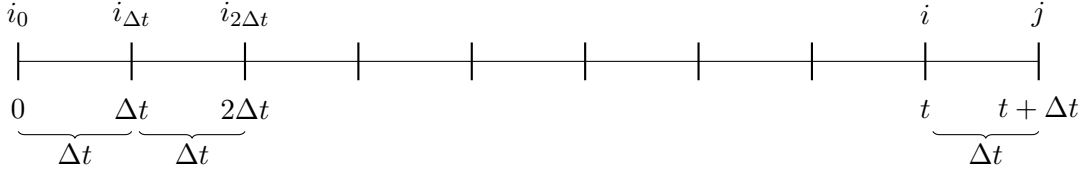
Figure 5. Trajectory of a Discrete Time SIS Model

A trajectory of a DTMC SIS model showing transition states and uniform holding times between consecutive state transitions.

by one and the infectious class goes up by one. A recovery in the population indicates that the infectious class decreases by one and the susceptible class goes up by one. For the SIS model, we define a trajectory as a sequence U of states with holding times as

$$U = (i_0, \Delta t, i_{\Delta t}, \Delta t, \ldots, i, \Delta t, j).$$

This implies that the system started at state i_0. Then, after a period of Δt units of time, the system transitioned to state $i_{\Delta t}$. The system stayed at state $i_{\Delta t}$ for another period of Δt units of time and then transitioned to the next state, and so on [23]. Figure 5 shows the trajectory of a discrete time Markov chain SIS model.

2.2.1 TRANSITION PROBABILITIES OF A DTMC SIS EPIDEMIC MODEL

Several factors affect the transmission of infectious disease in a population such as the climate, the population contact structure between the susceptible and the infectious populations, and the probability of transmission [16]. For a simple SIS epidemic model, we consider only the contact structure between the susceptible and infectious populations for disease transmission. We define $\beta > 0$ and $\gamma > 0$ as the transmission and recovery rates of the population, respectively. We make the assumption that there is homogeneous mixing of the susceptible and infectious populations and the contact structure is frequency dependent. The contact structure being frequency dependent implies that the transmission rate β does not change with population size. This means that the transmission rate remains constant even as the number of infectious people

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goes up. The number of susceptible individuals newly infected at time step t is therefore given by [16]

$$\frac{\beta S(t)I(t)}{N}.$$

The number of infectious individuals becoming susceptible is dependent on the number of infectious individuals in a population. In this case, it is solely determined by the recovery rate. The rate of infectious individuals becoming susceptible at any time t is therefore given by $\gamma I(t)$. We have that the change in the susceptible class is

$$\frac{dS(t)}{dt} = -\frac{\beta S(t)I(t)}{N} + \gamma I(t).$$

The probability of transiting from i to $i+1$ is

$$p_{i+1\leftarrow i}(\Delta t) = \frac{\beta i(N-i)}{N}\Delta t,$$

where $s = N - i$ because of the fixed population size. The number of individuals recovering at any time t is given by $\gamma I(t)$ and, for every recovery, the change in the infectious class is given by

$$\frac{dI(t)}{dt} = \frac{\beta S(t)I(t)}{N} - \gamma I(t).$$

The probability of transiting from i to $i-1$ is

$$p_{i-1\leftarrow i}(\Delta t) = \gamma i\Delta t.$$

The sum of the probabilities of all possible transitions must add up to one. So, the probability that the number of infectious remains unchanged after a time step is

$$p_{i\leftarrow i}(\Delta t) = 1 - \left[\frac{\beta i(N-i)}{N} + \gamma i\right]\Delta t.$$

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The transition probabilities of the DTMC SIS epidemic model are then given by

$$
p_{j \leftarrow i}(\Delta t) = \begin{cases} \dfrac{\beta i(N-i)}{N}\Delta t, & j = i+1 \\[2mm] \gamma i \Delta t, & j = i-1 \\[2mm] 1 - \left[\dfrac{\beta i(N-i)}{N} + \gamma i\right]\Delta t, & j = i \\[2mm] 0, & \text{otherwise.} \end{cases}
$$

For simplification and easy readability of the SIS epidemic model, we denote the transition probabilities of the birth of an infection and recovery or death of an infection as $b(i)\Delta t$ and $d(i)\Delta t$, respectively. Therefore, the SIS epidemic model can be represented as [2]

$$
p_{j \leftarrow i}(\Delta t) = \begin{cases} b(i)\Delta t, & j = i+1 \\[2mm] d(i)\Delta t, & j = i-1 \\[2mm] 1 - [b(i) + d(i)]\Delta t, & j = i \\[2mm] 0, & \text{otherwise.} \end{cases}
$$

To always have a valid transition probability between 0 and 1, we choose the time step Δt small enough so that [2]

$$
\max_{i \in \{1,2,\ldots,N\}} \{[b(i) + d(i)]\Delta t\} \leq 1.
$$

We form the tridiagonal transition matrix $P(\Delta t)$. Using the transition probabilities, $P(\Delta t)$ is given as

$$\begin{pmatrix} 1 & d(1)\Delta t & 0 & \dots & 0 & 0 \\ 0 & 1-[b(1)+d(1)]\Delta t & d(2)\Delta t & \dots & 0 & 0 \\ 0 & b(1)\Delta t & 1-[b(2)+d(2)]\Delta t & \dots & 0 & 0 \\ 0 & 0 & b(2)\Delta t & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & d(N-1)\Delta t & 0 \\ 0 & 0 & 0 & \dots & 1-[b(N-1)+d(N-1)]\Delta t & d(N)\Delta t \\ 0 & 0 & 0 & \dots & b(N-1)\Delta t & 1-d(N)\Delta t \end{pmatrix}.$$

The state $i = 0$ is an absorbing state of the matrix since it is impossible to transition from $i = 0$ to another state with $i > 0$. That is, it is not possible for a population with no infection to leave the disease free state. If there can be a transition from i to j and from j to i, i and j are said to be in the same communicating class. The state $i = 0$ forms a communicating class and the states with $i > 0$ forms another communicating class. In the class with states $i > 0$, the probability of transitioning between any two states in the class is positive, but also the probability of transitioning from any one of the states out of the class to $i = 0$ is also positive. Thus the states in the class with $i > 0$ are transient as it is possible to return after some time but not guaranteed.

2.2.2   PSEUDOCODE FOR DTMC SIS MODELS AND SIMULATED EXAMPLE

Provided all parameters and initial conditions are given, we can plot a graph of the SIS epidemic model comparing the changes in the number of infectious individuals against time. Using Allen's approach [2], the algorithm of the code is as follows:

1. Initialize the values of β, γ, population size N, time step Δt, and time duration of the outbreak t_{end}.

2. Create arrays $S(t)$ and $I(t)$. Set $t = 0$. Let $I(0)$ be the initial number of infectious individuals and $S(0) = N - I(0)$.

3. For t from 0 to t_{end} in an increment of Δt, while t is less than t_{end}:

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(a) Compute the probability of a new infection (p_1) using $\left(\dfrac{\beta S(t)I(t)}{N}\right)\Delta t.$

(b) Compute the probability of a recovery from infection (p_2) using $\gamma I(t)\Delta t.$

(c) Compute the probability of no change in the number of infectious using $1-(p_1+p_2).$

(d) Select a random number u from a uniform distribution of $(0,1)$.

(e) Compare u with p_1, p_2 and $1-(p_1+p_2)$.

(f) If $0 < u \le p_1$, decrease the number of susceptible individuals by 1 and increase the number of infectious individuals by 1. Hence $S(t+\Delta t) = S(t) - 1$ and $I(t+\Delta t) = I(t) + 1.$

(g) If $p_1 < u \le p_1 + p_2$, increase the number of susceptible individuals by 1 and decrease the number of infectious individuals by 1. Hence $S(t+\Delta t) = S(t) + 1$ and $I(t+\Delta t) = I(t) - 1.$

(h) Otherwise, $p_1 + p_2 < u < 1$. In this case, the number of susceptible and infectious remains the same. Hence $S(t+\Delta t) = S(t)$ and $I(t+\Delta t) = I(t)$.

4. Plot the graph of the times t against the number of infectious at each time, $I(t)$.

In the algorithm, we simulate a discrete random variable u to determine which of the events occurred. In general, for n events, we partition the interval $(0,1)$ into n parts, according to the probability of each of the individual events p_1, p_2, ..., p_n. The pieces of the partition are $(0,p_1]$, $(p_1, p_1 + p_2]$, ... , $(p_1 + p_2 + \ldots + p_{n-1}, 1)$, where $\sum_{i=1}^{n} p_i = 1$ is the sum of the column of the transition matrix [4]. The ith event occurs when u falls inside the ith interval. The random variable u has the same distribution as p_i. We use the default random number generator (Mersenne Twister) in Matlab with a period of $2^{19937} - 1$. The period is large enough to avoid internal correlations for the computations in this work. We use these ideas in all our models.

We simulate an example of a DTMC SIS epidemic model. Suppose that there is an influenza outbreak in a community of 100 people with 5 people initially infected. The transmission rate β is 1, the recovery rate γ is 0.5, and the fraction of time between consecutive events is 0.01. For 3 simulations, the graph of time against the number of infectious individuals is

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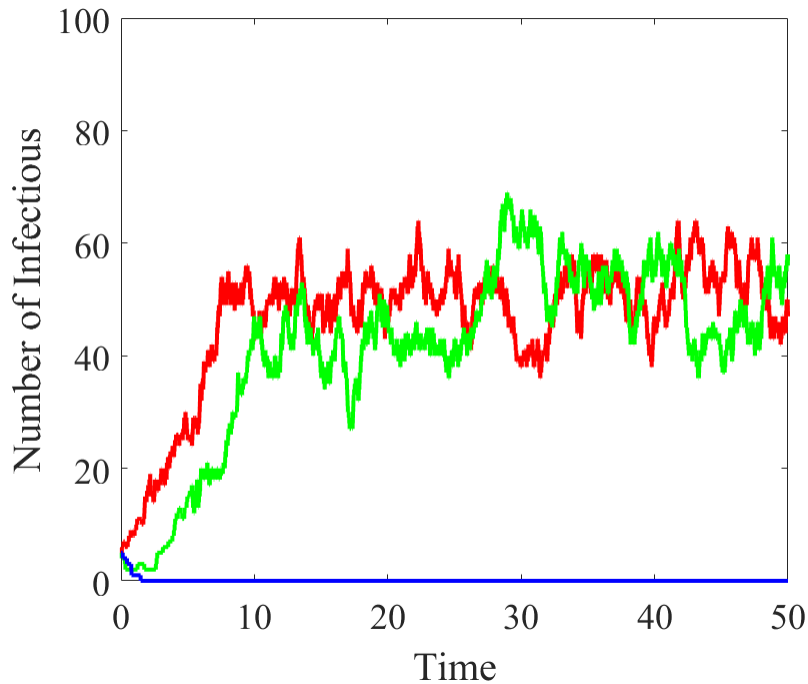
Figure 6. A DTMC SIS Epidemic Model

Simulations of a DTMC SIS Epidemic Model with three stochastic paths using parameters $N = 100$, $I(0) = 5$, $\beta = 1$, $\gamma = 0.5$ and $\Delta t = 0.01$.

presented in Figure 6. The graph was plotted by following the pseudocode in this section, with the aid of the epidemic model code used by Allen [2].

For this example, the basic reproduction number R_0 is 2. For two of the three outbreaks (red and green paths) in Figure 6, the population reaches an endemic equilibrium with about 50 infected people. The blue path in Figure 6 shows the infection quickly dies down even though $R_0 > 1$. This is due to the stochastic nature of the model.

2.3 SIR EPIDEMIC MODELS USING DISCRETE TIME MARKOV CHAINS

For SIR epidemic models, there are three compartments, and the random variables $S(t)$, $I(t)$ and $R(t)$ are required. As in SIS epidemic models, $S(t)$ and $I(t)$ count the number of infectious and susceptible individuals in the population at time $t \in T = \{0, \Delta t, 2\Delta t, ...\}$ with $S(t), I(t) \in \{0, 1, 2, ..., N\}$. The additional random variable $R(t)$ counts the number of recovered

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individuals in the population at time $t \in T$, also with $R(t) \in \{0, 1, 2, ..., N\}$. Recovered individuals are no longer susceptible and are immune to the infection. The assumption of a constant population still holds for the outbreak and, so, at any time t,

$$N = S(t) + I(t) + R(t).$$

Thus

$$\frac{dN}{dt} = \frac{dS(t)}{dt} + \frac{dI(t)}{dt} + \frac{dR(t)}{dt} = 0.$$

We use the susceptible and infectious classes to compute the recovered class to reduce the dimension of the system. The process is bivariate, with the recovered class depending on the susceptible and infectious class, and thus

$$R(t) = N - S(t) - I(t).$$

By choosing the time step small enough, we may assume that at most one transition happens during each step. For a time step of Δt, only one of the following can occur:

$$(s, i) \xrightarrow{\Delta t} (s - 1, i + 1), \quad (s, i) \xrightarrow{\Delta t} (s, i - 1) \quad or \quad (s, i) \xrightarrow{\Delta t} (s, i).$$

For every change in time, only one individual in the population may get infected, recover completely from an infection with no way of becoming susceptible again, or there may be no change in the number of infectious persons in the population. With a new infection in the population, the number of susceptible persons decreases by one and the infectious class goes up by one. A recovery indicates that the infectious class decrease by one and the recovered class goes up by 1. For the SIR model, we define a trajectory as a sequence U of states with holding times

$$U = ((s_0, i_0), \Delta t, (s_{\Delta t}, i_{\Delta t}), \Delta t, \dots, (s, i), \Delta t, (k, j)).$$

This implies that the system started at state (s_0, i_0). Then, after a period of Δt units of time, the system transitioned to state $(s_{\Delta t}, i_{\Delta t})$. The system stayed at state $(s_{\Delta t}, i_{\Delta t})$ for another Δt units of time and then transitioned to the next state, and so on. Figure 7 shows the trajectory of a

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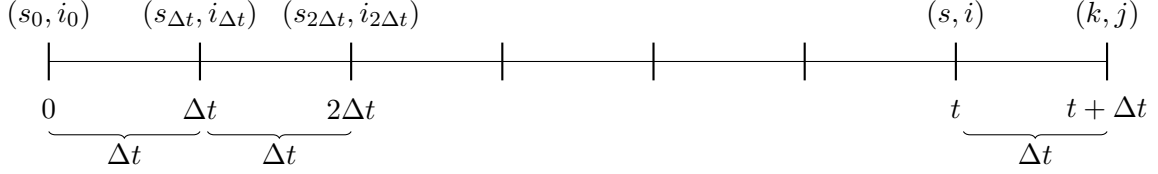
Figure 7. Trajectory of a Discrete Time SIR Model

A trajectory of a DTMC SIR model showing transition states and uniform holding times between consecutive state transitions.

discrete time Markov chain SIR model.

2.3.1 TRANSITION PROBABILITIES OF A DTMC SIR EPIDEMIC MODEL

For a DTMC SIR epidemic model, the change in the susceptible class at time t is

$$\frac{dS(t)}{dt} = -\frac{\beta S(t)I(t)}{N}.$$

This is because individuals are transitioning from the susceptible compartment to the infectious compartment, with no person returning back to the susceptible compartment. The number of susceptibles will continue to decrease with time. This decrease implies a new infection in the population and a transition from (s, i) to $(s - 1, i + 1)$. The probability of new infection is

$$p_{(s-1,i+1)\leftarrow(s,i)}(\Delta t) = \frac{\beta si}{N}\Delta t.$$

Individuals in the infectious compartment are also constantly transiting to the recovered compartment so that the change in the infectious class at time t is

$$\frac{dI(t)}{dt} = \frac{\beta S(t)I(t)}{N} - \gamma I(t).$$

Recovery means a transition from (s, i) to $(s, i - 1)$. The probability of recovery is

$$p_{(s,i-1)\leftarrow(s,i)}(\Delta t) = \gamma i\Delta t.$$

Since a constant population is assumed, the probability that the number of infectious remains unchanged after a time step is

$$p_{(s,i)\leftarrow(s,i)}(\Delta t) = 1 - \left[\frac{\beta si}{N} + \gamma i\right]\Delta t.$$

Therefore, we have transition probabilities of the SIR epidemic model as

$$p_{(s+k,i+j)\leftarrow(s,i)}(\Delta t) = \begin{cases} \dfrac{\beta si}{N}\Delta t, & (k,j) = (-1,1) \\[2ex] \gamma i\Delta t, & (k,j) = (0,-1) \\[2ex] 1 - \left[\dfrac{\beta si}{N} + \gamma i\right]\Delta t, & (k,j) = (0,0) \\[2ex] 0, & \text{otherwise.} \end{cases}$$

For simplicity, as in the SIS epidemic model, the SIR epidemic model can be represented as

$$p_{(s+k,i+j)\leftarrow(s,i)}(\Delta t) = \begin{cases} b(i)\Delta t, & (k,j) = (-1,1) \\[2ex] d(i)\Delta t, & (k,j) = (0,-1) \\[2ex] 1 - [b(i) + d(i)]\,\Delta t, & (k,j) = (0,0) \\[2ex] 0, & \text{otherwise.} \end{cases}$$

2.3.2   PSEUDOCODE FOR DTMC SIR MODELS AND SIMULATED EXAMPLE

Using Allen's approach [2], the algorithm of a DTMC SIR model code is as follows:

1. Initialize the values of β, γ, population size N, time step Δt, and time duration of the outbreak t_{end}.

2. Create arrays $S(t)$, $I(t)$ and $R(t)$. Set $t = 0$ and $R(0) = 0$. Let $I(0)$ be the initial number of infectious individuals and $S(0) = N - I(0)$.

3. For t from 0 to t_{end} in an increment of Δt, while t is less than t_{end}:

   (a) Compute the probability of a new infection (p_1) using $\left(\dfrac{\beta S(t)I(t)}{N}\right)\Delta t$.

(b) Compute the probability of a recovery from infection (p_2) using $\gamma I(t)\Delta t$.

(c) Compute the probability of no change in number of infectious using $1 - (p_1 + p_2)$.

(d) Select a random number u from a uniform distribution of (0,1).

(e) Compare u with p_1, p_2 and $1 - (p_1 + p_2)$.

(f) If $0 < u \leq p_1$, decrease the number of susceptible individuals by 1 and increase the number of infectious individuals by 1. Hence we have

$$S(t + \Delta t) = S(t) - 1, \quad I(t + \Delta t) = I(t) + 1, \quad \text{and } R(t + \Delta t) = R(t).$$

(g) If $p_1 < u \leq p_1 + p_2$, decrease the number of infectious individuals by 1 and increase the number of recovered individuals by 1. Hence we have

$$S(t + \Delta t) = S(t), \quad I(t + \Delta t) = I(t) - 1, \quad \text{and } R(t + \Delta t) = R(t) + 1.$$

(h) Otherwise, $p_1 + p_2 < u < 1$. In this case, the number of susceptible, infectious and recovered individuals remains the same. Hence

$$S(t + \Delta t) = S(t), \quad I(t + \Delta t) = I(t), \quad \text{and } R(t + \Delta t) = R(t).$$

4. Plot the graph of the times t against the number of infectious at each time, $I(t)$.

We simulate an example of a DTMC SIR epidemic model using the algorithm just stated. Suppose that there is a measles outbreak in a community of 100 people with 5 people initially infected. For this example, the transmission rate β is 1, the recovery rate γ is 0.5, and the time between consecutive events is 0.01. For 3 simulations, the graph of time against the number of infectious is given in Figure 8.

The path of the three simulations represented in Figure 8 shows that after the number of infections peak, individuals gradually recover and the infection dies down eventually. Due to the stochastic nature of the model, there may be no outbreak and the infection may die out quickly.
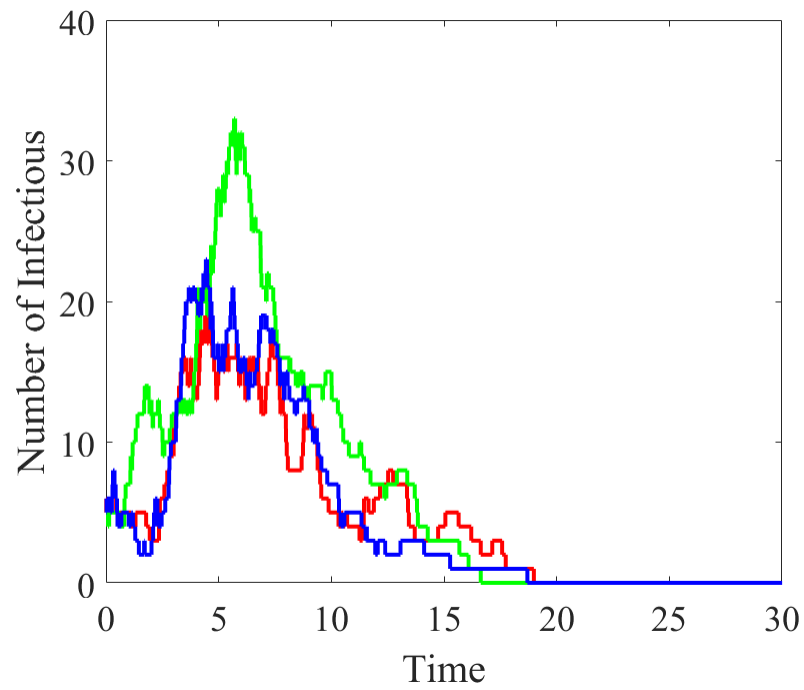
Figure 8. A DTMC SIR Epidemic Model

Simulations of a DTMC SIR Epidemic Model with three stochastic paths using parameters $N = 100$, $I(0) = 5$, $\beta = 1$, $\gamma = 0.5$ and $\Delta t = 0.01$.

CHAPTER 3

EPIDEMIC MODELS USING CONTINUOUS TIME MARKOV CHAINS

In this chapter, we use continuous time Markov chains to study SIS and SIR epidemic models.

3.1 CONTINUOUS TIME MARKOV CHAINS

Continuous time Markov chains are used to model systems where the process remains in a state for a random amount of time before transitioning to the next state. Let $\{X(t) : t \in T\}$ be random variables denoting the state of a system at time $t \in T = [0, \infty)$ with a discrete state space $S \subset \{0, 1, 2, ..., N\}$. The random variables $\{X(t) : t \in T\}$ form a Continuous Time Markov Chain (CTMC) if for any sequence of times, $t_0, t_1, \ldots, t_{n-1}, t_n, s, t$ with $t_0 < t_1 < ... < t_{n-1} < t_n < s < t$, the random variables $\{X(t) : t \in T\}$ satisfy the following equation

$$P[X(t) = j \mid X(s) = i, X(t_n) = i_n, ..., X(t_0) = i_0] = P[X(t) = j \mid X(s) = i] = p_{j \leftarrow i}(t - s). \quad (3.1)$$

The continuous time process satisfies the Markov property [2], that is, the process at time t depends only on the state of the immediate past process in time s, as in Equation 3.1. Unlike a discrete time Markov process, transitions in a continuous time Markov process do not happen at a fixed unit of time but can occur at any time. Similarly to the DTMC, we denote the probability that the process will transit from state i at time s, to state j at time t, to be $p_{j \leftarrow i}(t - s)$. We also make the assumption that $p_{j \leftarrow i}(t - s)$ is independent of t at any given time, hence, the process is time homogeneous and

$$P[X(t) = j \mid X(s) = i] = P[X(t - s) = j \mid X(0) = i] = p_{j \leftarrow i}(t - s).$$

The continuous time random process $X(s)$ will remain in its state for $\Delta t = t - s$ units of time, before transiting to $X(t)$ with a transition probability $p_{j \leftarrow i}(t - s) = p_{j \leftarrow i}(\Delta t)$. We call the time it takes for a process to transit from a state i to a state j the holding time or the interevent time. In general, for any two consecutive states i_n and i_{n+1}, a continuous time process in state i_n at

time t_n will remain at i_n for time $t_{n+1} - t_n$, before transiting to i_{n+1}. We denote the interevent time between i_n and i_{n+1} as T_n. For a CTMC, the memoryless property of the stochastic process along with time homogeneity forces the interevent times to also be memoryless. To show this, for $s, t \in T$, consider the conditional probability that $T_n > s + t$ given that $T_n > s$,

$$\text{Prob}(T_n > s + t \mid T_n > s).$$

For $T_n > s$, the process will remain in state i_n at any time $t_n + u$ while $0 \leq u \leq s$, so $X(t_n + u) = i_n$ for $0 \leq u \leq s$. Also, for $T_n > s + t$, the process will remain in state i_n at any time $t_n + u$ while $0 \leq u \leq s + t$, so $X(t_n + u) = i_n$ for $0 \leq u \leq s + t$. We want to show that

$$\text{Prob}(T_n > s + t \mid T_n > s) = \text{Prob}(T_n > t).$$

For $T_n > t$, the process will remain in state i_n at any time $t_n + u$ while $0 \leq u \leq t$, so $X(t_n + u) = i_n$ for $0 \leq u \leq t$. The conditional probability that $T_n > s + t$ given that $T_n > s$ is therefore

$$\text{Prob}(T_n > s + t \mid T_n > s)$$
$$= \text{Prob}(X(t_n + u) = i_n : 0 \leq u \leq s + t \mid X(t_n + u) = i_n : 0 \leq u \leq s).$$

Let A be the event that $X(t_n + u) = i_n$ for $0 \leq u \leq s$ and B be the event that $X(t_n + u) = i_n$ for $s \leq u \leq s + t$. The occurrence of both A and B, that is, $A \cap B$, is the event that $X(t_n + u) = i_n$ for $0 \leq u \leq s + t$. From the definition of conditional probability, we can show the property

$$\text{Prob}(A \cap B \mid A) = \text{Prob}(B \mid A).$$

Therefore, we have

$$\text{Prob}(T_n > s + t \mid T_n > s)$$
$$= \text{Prob}(X(t_n + u) = i_n : s \leq u \leq s + t \mid X(t_n + u) = i_n : 0 \leq u \leq s).$$

Using the Markov property, the conditional probability simplifies to

$$\text{Prob}(T_n > s + t \mid T_n > s) = \text{Prob}(X(t_n + u) = i_n : s \leq u \leq s + t \mid X(t_n + s) = i_n).$$

Since the random process is time homogeneous

$$\text{Prob}(T_n > s + t \mid T_n > s) = \text{Prob}(X(t_n + u) = i_n : 0 \leq u \leq t \mid X(t_n) = i_n),$$

and so

$$\text{Prob}(T_n > s + t \mid T_n > s) = \text{Prob}(X(t_n + u) = i_n : 0 \leq u \leq t)$$
$$= \text{Prob}(T_n > t).$$

This shows that T_n has a distribution with the memoryless property, which implies that T_n is exponentially distributed [26]. Let $\text{Prob}(T_n > t) = H_n(t)$, we have

$$H_n(t) = e^{-\lambda_n t},$$

where $\lambda_n > 0$ is the rate parameter. The cumulative distribution function $F_n(t)$ is given by

$$F_n(t) = 1 - e^{-\lambda_n t}.$$

3.1.1 GENERATOR MATRICES

A continuous time Markov chain can be exactly described by the probabilities of transitioning from one state to another and the mean times spent in each state. The probabilities of transitioning from one state to another form an embedded discrete time Markov chain as shown in Figure 9. The mean time spent in each state gives the exponential distribution for the interevent times. Next we show how to use the infinitesimal transition probabilities $p_{j \leftarrow i}(\Delta t)$ to form the embedded DTMC and find the mean interevent times.

To begin, we form the generator matrix Q of transition rates $q_{j \leftarrow i}$ as the one-sided derivatives of the infinitesimal transition probabilities at $\Delta t = 0$. Using Allen's approach [3] to
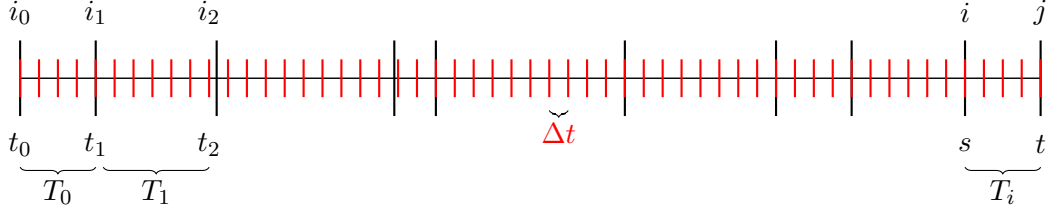
Figure 9. Embedded Discrete Time Process

An illustration of an embedded discrete time process in a continuous time process.

obtain the transition rates, we assume the probabilities $p_{j \leftarrow i}(\Delta t)$ are continuous and differentiable at $\Delta t \geq 0$. There are no transitions in a time period of $\Delta t = 0$ and so

$$p_{j \leftarrow i}(0) = 0, \quad i \neq j,$$

and

$$p_{j \leftarrow i}(0) = 1, \quad i = j.$$

To find the rates $q_{j \leftarrow i}$ when $i \neq j$, we compute

$$q_{j \leftarrow i} = \lim_{\Delta t \to 0^+} \frac{p_{j \leftarrow i}(\Delta t) - p_{j \leftarrow i}(0)}{\Delta t} = \lim_{\Delta t \to 0^+} \frac{p_{j \leftarrow i}(\Delta t)}{\Delta t}.$$

In this case, we have $\sum_{j=0}^{N} p_{j \leftarrow i}(\Delta t) = 1$, and it follows that

$$1 - p_{i \leftarrow i}(\Delta t) = \sum_{\substack{j=0, \\ j \neq i}}^{N} p_{j \leftarrow i}(\Delta t).$$

Therefore, we have

$$q_{i \leftarrow i} = \lim_{\Delta t \to 0^+} \frac{p_{i \leftarrow i}(\Delta t) - 1}{\Delta t} = \lim_{\Delta t \to 0^+} \frac{-\sum_{j \neq i} p_{j \leftarrow i}(\Delta t)}{\Delta t} = -\sum_{\substack{j=0, \\ j \neq i}}^{N} q_{j \leftarrow i}.$$

The relation between the infinitesimal transition probabilities $p_{j \leftarrow i}$ and the transition

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rates $q_{j \leftarrow i}$ is often expressed as

$$p_{j \leftarrow i}(\Delta t) = q_{j \leftarrow i} \cdot \Delta t + o(\Delta t), \quad i \neq j$$

and

$$p_{i \leftarrow i}(\Delta t) - 1 = q_{i \leftarrow i} \cdot \Delta t + o(\Delta t),$$

where a quantity $e(\Delta t)$ is $o(\Delta t)$ if it satisfies [18]

$$\lim_{\Delta t \to 0^+} \frac{e(\Delta t)}{\Delta t} = 0.$$

The rates $q_{j \leftarrow i}$ are used to form the generator matrix

$$Q = \begin{pmatrix} q_{0 \leftarrow 0} & q_{0 \leftarrow 1} & \cdots & q_{0 \leftarrow i} & \cdots & q_{0 \leftarrow N} \\ q_{1 \leftarrow 0} & q_{1 \leftarrow 1} & \cdots & q_{1 \leftarrow i} & \cdots & q_{1 \leftarrow N} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ q_{j \leftarrow 0} & q_{j \leftarrow 1} & \cdots & q_{j \leftarrow i} & \cdots & q_{j \leftarrow N} \\ \vdots & \vdots & \ddots & \vdots & \ddots & \vdots \\ q_{N \leftarrow 0} & q_{N \leftarrow 1} & \cdots & q_{N \leftarrow i} & \cdots & q_{N \leftarrow N} \end{pmatrix}.$$

Using the generator matrix, the probability of transitioning from state i to state j for the embedded DTMC is calculated as

$$\frac{q_{j \leftarrow i}}{\sum_{i \neq j} q_{j \leftarrow i}}. \tag{3.2}$$

In the embedded DTMC, the probability of transitioning from i to i is 0. The mean of the exponential interevent time in state i is

$$\frac{-1}{q_{i \leftarrow i}},$$

meaning $-q_{i \leftarrow i} = \lambda_i$ is the rate of the exponential distribution of the time for state i.
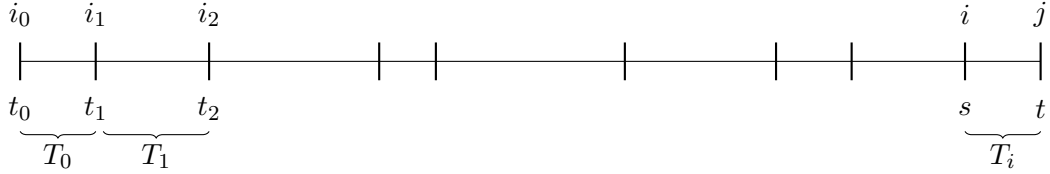
Figure 10. Trajectory of a Continuous Time SIS Model

A trajectory of a CTMC SIS model showing transition states and non-uniform holding times between consecutive state transitions.

3.2 SIS EPIDEMIC MODELS USING CONTINUOUS TIME MARKOV CHAINS

In formulating SIS epidemic models using continuous time Markov chains, we follow Allen's approach [2]. The model uses the two compartments: susceptible and infectious. Let $S(t)$ and $I(t)$ denote discrete random variables counting the numbers of susceptible and infectious persons at any instant of time $t \in [0, \infty)$ with $S(t), I(t) \in \{0, 1, 2, ..., N\}$. We make the assumption that the population is constant through the observed time and so $N = S(t) + I(t)$. The process is univariate, and at any time t we have $S(t) = N - I(t)$. For the continuous time SIS epidemic model, we define a trajectory as a sequence U of states with the holding times

$$U = (i_0, T_0, i_1, T_1, \ldots, i, T_i, j).$$

This implies that the system started at a state i_0. Then, after a period of T_0 units of time, the system transitioned to i_1, stayed at i_1 for a period of T_1 units of time, and then transitioned to the next state i_2, and so on. Figure 10 shows the trajectory of a continuous time Markov chain SIS model.

The infinitesimal transition probabilities of the embedded discrete time Markov chain are valid for sufficiently small Δt. If $I(t) = i$ only one of the following transitions can occur:

$$i \xrightarrow{\Delta t} i+1, \quad i \xrightarrow{\Delta t} i-1 \quad \text{or} \quad i \xrightarrow{\Delta t} i.$$

Since a constant population is assumed, for every change in time the number of infectious

increases by one, reduces by one or there is no change in the number of infectious. If the number of infectious increases by one, the susceptible compartment loses one person and the infectious compartment gains the loss. If the number of infectious reduces by one, the susceptible compartment gains one person. A recovery can mean a decrease in the number of infectious individuals.

3.2.1   TRANSITION PROBABILITIES OF A CTMC SIS EPIDEMIC MODEL

For a simple CTMC SIS epidemic model, we assume a similar contact structure as in the DTMC SIS epidemic model. The contact structure is frequency dependent. We also assume there is homogeneous mixing of the population, and given that the transmission rate β is greater than 0, the infinitesimal probability of transiting from i to $i+1$ is

$$p_{i+1\leftarrow i}(\Delta t) = \frac{\beta i(N-i)}{N}\Delta t + o(\Delta t).$$

If $\gamma > 0$ is the recovery rate, the number of individuals recovering at any time t is given by $\gamma I(t)$, and therefore the infinitesimal probability of transition from i to $i-1$ is

$$p_{i-1\leftarrow i}(\Delta t) = \gamma i \Delta t + o(\Delta t).$$

The sum of the probabilities of all possible transitions must add up to one. So, the infinitesimal probability that there is no change in the number of infected is

$$p_{i\leftarrow i}(\Delta t) = 1 - \left[\frac{\beta i(N-i)}{N} + \gamma i\right]\Delta t + o(\Delta t).$$

Combining the probabilities of the three different possible transitions with time, the transition probability of the embedded discrete time SIS epidemic model is then given by

$$
p_{j \leftarrow i}(\Delta t) = \begin{cases} \dfrac{\beta i(N-i)}{N} \Delta t + o(\Delta t), & j = i+1 \\[2ex] \gamma i \Delta t + o(\Delta t), & j = i-1 \\[2ex] 1 - \left[\dfrac{\beta i(N-i)}{N} + \gamma i \right] \Delta t + o(\Delta t), & j = i \\[2ex] o(\Delta t), & \text{otherwise.} \end{cases}
$$

This can be represented as [2]

$$
p_{j \leftarrow i}(\Delta t) = \begin{cases} b(i) \Delta t + o(\Delta t), & j = i+1 \\[2ex] d(i) \Delta t + o(\Delta t), & j = i-1 \\[2ex] 1 - [b(i) + d(i)] \Delta t + o(\Delta t), & j = i \\[2ex] o(\Delta t), & \text{otherwise.} \end{cases}
$$

We use these probabilities to compute the transition rates and then form the infinitesimal generator matrix

$$
Q = \begin{pmatrix} 0 & d(1) & 0 & \dots & 0 & 0 \\ 0 & -[b(1)+d(1)] & d(2) & \dots & 0 & 0 \\ 0 & b(1) & -[b(2)+d(2)] & \dots & 0 & 0 \\ 0 & 0 & b(2) & \dots & 0 & 0 \\ \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & 0 & \dots & d(N-1) & 0 \\ 0 & 0 & 0 & \dots & -[b(N-1)+d(N-1)] & d(N) \\ 0 & 0 & 0 & \dots & b(N-1) & -d(N) \end{pmatrix}.
$$

We use Equation 3.2 to find the transition probabilities of the embedded DTMC SIS model. From the generator matrix Q, the probability of transiting from i to $i+1$ (susceptible to infectious) is

$$\frac{b(i)}{b(i) + d(i)},$$

where $b(i) = \dfrac{\beta s i}{N}$ and $d(i) = \gamma i$. Therefore the probability of a new infection is

$$\frac{\left(\dfrac{\beta s i}{N}\right)}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

Similarly, the probability of transiting from i to $i-1$ (infectious to susceptible) is

$$\frac{d(i)}{b(i) + d(i)}.$$

Therefore the probability of a recovery is

$$\frac{\gamma i}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

The rate for the exponential interevent time for state i is

$$b(i) + d(i) = \frac{\beta s i}{N} + \gamma i.$$

3.2.2   PSEUDOCODE FOR CTMC SIS MODELS AND SIMULATED EXAMPLE

Given all parameters and initial conditions, we can plot a graph of the SIS epidemic model in continuous time, comparing the changes in the number of infectious individuals against time. Using Allen's approach [2], the algorithm of the code is given as follows:

1. Initialize the values of β, γ, the population size N, and the time duration of the outbreak t_{end}.

2. Create arrays $S(j)$, $I(j)$, and $t(j)$. Set $j = 1$ and $t(1) = 0$. Let $I(1)$ be the initial number of

infectious individuals and $S(1) = N - I(1)$.

3. While $I(j) > 0$ and $t(j) < t_{end}$,

   (a) Let $a = \dfrac{\beta S(j) I(j)}{N}$ and $b = \gamma I(j)$.

   (b) Compute the probability of a new infection (p_1) using $\dfrac{a}{a+b}$.

   (c) Compute the probability of a recovery from infection (p_2) using $\dfrac{b}{a+b}$.

   (d) Select two random numbers u_1 and u_2 from a uniform distribution of (0,1).

   (e) Compare u_1 with p_1 and p_2.

   (f) If $0 < u_1 \leq p_1$, decrease the number of susceptible individuals by 1, and increase the number of infectious individuals by 1. Hence $S(j+1) = S(j) - 1$ and $I(j+1) = I(j) + 1$.

   (g) Otherwise, $p_1 < u_1 \leq 1$. In this case, increase the number of susceptible individuals by 1, and decrease the number of infectious individuals by 1. Hence $S(j+1) = S(j) + 1$ and $I(j+1) = I(j) - 1$.

   (h) Select the time of the next event using u_2 as $t(j+1) = t(j) - \dfrac{\ln(u_2)}{a+b}$.

   (i) Update the vector index j to $j+1$ and repeat.

4. Plot the graph of the times $t(j)$ against the number of infectious at each time, $I(j)$.

In the algorithm, u_1 is used to determined which event occurred and u_2 is used to determine the time of occurrence. In the computation of the holding time, we can convert a uniform random variable, $u \in (0,1)$, to an exponentially distributed random number using a probability integral transform. The cumulative distribution function of the holding time is

$$F_i(t) = 1 - e^{-\lambda_i t}.$$

Since $F_i(F_i^{-1}(u)) = u$, then

$$1 - e^{-\lambda_i F_i^{-1}(u)} = u,$$

$$e^{-\lambda_i F_i^{-1}(u)} = 1 - u,$$
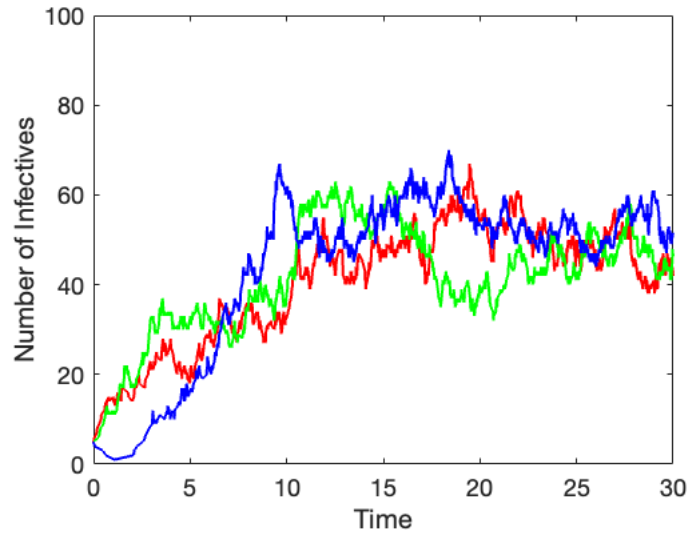
Figure 11. A CTMC SIS Epidemic Model

Simulations of a CTMC SIS Epidemic Model with three different stochastic paths using parameters $N = 100$, $I(1) = 5$, $\beta = 1$ and $\gamma = 0.5$.

$$F_i^{-1}(u) = -\frac{\ln{(1-u)}}{\lambda_i},$$

$$F_i^{-1}(u) = -\frac{\ln{(u)}}{\lambda_i}.$$

Therefore, for any u from a uniform random variable on $(0,1)$,

$$T_i = F_i^{-1}(u) = -\frac{\ln{(u)}}{\lambda_i}.$$

We simulate an example of a CTMC SIS epidemic model. We use a population of 100 people with 5 people initially infected. We use the transmission rate $\beta = 1$ and the recovery rate $\gamma = 0.5$. The graph of the time against the number of infectious individuals is presented in Figure 11.

3.3 SIR EPIDEMIC MODELS USING CONTINUOUS TIME MARKOV CHAINS

In the formulation of a CTMC SIR epidemic model, we define a new random variable $R(t)$ counting the number of recovered persons to the compartments of a CTMC SIS epidemic model.
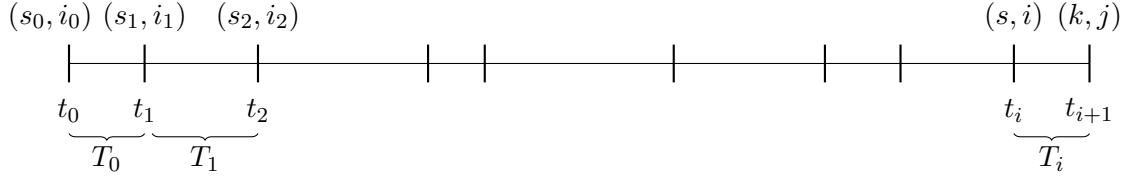
Figure 12. Trajectory of a Continuous Time SIR Model

A trajectory of a CTMC SIR model showing transition states and non-uniform holding times between consecutive states.

There are three compartments in this model: susceptible, infectious and recovered. The assumption of a constant population still holds for the observation and so, at any time t,

$$N = S(t) + I(t) + R(t).$$

The recovered class depends on the susceptible and the infectious class. The process is bivariate with

$$R(t) = N - S(t) - I(t).$$

We can define a trajectory U for the continuous time SIR model as a sequence of states with holding times

$$U = ((s_0, i_0), T_0, (s_1, i_1), T_1, \ldots, (s, i), T_i, (k, j)).$$

This implies that the system started at a state (s_0, i_0). Then, after T_0 units of time, the system transitioned to (s_1, i_1). The system stayed at state (s_1, i_1) for T_1 units of time and then transitioned to the next state (s_2, i_2), and so on.

The infinitesimal transition probabilities are valid for sufficiently small Δt, so for the bivariate process with random variables $(S(t), I(t))$ only one of the following transitions can occur:

$$(s, i) \xrightarrow{\Delta t} (s - 1, i + 1), \quad (s, i) \xrightarrow{\Delta t} (s, i - 1) \quad \text{or} \quad (s, i) \xrightarrow{\Delta t} (s, i).$$

Since a constant population is assumed, for every change in time the number of infectious increases by one, the number of recovered increases by one or no change happens. If the number of infectious increases by one, the susceptible compartment loses one person. If the number of

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recovered increases by one, the infectious compartment loses one person. Figure 12 shows the trajectory of a CTMC SIR model.

3.3.1 TRANSITION PROBABILITIES OF A CTMC SIR EPIDEMIC MODEL

The same contact structure and homogeneous mixing of the population as in the SIR DTMC model is assumed. The probability of a new infection, that is, transiting from (s, i) to $(s - 1, i + 1)$, is

$$p_{(s-1,i+1)\leftarrow(s,i)}(\Delta t) = \frac{\beta si}{N}\Delta t + o(\Delta t).$$

The probability of a recovery, that is, transiting from (s, i) to $(s, i - 1)$, is

$$p_{(s,i-1)\leftarrow(s,i)}(\Delta t) = \gamma i \Delta t + o(\Delta t).$$

The probability that the number of infectious and recovered remains unchanged is

$$p_{(s,i)\leftarrow(s,i)}(\Delta t) = 1 - \left[\frac{\beta si}{N} + \gamma i\right]\Delta t + o(\Delta t).$$

The transition probabilities of the embedded discrete time SIR epidemic model are

$$p_{(s+k,i+j)\leftarrow(s,i)}(\Delta t) = \begin{cases} \dfrac{\beta si}{N}\Delta t + o(\Delta t), & (k, j) = (-1, 1) \\[2mm] \gamma i \Delta t + o(\Delta t), & (k, j) = (0, -1) \\[2mm] 1 - \left[\dfrac{\beta si}{N} + \gamma i\right]\Delta t + o(\Delta t), & (k, j) = (0, 0) \\[2mm] o(\Delta t), & \text{otherwise.} \end{cases}$$

For simplification, this is denoted as

$$p_{(s+k,i+j)\leftarrow(s,i)}(\Delta t) = \begin{cases} b(i)\Delta t + o(\Delta t), & (k, j) = (-1, 1) \\[2mm] d(i)\Delta t + o(\Delta t), & (k, j) = (0, -1) \\[2mm] 1 - [b(i) + d(i)]\Delta t + o(\Delta t), & (k, j) = (0, 0) \\[2mm] o(\Delta t), & \text{otherwise.} \end{cases}$$

We use Equation 3.2 to find the transition probabilities of the embedded DTMC SIR model. From the generator matrix Q, the probability of transiting from (s, i) to $(s - 1, i + 1)$ (susceptible to infectious) is

$$\frac{\left(\dfrac{\beta s i}{N}\right)}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

Also, the probability of transiting from (s, i) to $(s, i - 1)$ (infectious to recovered) is

$$\frac{\gamma i}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

The rate for the exponential interevent time for state i is

$$b(i) + d(i) = \frac{\beta s i}{N} + \gamma i.$$

3.3.2   PSEUDOCODE FOR CTMC SIR MODELS AND SIMULATED EXAMPLE

Provided all parameters and initial conditions are given, we can plot a graph of the SIR epidemic model comparing the changes in the number of infectious individuals against time. The algorithm of the code is as follows:

1. Initialize the values of β, γ, population size N, and the time duration of the outbreak t_{end}.

2. Create arrays $S(j)$, $I(j)$, $R(j)$ and $t(j)$. Set $j = 1$, $R(1) = 0$ and $t(1) = 0$. Let $I(1)$ be the initial number of infectious individuals and $S(1) = N - I(1)$.

3. While $I(j) > 0$ and $t(j) < t_{end}$

    (a) Let $a = \dfrac{\beta S(j) I(j)}{N}$ and $b = \gamma I(j)$.

    (b) Compute the probability of a new infection (p_1) using $\dfrac{a}{a + b}$.

    (c) Compute the probability of a recovery from infection (p_2) using $\dfrac{b}{a + b}$.

    (d) Select two random numbers u_1 and u_2 from a uniform distribution of $(0, 1)$.

    (e) Compare u_1 with p_1 and p_2.

(f) If $0 < u_1 \leq p_1$, decrease the number of susceptible individuals by 1, and increase the number of infectious individuals by 1. Hence we have

$$S(j+1) = S(j) - 1, \quad I(j+1) = I(j) + 1, \quad \text{and } R(j+1) = R(t).$$

(g) Otherwise, $p_1 < u_1 < 1$. In this case, decrease the number of infectious individuals by 1, and increase the number of recovered individuals by 1. Hence we have

$$S(j+1) = S(j), \quad I(j+1) = I(j) - 1, \quad \text{and } R(j+1) = R(t) + 1.$$

(h) Select the time of the next event using u_2 as $t(j+1) = t(j) - \dfrac{\ln(u_2)}{a+b}$.

(i) Update the vector index j to $j+1$ and repeat.

4. Plot the graph of the times $t(j)$ against the number of infectious at each time, $I(j)$.

We simulate an example of a CTMC SIR epidemic model. We use a population of 100 people with 5 people initially infected. We use the transmission rate $\beta = 1$ and the recovery rate $\gamma = 0.5$. The graph of the time against the number of infectious individuals is presented in Figure 13.
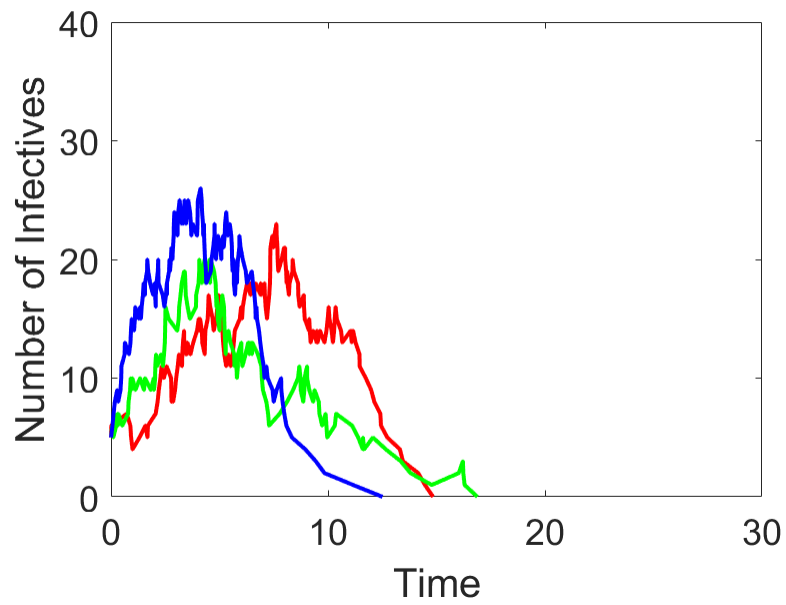
Figure 13. A CTMC SIR Epidemic Model

Simulations of a CTMC SIR epidemic model with three stochastic paths using parameters $N = 100$, $I(1) = 5$, $\beta = 1$ and $\gamma = 0.5$.

CHAPTER 4

METHOD OF MAXIMUM LIKELIHOOD

For independent random variables $X(0) = x_0$, $X(1) = x_1$, $\ldots$, $X(n) = x_n$ with joint density function $p(X(0), X(1), \ldots X(n) \mid \theta)$ with parameter θ, the likelihood function is

$$L(\theta) = L(\theta \mid x_0, x_1, \ldots, x_n) = p(x_0, x_1, \ldots, x_n \mid \theta) = \prod_{i=0}^{n} p(x_i \mid \theta).$$

For a Markov process, the transition probabilities are not independent. The transition probability to a new state depends on the current state. Assuming the transition probabilities depend on a parameter θ, the likelihood function of a Markov process is the product of the transition conditional probabilities,

$$L(\theta) = p(x_n \mid x_{n-1}, \theta) p(x_{n-1} \mid x_{n-2}, \theta) \ldots p(x_1 \mid x_0, \theta) p(x_0) = p(x_0) \prod_{i=1}^{n} p(x_i \mid x_{i-1}, \theta). \qquad (4.1)$$

The maximum likelihood estimate (MLE) $\hat{\theta}$ is the value of θ that maximizes $L(\theta)$. For computational convenience, we maximize the logarithm of the likelihood function by finding the value of θ that satisfies the equation

$$\frac{\partial \log L(\theta)}{\partial \theta} = 0.$$

Given some observed data, the MLE may be difficult to obtain analytically from the likelihood function, and so a suitable optimization algorithm may be used to approximate the MLE. Many optimization algorithms are designed to minimize the output of a function. A general optimization technique is to minimize the negative logarithm of the likelihood function. This process is equivalent to maximizing the logarithm of the likelihood function. We use the `fminsearch` algorithm in Matlab to approximate the MLEs of β and γ.

4.1 PARAMETER ESTIMATION FOR DTMC SIS MODELS

Consider a discrete time SIS model with transition probabilities

$$
p_{j \leftarrow i}(\Delta t) = \begin{cases}
\dfrac{\beta i(N-i)}{N}\Delta t, & j = i+1 \\[2mm]
\gamma i \Delta t, & j = i-1 \\[2mm]
1 - \left[\dfrac{\beta i(N-i)}{N} + \gamma i\right]\Delta t, & j = i \\[2mm]
0, & \text{otherwise}.
\end{cases}
$$

The parameters β and γ can be estimated for sufficiently observed data. The likelihood function is

$$
L(\beta, \gamma) = P(X(t=0) = i_0) \prod_{i,j=0}^{N} p_{j \leftarrow i}^{n_{ji}},
$$

where $X(t=0)$ is the random variable representing the initial number of infectious persons, N is the population size and n_{ji} is count of transitions from i to j. The product runs through all possible transition probabilities given by the transition matrix. We set $p_{j \leftarrow i} = 0$ when a transition did not occur from state i to state j, that is, $n_{ji} = 0$, and let $0^0 = 1$. The initial number of infectious persons is known and so $P((X(t=0) = i_0) = 1$. The likelihood function from Equation 4.1 is

$$
L(\beta, \gamma) = \prod_{i=1}^{N} \left[(p_{i+1 \leftarrow i})^{n_{i+1,i}} (p_{i-1 \leftarrow i})^{n_{i-1,i}} (p_{i \leftarrow i})^{n_{i,i}} \right].
$$

The logarithm of a function is strictly increasing, so the logarithm of the likelihood function will be maximized exactly when the likelihood function is maximized. Taking the logarithm of the likelihood function converts the products to sums for easier computation. We have

$$
\log L(\beta, \gamma) = \sum_{i=1}^{N} \left[n_{i+1,i} \log\left(\frac{\beta i}{N}(N-i)\right) + n_{i-1,i} \log(\gamma i) + n_{i,i} \log\left(1 - \left(\gamma i + \frac{\beta i}{N}(N-i)\right)\right) \right].
$$

Taking the partial derivative of the logarithm of the likelihood function with respect to β, we have

$$
\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = \sum_{i=1}^{N} \left[(n_{i+1,i})\left(\frac{1}{\beta}\right) - \frac{(n_{i,i})i(N-i)}{(N - N\gamma i - \beta i(N-i))} \right].
$$

Also, taking the partial derivative of the logarithm of the likelihood function with respect to γ, we have

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = \sum_{i=1}^{N} \left[(n_{i-1,i}) \left(\frac{1}{\gamma} \right) - \frac{(n_{i,i})i}{(N - N\gamma i - \beta i(N - i))} \right].$$

The MLE of β is $\hat{\beta}$, the value β that satisfies the equation

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = 0.$$

The MLE of γ is $\hat{\gamma}$, the value γ that satisfies the equation

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = 0.$$

4.1.1   ESTIMATION ALGORITHM AND RESULTS FOR DTMC SIS MODELS

Given some observed data, the likelihood function can be computed using Matlab. For this algorithm, we need not count the number of transitions between any two consecutive states. We compute the probabilities for the likelihood function at any point in time using data from the simulated outbreak. We progress through the data in time steps to compute the likelihood function. The Matlab algorithm to compute the MLE of β and γ is:

1. Simulate an outbreak with known β and γ while discarding simulations with no infections at $t = 10$. Let k be the smaller of the first index when the I vector is 0 ($I(k) = 0$) or the length of the infectious vector.

2. The following steps are used to compute a function $l(\tilde{\beta}, \tilde{\gamma})$, where $\tilde{\beta}$ and $\tilde{\gamma}$ are parameters. The algorithm uses the vector I from step (1) and the population size N.

   (a) Initialize a vector p with length $k - 1$ for the transition probabilities.

   (b) For j from 2 to k in an increment of 1:

      i. If $I(j) = I(j - 1) + 1$, the number of susceptible individuals decreased by 1, and the number of infectious individuals increased by 1. Hence we have

$$p(j - 1) = \frac{\tilde{\beta}[N - I(j-1)]I(j-1)}{N} \Delta t.$$

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ii. If $I(j) = I(j-1) - 1$, the number of susceptible individuals increased by 1, and the number of infectious individuals decreased by 1. Hence we have

$$p(j-1) = \tilde{\gamma}I(j-1)\Delta t.$$

iii. Otherwise, we have $I(j) = I(j-1)$. In this case, the number of susceptible and infectious remains the same. Hence

$$p(j-1) = 1 - \left(\frac{\tilde{\beta}[N - I(j-1)]I(j-1)}{N} + \tilde{\gamma}I(j-1) \right) \Delta t.$$

(c) Let $l(\tilde{\beta}, \tilde{\gamma}) = -\sum_{j=1}^{k-1}(\log p(j))$. Hence l represents the negative of the logarithm of the likelihood function.

3. Use `fminsearch` on the function $l(\tilde{\beta}, \tilde{\gamma})$ to identify values of $\tilde{\beta}$ and $\tilde{\gamma}$ that minimize l starting with initial search values of $\tilde{\beta} = 0.1$ and $\tilde{\gamma} = 0.01$. This process produces approximations to the MLE values $\hat{\beta}$ and $\hat{\gamma}$, respectively.

4. Repeat steps (1) to (3) 10,000 times, and store the approximations to $\hat{\beta}$ and $\hat{\gamma}$ found in step (3) each time.

5. Plot the distribution of data from step (4).

We use the algorithm just described to computationally produce a distribution of the MLE values $\hat{\beta}$ and $\hat{\gamma}$. We use a discrete time SIS model with parameters $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$ for $\beta = 1.5$ and $\gamma = 0.5$ and for $\beta = 0.9$ and $\gamma = 0.3$. For 10,000 simulations, the histograms of $\hat{\beta}$ and $\hat{\gamma}$ are given in Figure 14 and in Figure 15, respectively, for the different values of β and γ. Simulations with infections dying out before $t = 10$ are discarded and the simulations are repeated. The discarded simulations did not reach endemic equilibrium, and therefore did not last long enough for the `fminsearch` algorithm to accurately determine $\hat{\beta}$ and $\hat{\gamma}$.

The number of repeated simulations is given in Table 2. From the histograms in Figure 14 and Figure 15, we see that the distributions of $\hat{\beta}$ and $\hat{\gamma}$ are normal and symmetric about the known values of β and γ.
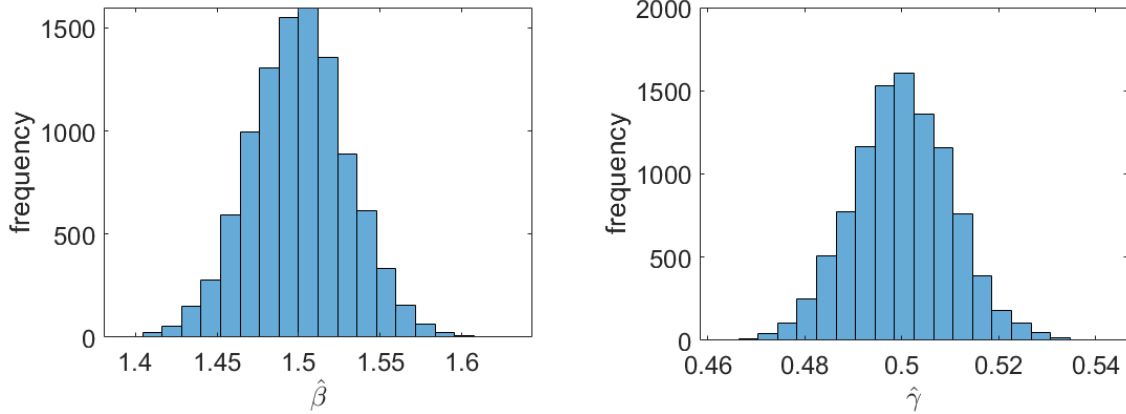
Figure 14. Histogram of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIS Model with $\beta = 1.5$ and $\gamma = 0.5$

Parameter estimation distribution of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIS model with $\beta = 1.5$ and $\gamma = 0.5$. Each distribution has 10,000 simulations with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$. Left panel: Parameter distribution of $\hat{\beta}$. Right panel: Parameter distribution of $\hat{\gamma}$.

Figure 15. Histogram of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIS Model with $\beta = 0.9$ and $\gamma = 0.3$

Parameter estimation distribution of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIS model with $\beta = 0.9$ and $\gamma = 0.3$. Each distribution has 10,000 simulations with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$. Left panel: Parameter distribution of $\hat{\beta}$. Right panel: Parameter distribution of $\hat{\gamma}$.
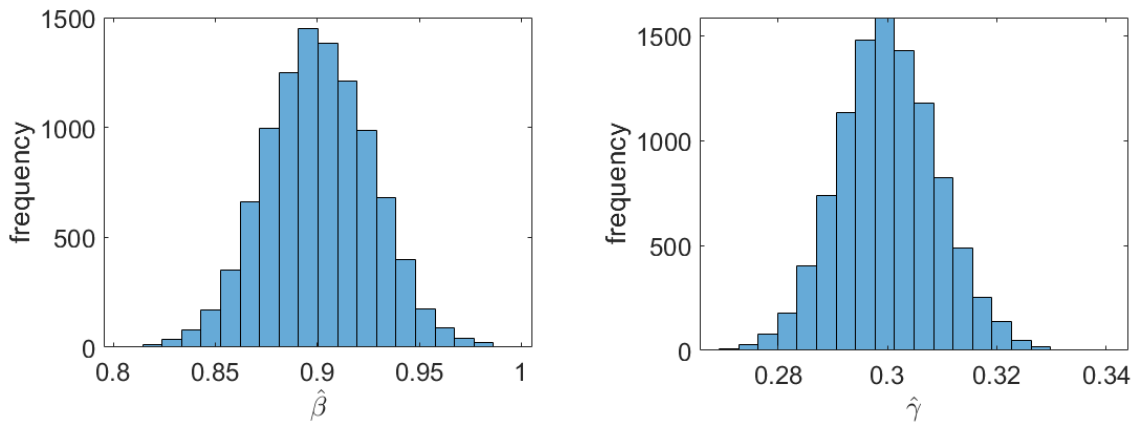
$\beta = 1.5$	$\gamma = 0.5$	$\beta = 0.9$	$\gamma = 0.3$	$\beta = 1.5$	$\gamma = 0.5$	$\beta = 0.9$	$\gamma = 0.3$
$\hat{\beta}$	$\hat{\gamma}$	$\hat{\beta}$	$\hat{\gamma}$	$\hat{\beta}$	$\hat{\gamma}$	$\hat{\beta}$	$\hat{\gamma}$
1.4962	0.5177	0.8669	0.3023	1.4900	0.5007	0.8875	0.3080
1.4980	0.4983	0.8852	0.3087	1.5303	0.5038	0.8785	0.3260
1.5413	0.4825	0.9029	0.3103	1.4910	0.4975	0.8922	0.2945
1.4911	0.5036	0.9389	0.2938	1.4963	0.4909	0.9309	0.3038
1.4947	0.5064	0.8786	0.3037	1.5217	0.4924	0.9158	0.2875
1.4622	0.5102	0.9112	0.2978	1.5587	0.4950	0.9202	0.2980
1.4841	0.5140	0.8869	0.2962	1.5018	0.4954	0.9312	0.3042
1.4627	0.5109	0.9075	0.3057	1.4914	0.5077	0.9365	0.3077
1.4851	0.4889	0.8914	0.2963	1.4709	0.5010	0.8791	0.3108
1.4984	0.4995	0.9087	0.3029	1.5203	0.5051	0.9206	0.2971

Table 1. Simulation Parameter Estimates for a DTMC SIS Model

Parameter estimations of $\hat{\beta}$ and $\hat{\gamma}$ for simulations of DTMC SIS model with $\beta = 1.5$ and $\gamma = 0.5$ (left) and with $\beta = 0.9$ and $\gamma = 0.3$ (right). All simulations are performed with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$.

For the two pairs of β and γ, 20 estimates of $\hat{\beta}$ and $\hat{\gamma}$ are presented in Table 1. The bias and MSE are presented in Table 2. The bias and MSE are small and so the MLE gives good estimates of β and γ.

Known values	$\beta = 1.5$	$\gamma = 0.5$	$\beta = 0.9$	$\gamma = 0.3$
	$\hat{\beta}$	$\hat{\gamma}$	$\hat{\beta}$	$\hat{\gamma}$
Bias	0.2485×10^{-3}	0.1545×10^{-3}	0.7072×10^{-3}	0.1104×10^{-3}
MSE	0.9019×10^{-3}	0.1054×10^{-3}	0.6850×10^{-3}	0.0787×10^{-3}
Number of Repeated simulations	48		60	

Table 2. Computational Results for a DTMC SIS Model

Computational results of $\hat{\beta}$ and $\hat{\gamma}$ for simulations of DTMC SIS model with $\beta = 1.5$ and $\gamma = 0.5$ (left) and $\beta = 0.9$ and $\gamma = 0.3$ (right). Computational results for 10,000 simulations of discrete time SIS model with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$.

4.2 PARAMETER ESTIMATION FOR DTMC SIR MODELS

Consider a discrete time SIR model with transition probabilities

$$p_{(k,j)\leftarrow(s,i)}(\Delta t) = \begin{cases} \dfrac{\beta s i}{N}\Delta t, & (k,j) = (s-1, i+1) \\[2mm] \gamma i \Delta t, & (k,j) = (s, i-1) \\[2mm] 1 - \left[\dfrac{\beta s i}{N} + \gamma i\right]\Delta t, & (k,j) = (s,i) \\[2mm] 0, & \text{otherwise.} \end{cases}$$

As with the SIS model, we can estimate parameters β and γ. The likelihood function is

$$L(\beta, \gamma) = P(X(t=0) = (s_0, i_0)) \prod_{i,j,s,k=0}^{N} (p_{(k,j)\leftarrow(s,i)})^{n_{(k,j)(s,i)}},$$

where $n_{(k,j)(s,i)}$ is the transition count from state (s,i) to state (k,j). The likelihood function is

$$L(\beta, \gamma) = \prod_{i=1}^{N}\prod_{s=0}^{N}(p_{(s-1,i+1)\leftarrow(s,i)})^{n_{(s-1,i+1),(s,i)}}(p_{(s,i-1)\leftarrow(s,i)})^{n_{(s,i-1),(s,i)}}(p_{(s,i)\leftarrow(s,i)})^{n_{(s,i),(s,i)}}.$$

Taking the logarithm of the likelihood function, we have

$$\log L(\beta, \gamma) = \sum_{i=1}^{N}\sum_{s=0}^{N}\left[n_{(s-1,i+1),(s,i)}\log\left(\frac{\beta s i}{N}\right) + n_{(s,i-1),(s,i)}\log(\gamma i)\right.$$
$$\left. + n_{(s,i),(s,i)}\log\left(1 - \left[\frac{\beta s i}{N} + \gamma i\right]\right)\right].$$

Taking the partial derivative of the logarithm of the likelihood function with respect to β, we have

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = \sum_{i=1}^{N}\sum_{s=0}^{N}\left[n_{(s-1,i+1),(s,i)}\left(\frac{1}{\beta}\right) - \frac{n_{(s,i),(s,i)}s i}{(N - N\gamma i - \beta s i)}\right].$$

Also, taking the partial derivative of the logarithm of the likelihood function with respect to γ, we have

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = \sum_{i=1}^{N}\sum_{s=0}^{N}\left[(n_{i-1,i})\left(\frac{1}{\gamma}\right) - \frac{(n_{i,i})i}{(N - N\gamma i - \beta s i)}\right].$$

We denote the MLE of β as $\hat{\beta}$, the value of β that satisfies the equation

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = 0.$$

We denote the MLE of γ as $\hat{\gamma}$, the value γ that satisfies the equation

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = 0.$$

4.2.1 ESTIMATION ALGORITHM AND RESULTS FOR DTMC SIR MODELS

Given some observed data, the likelihood function can also be obtained using Matlab. For this algorithm, we need not count the number of transitions between any two consecutive states. We progress through the data in time steps to get the likelihood function. The Matlab algorithm of the MLE of β and γ is given as follows:

1. Simulate an outbreak with known β and γ while discarding simulations with no infections at $t = 7$. Let k be the smaller of the first index when the I vector is 0 ($I(k) = 0$) or the length of the infectious vector.

2. The following steps are used to compute a function $l(\tilde{\beta}, \tilde{\gamma})$, where $\tilde{\beta}$ and $\tilde{\gamma}$ are parameters. The algorithm uses the vectors I and S from step (1) and the population size N.

   (a) Initialize a vector p for the transition probabilities with length $k - 1$.

   (b) For j from 2 to k in an increment of 1:

      i. If $I(j) = I(j-1) + 1$, the number of susceptible individuals decreased by 1, and the number of infectious individuals increased by 1. Hence we have

$$p(j-1) = \frac{\tilde{\beta} S(j-1) I(j-1)}{N} \Delta t.$$

      ii. If $I(j) = I(j-1) - 1$, the number of infectious individuals decreased 1, and the number of recovered individuals increased by 1. Hence we have

$$p(j-1) = \tilde{\gamma} I(j-1) \Delta t.$$

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iii. Otherwise, $I(j) = I(j-1)$. In this case, the numbers of susceptible, infectious and recovered remained the same. Hence we have

$$p(j-1) = 1 - \left(\frac{\tilde{\beta} S(j-1) I(j-1)}{N} + \tilde{\gamma} I(j-1) \right) \Delta t.$$

(c) Let $l(\tilde{\beta}, \tilde{\gamma}) = -\sum_{j=1}^{k-1} (\log p(j))$ where l is the negative of the logarithm of the likelihood function.

3. Use `fminsearch` on the function $l(\tilde{\beta}, \tilde{\gamma})$ to identify values of $\tilde{\beta}$ and $\tilde{\gamma}$ that minimize l starting with initial search values of $\tilde{\beta} = 0.1$ and $\tilde{\gamma} = 0.01$. This process produces approximations to the MLE values $\hat{\beta}$ and $\hat{\gamma}$, respectively.

4. Repeat steps (1) to (3) 10,000 times, and store the approximations to $\hat{\beta}$ and $\hat{\gamma}$ found in step (3) each time.

5. Plot the distribution of data from step (4).

We computationally produce a distribution for the MLE values of $\hat{\beta}$ and $\hat{\gamma}$, for a discrete time SIR model. We use parameters $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$ for $\beta = 1.5$ and $\gamma = 0.5$ and for $\beta = 0.9$ and $\gamma = 0.3$. For 10,000 simulations, the histograms of $\hat{\beta}$ and $\hat{\gamma}$ are given in Figure 16 and Figure 17. Simulations with infections dying out before $t = 7$ are discarded. The discarded simulations are presumed to not last long enough for `fminsearch` to accurately determine the values of $\hat{\beta}$ and $\hat{\gamma}$. The choice of which simulations to discard may be adjusted to increase the accuracy of the histogram. The choice of $t = 7$ in this simulation improved the accuracy of the histogram.

For the two pairs of β and γ, 20 estimates of $\hat{\beta}$ and $\hat{\gamma}$ are presented in Table 3. The bias, MSE and the number of repeated simulations are presented in Table 4. The histogram of $\hat{\gamma}$ for $\gamma = 0.5$ and $\gamma = 0.3$ is right skewed due to some simulations having the number of infectious dying out right after time $t = 7$. The bias and MSE are small, so the MLE gives a good estimate of β and γ.
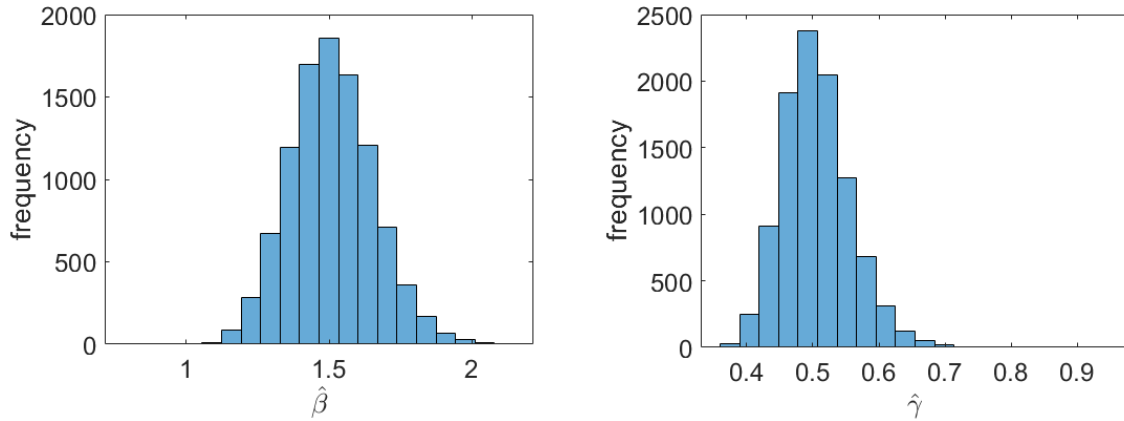
Figure 16. Histogram of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIR Model with $\beta = 1.5$ and $\gamma = 0.5$

Parameter estimation distribution of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIR model with $\beta = 1.5$ and $\gamma = 0.5$. Each distribution has 10,000 simulations with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\beta}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`.

Figure 17. Histogram of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIR Model with $\beta = 0.9$ and $\gamma = 0.3$

Parameter estimation distribution of $\hat{\beta}$ and $\hat{\gamma}$ for a DTMC SIR model with $\beta = 0.9$ and $\gamma = 0.3$. Each distribution has 10,000 simulations with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\beta}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`.
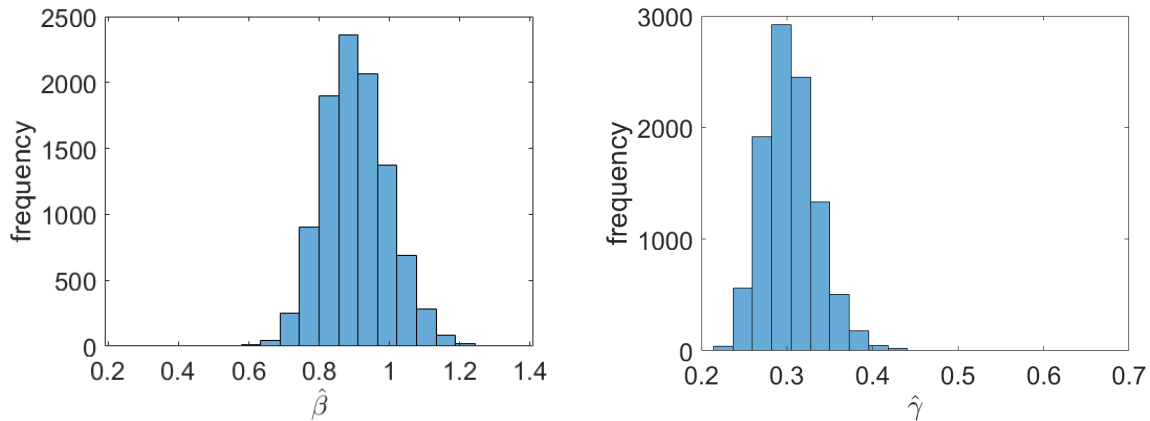
$\beta = 1.5$	$\gamma = 0.5$	$\beta = 0.9$	$\gamma = 0.3$
$\hat{\beta}$	$\hat{\gamma}$	$\hat{\beta}$	$\hat{\gamma}$
1.4633	0.5591	0.7789	0.3253
1.2879	0.4374	0.8381	0.2830
1.5262	0.4609	0.9281	0.2838
1.4284	0.5318	0.8760	0.3374
1.5316	0.5614	0.9036	0.2666
1.6757	0.5359	0.8930	0.2949
1.6276	0.4807	0.8867	0.2697
1.6627	0.4845	1.1176	0.2861
1.6689	0.4842	0.9544	0.2661
1.5112	0.4741	0.8565	0.2907
1.3503	0.5216	0.9925	0.3355
1.4809	0.4800	0.8543	0.3179
1.3747	0.5022	0.8397	0.3273
1.4969	0.4755	0.9436	0.3502
1.5238	0.4881	0.8017	0.3159
0.7832	0.7964	0.7801	0.3250
1.2235	0.5122	1.0029	0.2808
1.5345	0.4659	0.7896	0.3064
1.7693	0.4678	0.8152	0.2559
1.5651	0.4744	0.8291	0.3225

Table 3. Simulation Parameter Estimates for a DTMC SIR Model

Parameter estimations of $\hat{\beta}$ and $\hat{\gamma}$ for simulations of DTMC SIR model with $\beta = 1.5$ and $\gamma = 0.5$ (left) and $\beta = 0.9$ and $\gamma = 0.3$ (right). All simulations are performed with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$.

Known values	$\beta = 1.5$	$\gamma = 0.5$	$\beta = 0.9$	$\gamma = 0.3$
	$\hat{\beta}$	$\hat{\gamma}$	$\hat{\beta}$	$\hat{\gamma}$
Bias	0.0083	0.0058	0.0060	0.0041
MSE	0.0217	0.0027	0.0087	0.0011
Number of Repeated simulations	59		60	

Table 4. Computational Results for a DTMC SIR Model

Computational results of $\hat{\beta}$ and $\hat{\gamma}$ for simulations of DTMC SIR model with $\beta = 1.5$ and $\gamma = 0.5$ (left) and $\beta = 0.9$ and $\gamma = 0.3$ (right). Computational results for 10,000 simulations with $N = 100$, $I(0) = 5$, $\Delta t = 0.01$ and $t = 50$.
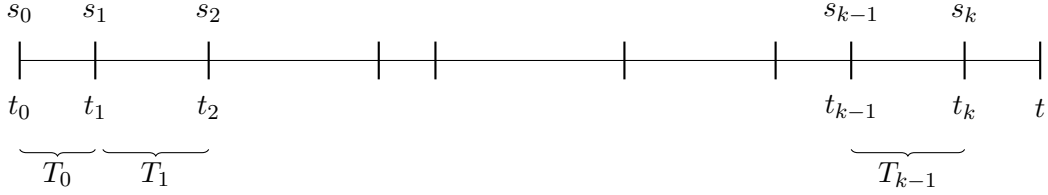
Figure 18. Estimating Maximum Likelihood for Continuous Time SIS Model

Illustration of a continuous time stochastic process observed between t_0 units of time and t units of time.

4.3 PARAMETER ESTIMATION FOR CTMC SIS MODELS

We follow the approach of Perkins [23]. Consider a CTMC SIS model with trajectory

$$U = (s_0, T_0, s_1, T_1, ..., s_{k-1}, T_{k-1}, s_k),$$

The system starts at state s_0 at t_0 units of time and enters the last state s_k at t_k units of time as shown in Figure 18. There are a total of k transitions in this process. At any given time, all observations occur within the time interval (t_0, t) where $t \geq t_k$, and there is no transition in the interval (t_k, t).

The likelihood function is

$$L(\beta, \gamma) = \prod_{i=0}^{k-1} (\lambda_{s_i} e^{-\lambda_{s_i} T_i})(p_{s_{i+1} \leftarrow s_i})(e^{-\lambda_{s_k}(t - \sum_{i=0}^{k-1} T_i)}),$$

where $\lambda_{s_i} e^{-\lambda_{s_i} T_i}$ is the probability of the holding time T_i in state s_i, $p_{s_{i+1} \leftarrow s_i}$ is the probability of transiting from state s_i to s_{i+1} and $e^{-\lambda_{s_k}(t - \sum_{i=0}^{k-1} T_i)}$ is the probability that no additional transitions occur after time s_k up to time t. We observe that $\sum_{i=0}^{k-1} T_i = t_k$. Let $t - t_k = T_k$, so that

$$e^{-\lambda_{s_k}(t - \sum_{i=0}^{k-1} T_i)} = e^{-\lambda_{s_k}(T_k)},$$

and

$$L(\beta, \gamma) = e^{-\lambda_{s_k}(T_k)} \prod_{i=0}^{k-1} (\lambda_{s_i} e^{-\lambda_{s_i} T_i})(p_{s_{i+1} \leftarrow s_i}).$$

For a continuous time SIS model, only two types of transitions can occur. Either a susceptible person becomes infected or an infected person becomes susceptible. For any transition from state s_i to state s_{i+1}, there is either a transition from i to $i+1$ or from i to $i-1$.

Let $\{t_{\beta_1}, t_{\beta_2}, ..., t_{\beta_n}\}$ be the set of times when there is a transition from i to $i+1$ and let $\{t_{\gamma_1}, t_{\gamma_2}, ..., t_{\gamma_m}\}$ be the set of times when there is a transition from i to $i-1$. This means that the first transition from i to $i+1$ in the system happened at time t_{β_1}, the first transition from i to $i-1$ in the system happened at time t_{γ_1} and so on. There are n transitions from i to $i+1$ and m transitions from i to $i-1$. There are a total of k transitions in the system from state s_0 up to state s_k.

From the generator matrix Q, the probability of transiting from i to $i+1$ (susceptible to infectious) is

$$p_{i+1 \leftarrow i} = \frac{b(i)}{b(i) + d(i)},$$

where $b(i) = \dfrac{\beta s i}{N}$ and $d(i) = \gamma i$. The probability of a new infection is

$$p_{i+1 \leftarrow i} = \frac{\left(\dfrac{\beta s i}{N}\right)}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

Similarly, the probability of transiting from i to $i-1$ (infectious to susceptible) is

$$p_{i-1 \leftarrow i} = \frac{d(i)}{b(i) + d(i)},$$

and so the probability of transiting from infectious to susceptible is

$$p_{i-1 \leftarrow i} = \frac{\gamma i}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

We split the state transition probabilities, $p_{s_{i+1} \leftarrow s_i}$, into the two possible cases of transitions:

from susceptible to infectious and infectious to susceptible. The likelihood function becomes

$$
\prod_{i=0}^{k-1}(\lambda_{s_i}e^{-\lambda_{s_i}T_i})(p_{s_{i+1}\leftarrow s_i}) =
$$

$$
\overbrace{\left[\prod_{a=t_{\beta_1}}^{t_{\beta_n}}\left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)\exp\left(-\left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)T_a\right)\left(\frac{\frac{\beta S(a)I(a)}{N}}{\frac{\beta S(a)I(a)}{N}+\gamma I(a)}\right)\right]}^{\text{susceptible to infectious}}
$$

$$
\underbrace{\times\left[\prod_{b=t_{\gamma_1}}^{t_{\gamma_m}}\left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)\exp\left(-\left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)T_b\right)\left(\frac{\gamma I(b)}{\frac{\beta S(b)I(b)}{N}+\gamma I(b)}\right)\right]}_{\text{infectious to susceptible}},
$$

where $S(a) = N - I(a)$ and $S(b) = N - I(b)$. The equation then simplifies to

$$
\prod_{i=0}^{k-1}(\lambda_{s_i}e^{-\lambda_{s_i}T_i})(p_{s_{i+1}\leftarrow s_i}) = \prod_{a=t_{\beta_1}}^{t_{\beta_n}}\left[\frac{\beta S(a)I(a)}{N}\exp\left(-\left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)T_a\right)\right]
$$

$$
\times\prod_{b=t_{\gamma_1}}^{t_{\gamma_m}}\left[\gamma I(b)\exp\left(-\left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)T_b\right)\right].
$$

The likelihood function can be written as

$$
L(\beta,\gamma) = \exp\left(-\left(\frac{\beta S(t_k)I(t_k)}{N}+\gamma I(t_k)\right)T_k\right)\prod_{b=t_{\gamma_1}}^{t_{\gamma_m}}\left[\gamma I(b)\exp\left(-\left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)T_b\right)\right]
$$

$$
\times\prod_{a=t_{\beta_1}}^{t_{\beta_n}}\left[\frac{\beta S(a)I(a)}{N}\exp\left(-\left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)T_a\right)\right],
$$

By taking the logarithm of the likelihood function, we have

$$
\log L(\beta,\gamma) = -\left(\frac{\beta S(t_k)I(t_k)}{N}+\gamma I(t_k)\right)T_k + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}}\left[\log(\gamma I(b)) - \left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)T_b\right]
$$

$$
+ \sum_{a=t_{\beta_1}}^{t_{\beta_n}}\left[\log\left(\frac{\beta S(a)I(a)}{N}\right) - \left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)T_a\right].
$$

Taking the partial derivative of the logarithm of likelihood function with respect to β, we have

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = \sum_{a=t_{\beta_1}}^{t_{\beta_n}} \left[\left(\frac{1}{\beta} \right) - \left(\frac{S(a)I(a)}{N} \right) T_a \right] + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}} \left[- \left(\frac{S(b)I(b)}{N} \right) T_b \right]$$
$$- \left(\frac{S(t_k)I(t_k)}{N} \right) T_k.$$

Distributing the sums, we have

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = - \left(\sum_{a=t_{\beta_1}}^{t_{\beta_n}} \left[\left(\frac{S(a)I(a)}{N} \right) T_a \right] + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}} \left[\left(\frac{S(b)I(b)}{N} \right) T_b \right] \right)$$
$$- \left[\frac{S(t_k)I(t_k)}{N} \right] T_k + \sum_{a=t_{\beta_1}}^{t_{\beta_n}} \left(\frac{1}{\beta} \right).$$

We combine the first two terms since together, they consist of all possible transitions from state s_0 up to state s_k, and so

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = - \left[\frac{S(t_k)I(t_k)}{N} \right] T_k + \sum_{a=t_{\beta_1}}^{t_{\beta_n}} \left(\frac{1}{\beta} \right) - \sum_{i=0}^{k-1} \left[\left(\frac{S(t_i)I(t_i)}{N} \right) T_i \right].$$

Adding the first term to the last term and since there is a total of n transitions from t_{β_1} to t_{β_n}

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = \frac{n}{\beta} - \sum_{i=0}^{k} \left[\left(\frac{S(t_i)I(t_i)}{N} \right) T_i \right].$$

The maximum likelihood estimate $\hat{\beta}$ is the value of β such that

$$\frac{\partial \log L(\beta, \gamma)}{\partial \beta} = 0.$$

Therefore, we have that

$$\hat{\beta} = \frac{n}{\displaystyle\sum_{i=0}^{k} \left[\frac{S(t_i)I(t_i)T_i}{N} \right]}. \tag{4.2}$$

Similarly, to obtain the maximum likelihood estimate $\hat{\gamma}$, we take the partial derivative of

the log likelihood function with respect to γ, obtaining

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = -I(t_k)T_k - \sum_{a=t_{\beta_1}}^{t_{\beta_n}} [I(a)T_a] + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}} \left[\frac{1}{\gamma} - I(b)T_b \right].$$

Distributing the sum, we have

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = -I(t_k)T_k + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}} \left(\frac{1}{\gamma} \right) - \left(\sum_{a=t_{\beta_1}}^{t_{\beta_n}} [I(a)T_a] + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}} [I(b)T_b] \right).$$

We combine the last two terms since together, both terms sum all possible times of transitions from state s_0 up to state s_k, and so

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = -I(t_k)T_k + \sum_{b=t_{\gamma_1}}^{t_{\gamma_m}} \left(\frac{1}{\gamma} \right) - \sum_{i=0}^{k-1} [I(i)T_i].$$

Adding the first term to the last term, and since there is a total of m transitions from t_{γ_1} to t_{γ_m}

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = \frac{m}{\gamma} - \sum_{i=0}^{k} [I(i)T_i].$$

The maximum likelihood estimate $\hat{\gamma}$, is the value of γ such that

$$\frac{\partial \log L(\beta, \gamma)}{\partial \gamma} = 0,$$

therefore, we have that

$$\hat{\gamma} = \frac{m}{\sum_{i=0}^{k} [I(t_i)T_i]}. \tag{4.3}$$

4.3.1   ESTIMATION ALGORITHM AND RESULTS FOR CTMC SIS MODELS

The likelihood function for simulated data can be approximated using Matlab. We use `fminsearch` and the theoretical formulas Equation 4.2 and Equation 4.3 to compute the maximum likelihood estimate of β and γ. The Matlab algorithm is:

1. Simulate an outbreak with known β and γ while discarding simulations with no infectious

individuals at $t = 10$. Let k be the smaller of the first index when the I vector is 0 ($I(k) = 0$) or the length of the infectious vector.

2. The following steps are used to compute a function $l(\tilde{\beta}, \tilde{\gamma})$, where $\tilde{\beta}$ and $\tilde{\gamma}$ are parameters. The algorithm uses the vector I and t from step (1) and the population size N.

(a) Initialize counters n and m as $n = 0$ and as $m = 0$ for counting transitions from $I(j)$ to $I(j) + 1$ and from $I(j)$ to $I(j) - 1$, respectively.

(b) Initialize a vector p of length $k - 1$ for the transition probabilities.

(c) For j from 2 to k in an increment of 1:

    i. Calculate the interevent time between consecutive states using the time vector from the simulated outbreak as $T(j - 1) = t(j) - t(j - 1)$.

    ii. If $I(j) = I(j - 1) + 1$, the number of susceptible individuals decreased by 1, and the number of infectious individuals increased by 1. Hence we have

$$p(j - 1) = \left(\frac{\tilde{\beta}[N - I(j - 1)]I(j - 1)}{N} \right) \times$$
$$\exp\left(-\left(\frac{\tilde{\beta}[N - I(j - 1)]I(j - 1)}{N} + \tilde{\gamma}I(j - 1) \right) \right) T(j - 1),$$

and we increase the counter from n to $n + 1$.

    iii. Otherwise, $I(j) = I(j - 1) - 1$, so the number of susceptible individuals increased by 1, and the number of infectious individuals decreased by 1. Hence we have

$$p(j - 1) = (\tilde{\gamma}I(j - 1)) \times \exp\left(-\left(\frac{\tilde{\beta}[N - I(j - 1)]I(j - 1)}{N} + \tilde{\gamma}I(j - 1) \right) \right) T(j - 1),$$

and we increase the counter from m to $m + 1$.

(d) Let $l(\tilde{\beta}, \tilde{\gamma})$ be the negative log likelihood

$$l(\tilde{\beta}, \tilde{\gamma}) = \left[-\sum_{j=1}^{k-1} \log p(k) \right] - \left(\frac{\tilde{\beta}[N - I(k)]I(k)}{N} + \tilde{\gamma}I(k) \right) \cdot (t_{end} - t(k)),$$

where $t(k)$ is the time of the last event and t_{end} is the length of time of the outbreak.

3. Use `fminsearch` to identify values of $\tilde{\beta}$ and $\tilde{\gamma}$ that minimize l starting with initial search values of $\tilde{\beta} = 0.1$ and $\tilde{\gamma} = 0.01$. These values are our approximations of $\hat{\beta}$ and $\hat{\gamma}$.

4. Use Equation 4.2 and Equation 4.3 with m and n to find the theoretical MLE of β and γ.

5. Store the approximations of $\hat{\beta}$ and $\hat{\gamma}$ from step (3) and the theoretical values from step (4).

6. Repeat steps (1) through (5) 10,000 times.

7. Plot the distribution of the data from step (6).

We computationally produce a distribution for the MLE values of $\hat{\beta}$ and $\hat{\gamma}$, for a continuous time SIS model. We use parameters $N = 100$, $I(1) = 5$ and $t = 50$ for $\beta = 1.5$ and $\gamma = 0.5$ and for $\beta = 0.9$ and $\gamma = 0.3$. For 10,000 simulations, the histograms of $\hat{\beta}$ are given in Figure 19 and Figure 21. The histograms for $\hat{\gamma}$ are given in Figure 20 and Figure 22. Simulations with infections dying out before $t = 10$ are repeated.

For the two pairs of β and γ, 20 estimates of $\hat{\beta}$ and $\hat{\gamma}$ obtained using `fminsearch` and the theoretical formulas are presented in Table 5. The bias, MSE and the number of repeated simulations are presented in Table 6 and Table 7. From the histograms of the MLEs, we see that the distributions of $\hat{\beta}$ and $\hat{\gamma}$ are normal and symmetric about the known values of β and γ. The bias and MSE are small, so the MLE gives a good estimate of β and γ.

4.4 PARAMETER ESTIMATION FOR CTMC SIR MODELS

For a continuous time SIR model, the MLEs are derived in a similar manner to the continuous time SIS model. The likelihood function is

$$L(\beta, \gamma) = e^{-\lambda_{s_k}(T_k)} \prod_{i=0}^{k-1} (\lambda_{s_i} e^{-\lambda_{s_i} T_i})(p_{s_{i+1} \leftarrow s_i}).$$

For a continuous time SIR model, only two types of transitions can occur. Either a susceptible person becomes infected or an infected person recovers. For any transition from state s_i to state s_{i+1}, there is either a transition from (s, i) to $(s - 1, i + 1)$ (susceptible to infectious) or from (s, i) to $(s, i - 1)$ (infectious to recovered).
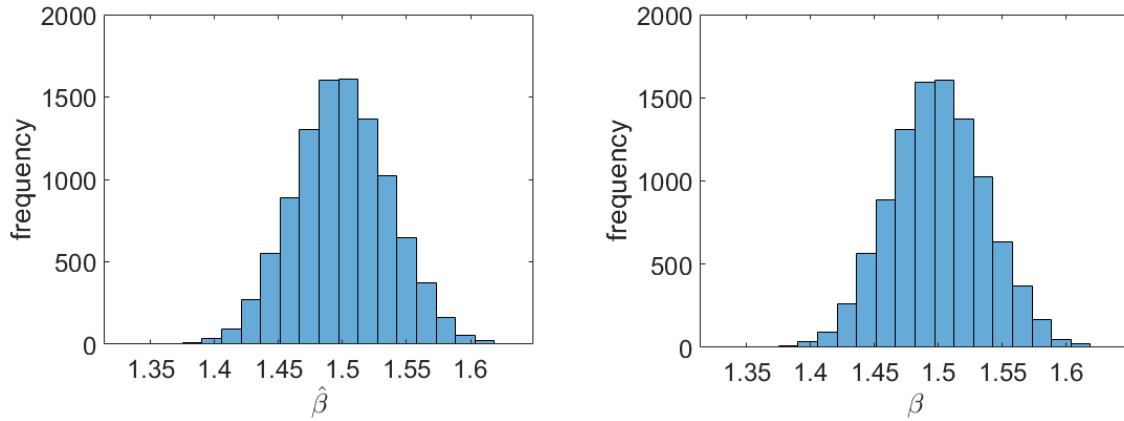
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Figure 19. Histogram of $\hat{\beta}$ for a CTMC SIS Model with $\beta = 1.5$ and $\gamma = 0.5$

Parameter estimation distribution of $\hat{\beta}$ for a CTMC SIS model with $\beta = 1.5$ and $\gamma = 0.5$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\beta}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\beta}$ using theoretical estimates.

Figure 20. Histogram of $\hat{\gamma}$ for a CTMC SIS Model with $\beta = 1.5$ and $\gamma = 0.5$

Parameter estimation distribution of $\hat{\gamma}$ for a CTMC SIS model with $\beta = 1.5$ and $\gamma = 0.5$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using theoretical estimates.
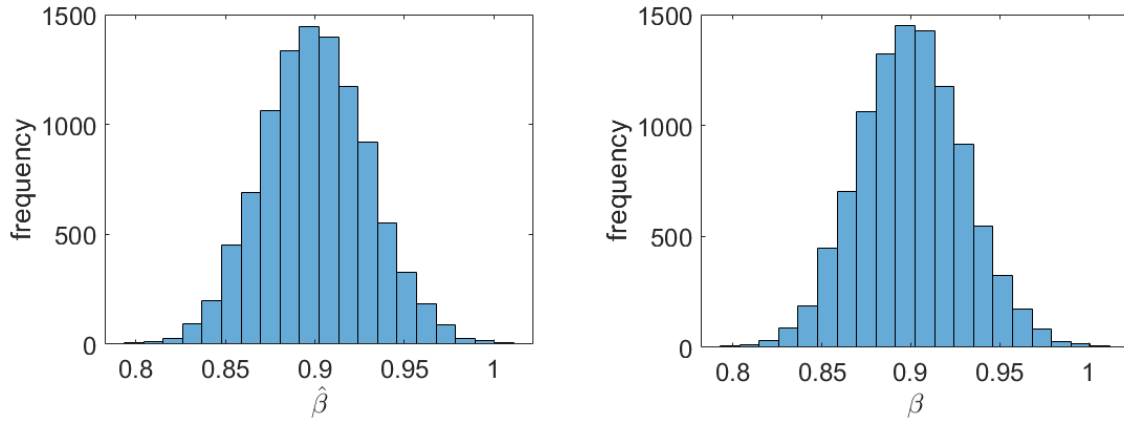
Figure 21. Histogram of $\hat{\beta}$ for a CTMC SIS Model with $\beta = 0.9$ and $\gamma = 0.3$

Parameter estimation distribution of $\hat{\beta}$ for a CTMC SIS model with $\beta = 0.9$ and $\gamma = 0.3$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using theoretical estimates.
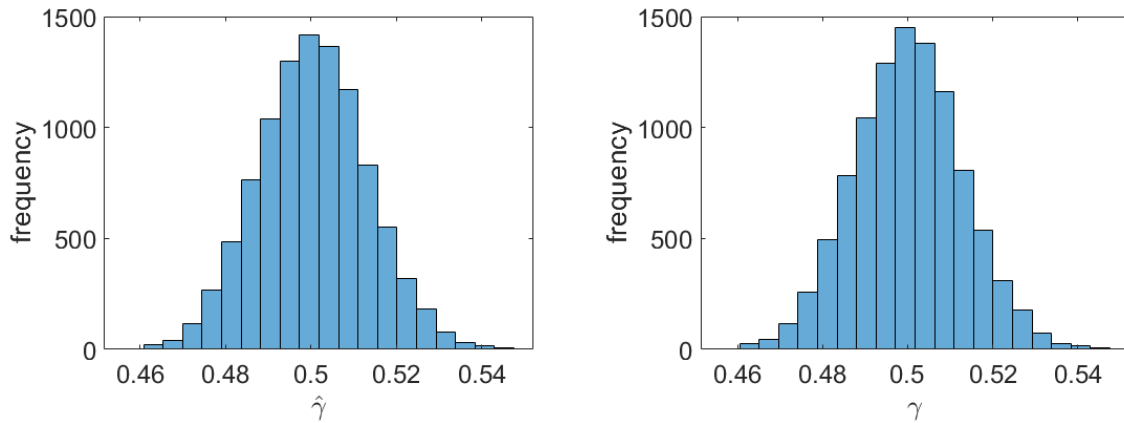

Figure 22. Histogram of $\hat{\gamma}$ for a CTMC SIS Model with $\beta = 0.9$ and $\gamma = 0.3$

Parameter estimation distribution of $\hat{\gamma}$ for a CTMC SIS model with $\beta = 0.9$ and $\gamma = 0.3$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using theoretical estimates.
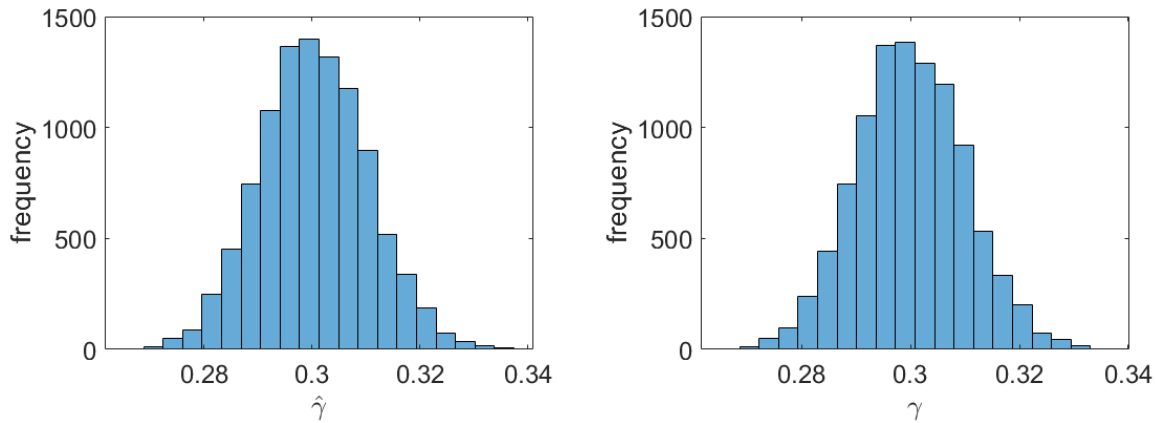
$\beta = 1.5$		$\gamma = 0.5$		$\beta = 0.9$		$\gamma = 0.3$	
$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$	$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$
1.4522	1.4524	0.5006	0.5002	0.8591	0.8598	0.2936	0.2935
1.5399	1.5404	0.4774	0.4764	0.8910	0.8895	0.3099	0.3095
1.5113	1.5121	0.4925	0.4921	0.9411	0.9407	0.3160	0.3160
1.5135	1.5135	0.5173	0.5173	0.8783	0.8793	0.2768	0.2767
1.5244	1.5252	0.4900	0.4894	0.8874	0.8883	0.2940	0.2938
1.5148	1.5147	0.5111	0.5112	0.8568	0.8565	0.2841	0.2841
1.4694	1.4703	0.4952	0.4949	0.9116	0.9111	0.3206	0.3206
1.4799	1.4805	0.5009	0.5006	0.8721	0.8717	0.2943	0.2943
1.4761	1.4766	0.4787	0.4783	0.8727	0.8733	0.2962	0.2956
1.4809	1.4812	0.5055	0.5049	0.9104	0.9099	0.2978	0.2975
1.4295	1.4300	0.5039	0.5033	0.9292	0.9292	0.3014	0.3010
1.5412	1.5418	0.4988	0.4983	0.9104	0.9098	0.3063	0.3054
1.4836	1.4826	0.4952	0.4950	0.8901	0.8900	0.3021	0.3023
1.4908	1.4905	0.5168	0.5170	0.9559	0.9553	0.3012	0.3013
1.5157	1.5156	0.5022	0.5021	0.8737	0.8726	0.2977	0.2976
1.5384	1.5375	0.5032	0.5032	0.9174	0.9165	0.3128	0.3127
1.4619	1.4626	0.5222	0.5217	0.9044	0.9039	0.2824	0.2825
1.4518	1.4514	0.4725	0.4726	0.8735	0.8734	0.3054	0.3039
1.4921	1.4930	0.5096	0.5094	0.8644	0.8649	0.3051	0.3048
1.5359	1.5359	0.5053	0.5053	0.9290	0.9297	0.2967	0.2965

Table 5. Simulation Parameter Estimates for a CTMC SIS Model

All simulations are performed with $N = 100$, $I(1) = 5$ and $t = 50$.

Known values	$\beta = 1.5$		$\gamma = 0.5$	
	$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$
Bias	0.6029×10^{-3}	0.0361	0.5303×10^{-3}	0.0169
MSE	0.0014	0.0027	0.0002	0.0004
Number of Repeated simulations	50			

Table 6. Computational Results for a CTMC SIS Model with $\beta = 1.5$ and $\gamma = 0.5$

Computational results for 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$.

Known values	$\beta = 0.9$		$\gamma = 0.3$	
	$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$
Bias	-0.2547×10^{-3}	0.0187	0.5441×10^{-3}	0.0046
MSE	0.8401×10^{-3}	0.0012	0.1000×10^{-3}	0.0001
Number of Repeated Simulations	45			

Table 7. Computational Results for a CTMC SIS Model with $\beta = 0.9$ and $\gamma = 0.3$

Computational results for 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$.

Let $\{t_{\beta_1}, t_{\beta_2}, ..., t_{\beta_n}\}$ be the set of times when there is a transition from i to $i+1$ and let $\{t_{\gamma_1}, t_{\gamma_2}, ..., t_{\gamma_m}\}$ be the set of times when there is a transition from i to $i-1$. This means that the first transition from i to $i+1$ in the system happened at time t_{β_1}, the first transition from i to $i-1$ in the system happened at time t_{γ_1} and so on. There are n transitions from i to $i+1$ and m transitions from i to $i-1$. There are a total of k transitions in the system from state s_0 up to state s_k.

The probability of transiting from (s, i) to $(s-1, i+1)$ (susceptible to infectious) is

$$p_{(s-1,i+1)\leftarrow(s,i)} = \frac{\left(\dfrac{\beta s i}{N}\right)}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

Also, the probability of transiting from (s, i) to $(s, i-1)$ (infectious to recovered) is

$$p_{(s,i-1)\leftarrow(s,i)} = \frac{\gamma i}{\left(\dfrac{\beta s i}{N} + \gamma i\right)}.$$

We split the state transition probabilities, $p_{s_{i+1}\leftarrow s_i}$, into the two possible types of state transitions in an SIR model. Transition can be from susceptible to infectious or from infectious to recovered.

The likelihood function becomes

$$\prod_{i=0}^{k-1}(\lambda_{s_i}e^{-\lambda_{s_i}T_i})(p_{s_{i+1}\leftarrow s_i}) =$$

$$\overbrace{\left[\prod_{a=t_{\beta_1}}^{t_{\beta_n}}\left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)\exp\left(-\left(\frac{\beta S(a)I(a)}{N}+\gamma I(a)\right)T_a\right)\left(\frac{\frac{\beta S(a)I(a)}{N}}{\frac{\beta S(a)I(a)}{N}+\gamma I(a)}\right)\right]}^{\text{susceptible to infectious}}$$

$$\underbrace{\times\left[\prod_{b=t_{\gamma_1}}^{t_{\gamma_m}}\left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)\exp\left(-\left(\frac{\beta S(b)I(b)}{N}+\gamma I(b)\right)T_b\right)\left(\frac{\gamma I(b)}{\frac{\beta S(b)I(b)}{N}+\gamma I(b)}\right)\right]}_{\text{infectious to recovered}},$$

where $S(a) = N - I(a) - R(a)$ and $S(b) = N - I(b) - R(b)$. In finding the MLEs, we follow the same steps as in the continuous time SIS, and we obtain $\hat{\beta}$ as

$$\hat{\beta} = \frac{n}{\sum_{i=0}^{k}\left[\frac{S(t_i)I(t_i)T_i}{N}\right]}, \tag{4.4}$$

and $\hat{\gamma}$ as

$$\hat{\gamma} = \frac{m}{\sum_{i=0}^{k}[I(t_i)T_i]}. \tag{4.5}$$

4.4.1 ESTIMATION ALGORITHM AND RESULTS FOR CTMC SIR MODELS

For simulated data, the likelihood function can be obtained using Matlab. We use `fminsearch` and the theoretical formulas Equation 4.4 and Equation 4.5 to find the maximum likelihood estimate of β and γ. The Matlab algorithm is given as follows:

1. Simulate an outbreak with known β and γ while discarding simulations with no infectious at $t = 9$. Let k be the smaller of the first index when the I vector is 0 ($I(k) = 0$) or the length of the infectious vector.

2. The following steps are used to compute a function $l(\tilde{\beta}, \tilde{\gamma})$, where $\tilde{\beta}$ and $\tilde{\gamma}$ are parameters.

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The algorithm uses the vector I and t from step (1) and the population size N.

(a) Initialize counters n and m as $n = 0$ and $m = 0$ for counting transitions from $I(j)$ to $I(j) + 1$ and from $I(j)$ to $I(j) - 1$, respectively.

(b) Initialize a vector p of length $k - 1$ for the transition probabilities.

(c) For j from 2 to k in an increment of 1:

    i. Calculate the interevent time between consecutive states using the time array from the simulated outbreak as $T(j - 1) = t(j) - t(j - 1)$.

    ii. If $I(j) = I(j - 1) + 1$, the number of susceptible individuals decreased by 1, and the number of infectious individuals increased by 1. Hence we have

$$p(j-1) = \left(\frac{\tilde{\beta} S(j-1) I(j-1)}{N} \right) \exp\left(-\left(\frac{\tilde{\beta} S(j-1) I(j-1)}{N} + \gamma I(j-1) \right) \right) T(j-1)$$

    and we increase the counter from n to $n + 1$.

    iii. Otherwise $I(j) = I(j - 1) - 1$, the number of infectious individuals decreased by 1, and the number of recovered individuals increased by 1. Hence we have

$$p(j - 1) = \gamma I(j - 1) \exp\left(-\left(\frac{\tilde{\beta} [S(j-1)] I(j-1)}{N} + \tilde{\gamma} I(j-1) \right) \right) T(j - 1),$$

    and we increase the counter from m to $m + 1$.

(d) Let $l(\tilde{\beta}, \tilde{\gamma})$ be the negative log likelihood

$$l(\tilde{\beta}, \tilde{\gamma}) = \left[-\sum_{j=1}^{k-1} \log p(j) \right] + \left(-\left(\frac{\tilde{\beta} S(k) I(k)}{N} + \tilde{\gamma} I(k) \right) \right) \cdot (t_{end} - t(k))$$

where $t(k)$ is the last event and t_{end} is the length of time of the outbreak.

3. Use `fminsearch` to identify values of $\tilde{\beta}$ and $\tilde{\gamma}$ that minimize l starting with initial search values of $\beta = 0.1$ and $\gamma = 0.01$. The final values of $\tilde{\beta}$ and $\tilde{\gamma}$ will be our approximations to $\hat{\beta}$ and $\hat{\gamma}$, respectively.

4. Use Equation 4.5 and Equation 4.4 with m and n to find the theoretical MLE of β and γ.

5. Store the approximations of $\hat{\beta}$ and $\hat{\gamma}$ from step (3) and the theoretical values from step (4).

6. Repeat steps (1) through (5) 10,000 times.

7. Plot the distribution of the data from step (6).

We find the MLEs $\hat{\beta}$ and $\hat{\gamma}$ for a continuous time SIR model using `fminsearch` and the theoretical MLE formulas Equation 4.4 and Equation 4.5, respectively. We simulate a continuous time SIR model with parameters $N = 100$, $I(1) = 5$ and $t = 50$ for $\beta = 1.5$ and $\gamma = 0.5$ and for $\beta = 0.9$ and $\gamma = 0.3$. For 10,000 simulations, the histograms of $\hat{\beta}$ are given in Figure 23 and Figure 25 while the histograms of $\hat{\gamma}$ are given in Figure 24 and Figure 26. Simulations with infections dying out at $t = 7$ are repeated for simulations with $\beta = 1.5$ and $\gamma = 0.5$. Simulations with infections dying out at $t = 9$ are repeated for simulations with $\beta = 0.9$ and $\gamma = 0.3$.

For the two pairs of β and γ, 20 estimates of $\hat{\beta}$ and $\hat{\gamma}$ obtained using `fminsearch` and the theoretical formulas are presented in Table 8. The bias and MSE are presented in Table 9 and Table 10. The histograms of $\hat{\gamma}$ for $\gamma = 0.5$ and $\gamma = 0.3$ are right skewed due to some simulations having the number of infectious dying out right after time $t = 7$ (or $t = 9$). The time constraint may be increased to allow only simulations that last long enough to predict β and γ. The bias and MSE are small, so the MLE gives a good estimate of β and γ.
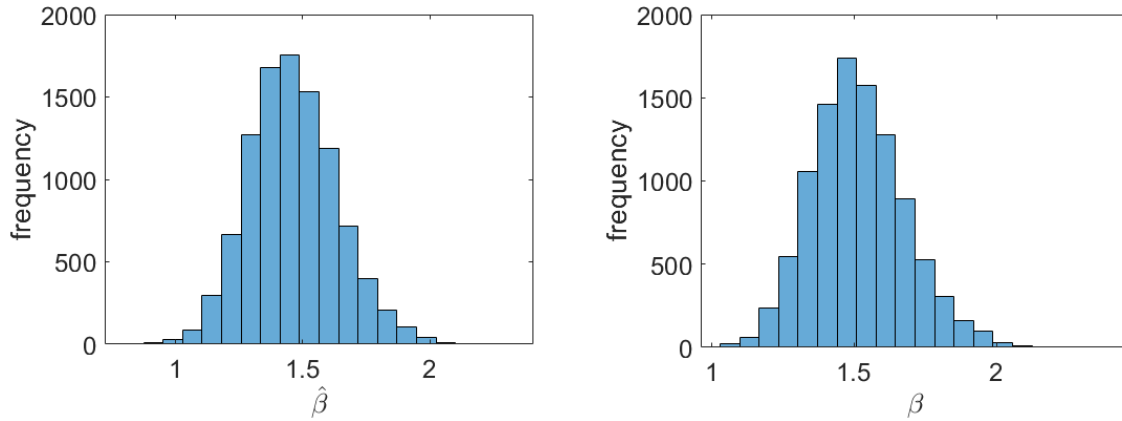
Figure 23. Histogram of $\hat{\beta}$ for a CTMC SIR Model with $\beta = 1.5$ and $\gamma = 0.5$

Parameter estimation distribution of $\hat{\beta}$ for a CTMC SIR model with $\beta = 1.5$ and $\gamma = 0.5$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\beta}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\beta}$ using theoretical estimates.
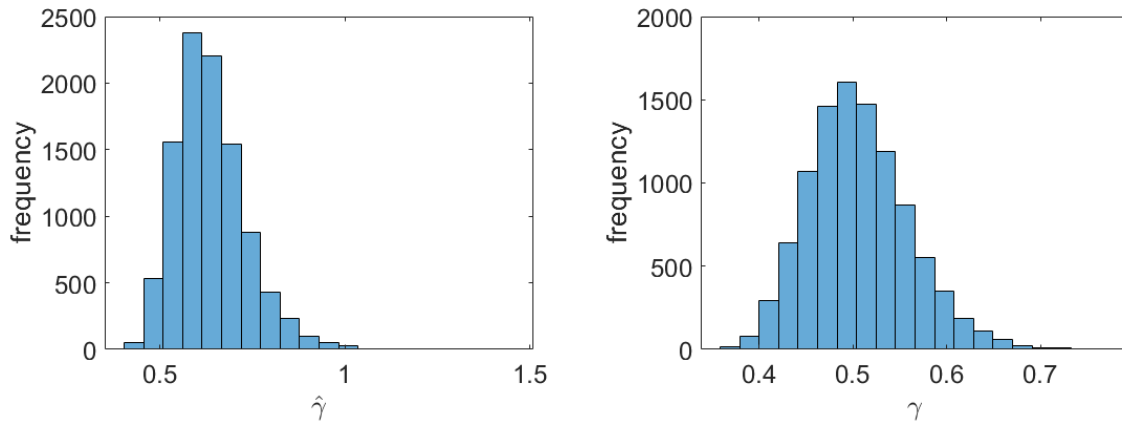

Figure 24. Histogram of $\hat{\gamma}$ for a CTMC SIR Model with $\beta = 1.5$ and $\gamma = 0.5$

Parameter estimation distribution of $\hat{\gamma}$ for a CTMC SIR model with $\beta = 1.5$ and $\gamma = 0.5$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using theoretical estimates.
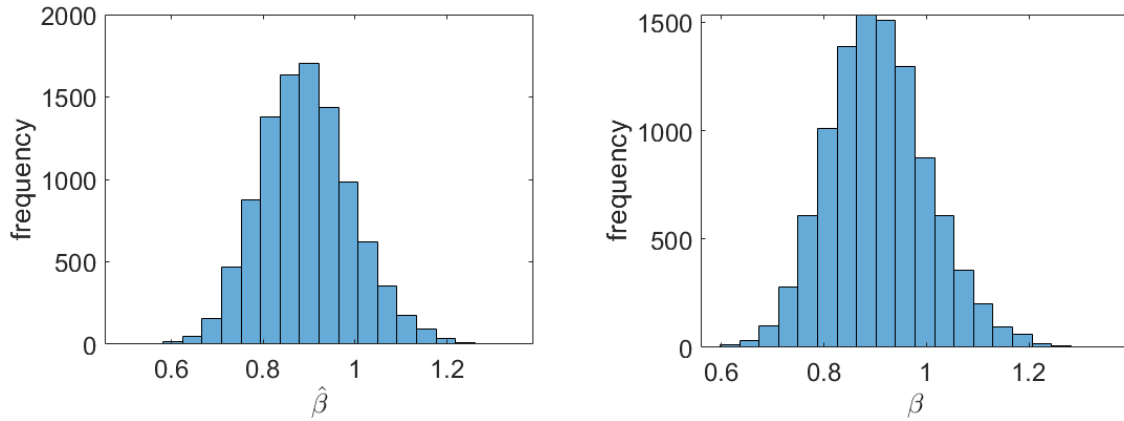
Figure 25. Histogram of $\hat{\beta}$ for a CTMC SIR Model with $\beta = 0.9$ and $\gamma = 0.3$

Parameter estimation distribution of $\hat{\beta}$ for a CTMC SIR model with $\beta = 0.9$ and $\gamma = 0.3$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\beta}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\beta}$ using theoretical estimates.

Figure 26. Histogram of $\hat{\gamma}$ for a CTMC SIR Model with $\beta = 0.9$ and $\gamma = 0.3$

Parameter estimation distribution of $\hat{\gamma}$ for a CTMC SIR model with $\beta = 0.9$ and $\gamma = 0.3$. Each distribution has 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$. Left panel: Parameter estimation distribution of $\hat{\gamma}$ using `fminsearch`. Right panel: Parameter estimation distribution of $\hat{\gamma}$ using theoretical estimates.
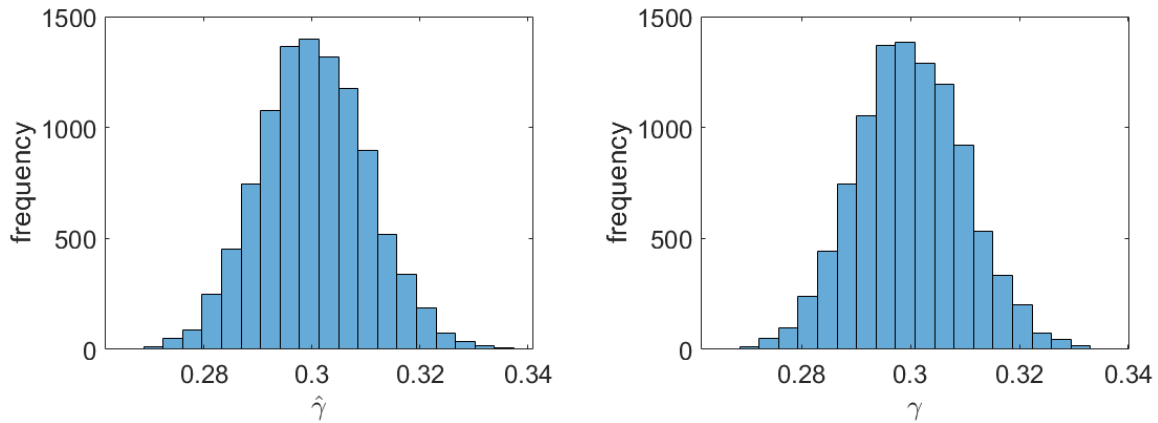
| β = 1.5 | | γ = 0.5 | | β = 0.9 | | γ = 0.3 | |
$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$	$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$
1.7428	1.7550	0.5171	0.4354	0.8892	0.8998	0.3570	0.3224
1.4552	1.4885	0.5192	0.4375	0.8338	0.8497	0.3335	0.3046
1.4008	1.4411	0.6393	0.5085	0.8571	0.8595	0.2753	0.2588
1.3492	1.3850	0.4775	0.4095	0.9494	0.9601	0.3277	0.3010
1.3213	1.3805	0.6281	0.5163	0.8495	0.8687	0.3545	0.3200
1.5680	1.6086	0.6607	0.5244	0.7703	0.7768	0.2697	0.2476
1.7140	1.7373	0.4758	0.4054	0.8451	0.8705	0.3595	0.3268
1.7136	1.7485	0.5850	0.4837	0.7937	0.8104	0.33201	0.3046
1.4325	1.4941	0.6208	0.4942	0.7923	0.8076	0.3291	0.3009
1.4730	1.5110	0.5763	0.4874	0.7715	0.7910	0.3785	0.3415
1.2484	1.2705	0.5198	0.4433	0.9420	0.9527	0.3555	0.3295
1.7468	1.7579	0.5171	0.4309	0.8796	0.8895	0.2907	0.2741
1.7136	1.7377	0.6328	0.5137	1.0995	1.1070	0.3330	0.2982
1.5640	1.6160	0.5470	0.4542	0.8160	0.8361	0.3834	0.3441
1.6864	1.6974	0.5714	0.4718	0.8322	0.8431	0.3176	0.2956
1.5315	1.5705	0.5602	0.4528	0.7607	0.7753	0.3027	0.2769
1.7573	1.7836	0.5937	0.4768	0.8772	0.8787	0.3044	0.2869
1.3245	1.3807	0.6570	0.5254	0.9978	1.0160	0.3597	0.3228
1.5227	1.5504	0.6453	0.5235	0.8028	0.8145	0.3013	0.2787
1.4305	1.4797	0.5761	0.4676	0.7542	0.7748	0.3449	0.3111

Table 8. Simulation Parameter Estimates for a CTMC SIR Model

All simulations are performed with $N = 100$, $I(1) = 5$ and $t = 50$.

Known values	β = 1.5		γ = 0.5	
	$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$
Bias	-0.0375	0.1877	0.1372	-0.0230
MSE	0.0318	0.0621	0.0281	0.0034
Number of Repeated Simulations	52			

Table 9. Computational Results for a CTMC SIR Model with $\beta = 1.5$ and $\gamma = 0.5$

Computational results for 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$.

Known values	$\beta = 0.9$		$\gamma = 0.3$	
	$\hat{\beta}_{\text{fminsearch}}$	$\hat{\beta}_{\text{theoretical}}$	$\hat{\gamma}_{\text{fminsearch}}$	$\hat{\gamma}_{\text{theoretical}}$
Bias	-0.0069	0.0816	0.0350	0.0117
MSE	0.0101	0.0162	0.0030	0.0012
Number of Repeated Simulations	84			

Table 10. Computational Results for a CTMC SIR Model with $\beta = 0.9$ and $\gamma = 0.3$

Computational results for 10,000 simulations with $N = 100$, $I(1) = 5$ and $t = 50$.

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APPENDIX A

APPROVAL LETTER

Office of Research Integrity

February 10, 2020

Oluwatobiloba Ige
2100 7th Ave. Apt 413
Huntington, WV 25703

Dear Oluwatobiloba:

This letter is in response to the submitted thesis abstract entitled *"Markov Chain Epidemic Models and Maximum Likelihood Parameter Estimation."* After assessing the abstract, it has been deemed not to be human subject research and therefore exempt from oversight of the Marshall University Institutional Review Board (IRB). The Code of Federal Regulations (45CFR46) has set forth the criteria utilized in making this determination. Since the information in this study does not involve human subjects as defined in the above referenced instruction, it is not considered human subject research. If there are any changes to the abstract you provided then you would need to resubmit that information to the Office of Research Integrity for review and a determination.

I appreciate your willingness to submit the abstract for determination. Please feel free to contact the Office of Research Integrity if you have any questions regarding future protocols that may require IRB review.

Sincerely,

Bruce F. Day, ThD, CIP
Director