



**Deterministic and Stochastic SIS Models of Common  
Cold in Universiti Malaysia Perlis**

by

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## LIST OF ABBREVIATIONS

UniMAP	University Malaysia Perlis
SIS	Susceptible-Infected- Susceptible
ODE	Ordinary Differential Equations
DTMC	Discrete Time Markov Chain
DFE	Disease Free Equilibrium

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## LIST OF SYMBOLS

$R$	R project for statistically computing
$S$	Susceptible humans
$I$	Infected humans
$R_0$	Reproductive number
$\mu$	Birth/ Death rate
$\beta$	Transmission rate
$\gamma$	Recovery rate
$p$	Recovery rate from pharmacological treatment

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## Model SIS Berketentuan dan Stokastik bagi Selsema di Universiti Malaysia Perlis

### ABSTRAK

Model SIS epidemiologi adalah keterangan dinamik penyakit yang hubungan dihantar dan imuniti tidak tahan lama. Selsema biasa boleh dikategorikan sebagai model SIS. Penyakit ini telah disebabkan oleh jangkitan virus yang terletak di hidung dan virus itu telah disebarkan kepada individu. Mereka akan pulih tanpa imuniti terhadap selsema dan segera terdedah apabila mereka telah pulih dari selsema. Ini adalah percubaan pertama untuk menjalankan kajian terhadap model SIS bagi selsema. Tujuan kajian ini adalah untuk menentukan tingkah laku model SIS berketentuan dan stokastik terhadap demografi (kelahiran dan kematian) dan tanpa demografi (tiada kelahiran, tiada kematian dan tiada migrasi) atau juga dikenali sebagai populasi tertutup, untuk memperolehi nombor pembiakan,  $R_0$  antara model dan untuk menentukan model SIS dengan dan tanpa rawatan farmakologi. Terdapat dua kumpulan telah diuji dalam model SIS iaitu pelajar UNIMAP dan kakitangan UNIMAP dan data ini telah diambil daripada pusat kesihatan UNIMAP dari September 2015. Dalam kajian ini, model SIS telah dilaksanakan sebagai set persamaan perbezaan biasa (ODE) yang boleh diselesaikan dengan menggunakan kaedah berangka yang berbeza dan proses Markov masa diskret dalam simulasi stokastik. Algoritma Gillespie telah digunakan untuk menjana simulasi stokastik sangat cekap dengan program R dalam satu proses rawak daripada semua acara dalam proses mengikut kebarangkalian masing-masing. Kemudian, persamaan pembezaan akan dibina untuk menerangkan statistik minima setiap proses. Oleh itu, terbitan bilangan pembiakan,  $R_0$  telah diperolehi dengan menggunakan kaedah operator generasi akan datang dan ditakrifkan sebagai jangkaan bilangan kes sekunder dihasilkan, dalam populasi yang sama sekali terdedah. Dalam kes ini, bilangan yang dijangkiti dalam demografi SIS secara berterusan akan berkurangan kerana ada semasa kelahiran dan kematian penduduk. Rawatan farmakologi telah digunakan untuk memperbaiki dan mengawal jangkitan selsema dari merebak kepada penduduk. Kawalan ini dapat membantu untuk mengurangkan bilangan individu yang dijangkiti dalam populasi. Dinamik berketentuan dan proses Markov masa diskret stokastik model SIS dengan dan tanpa rawatan farmakologi telah ditentukan dan dibandingkan dengan menggunakan nilai-nilai parameter yang berbeza bagi kadar pemulihan untuk mendapatkan tingkah laku penduduk dijangkiti. Oleh itu, rawatan farmakologi meningkatkan nilai kadar pemulihan dan membantu mereka untuk pulih dengan lebih cepat. Selain daripada itu, bilangan pembiakan asas,  $R_0$  untuk setiap model tanpa demografi dan dengan demografi diperolehi untuk menentukan sama ada penyakit adalah berterusan dalam populasi atau tidak. Penyakit ini akan terus tersebar ke dalam penduduk jika  $R_0 > 1$  dan semua model dalam kajian ini adalah lebih besar daripada 1.

## Deterministic and Stochastic SIS Model of Common Cold in Universiti Malaysia Perlis

### ABSTRACT

The epidemiological with SIS model is the description of the dynamics of a disease that is contact transmitted with no long lasting immunity. Common cold can be categorized as a SIS model. This illness caused by a virus infection located in the nose and the virus is transmitted to individuals. They will recover with no immunity to the common cold and immediately susceptible once they have recovered. This is the first attempt to develop SIS model on common cold. The purpose of this study is to compare between the deterministic and stochastic SIS model with demography and without demography (presence of births and deaths), to derive the reproductive number,  $R_0$  between the models and to compare the SIS models demography without pharmacological treatment and with pharmacological treatment. There are two groups tested in SIS models which are UNIMAP's students and UNIMAP's staffs and these data were taken from UNIMAP's university health centre on September 2015. In this study, SIS models were implemented as set of deterministic ordinary differential equations (ODE) that can be solved by using different numerical methods and a discrete time Markov chain (DTMC) process in stochastic simulations. Gillespie algorithm had been used to generate stochastic simulations very efficiently in R program by drawing a random process from all events in process according to their respective probabilities. Then, differential equations will be constructed which describe the mean statistics of each process. Hence, the derivation of reproductive number,  $R_0$  had been obtained by using the next generation operator method and defined as 'the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual'. In these cases, the number of infected persons in SIS demography will continuously decrease as there are presence of births and deaths in the population. Pharmacological treatment had been used to improve and control the infection of common cold from spread to population. This control measure help to minimize the number of infected individuals in the population. The dynamics of deterministic and stochastic discrete time Markov Chain (DTMC) SIS models with and without pharmacological treatment are determined and compared by using different parameter values of recovery rate to obtain the behaviour of infected population. Therefore, the pharmacological treatment increases the value of recovery rate and help them to recover more quickly. Other than that, basic reproductive number,  $R_0$  for every models without demography and with demography were derived for determining whether a disease persist in the population or not. The disease will continuously spread out into population if  $R_0 > 1$  as all the models are greater than 1.

# CHAPTER 1

## INTRODUCTION

### 1.1 Mathematical modelling

SIS (Susceptible- Infected- Susceptible) model is a model of the behaviour of an infectious disease in a large population. These states are generally called compartments, and the corresponding models are called compartment models. Individuals in population are appoint into different compartments and letters are used to show the different stages in compartmental models. Compartmental models explains briefly what happens at the population scale (Vynncycky & White, 2010).

### 1.2 Deterministic modelling

Deterministic modelling is described by ordinary differential equations (ODEs) that can be deal with by using different numerical methods. It is applicable for large population and deterministic simulation contain no random variables and no degree of randomness. The output of the model is fully determined by the parameter values and the initial conditions.

Equilibrium state can be gain when the system is at equilibrium with  $\frac{dS}{dt} + \frac{dI}{dt} = 0$ . Hence, each set of equations in the system are equal to zero. The values of the variables were denoted by  $S^*$  and  $I^*$  to satisfy the condition. The disease free equilibrium is self- evident. This is the event where the disease suffered extinction.  $R_0$  or known as basic reproductive number is ‘the expected number of new infections from one

infected individuals in a fully susceptible population through the entire duration of the infectious period' (Chitnis, 2011). In this study, all models are set to disease free states to obtain  $R_0$ .

### 1.3 Stochastic modelling

Stochastic model is developed as a stochastic process with a collection of random variables evolving in time (Allen, 2008). The behaviour of dynamics stochastic modeling can be interpret by discrete time Markov Chain (DTMC) (Vynnycky & White, 2010). The discrete time stochastic SIS model is a Markov chain with finite state space and assumed that at most one event occurs in the time period  $\Delta t$  (Allen & Burgin, 2000). The same set of parameter values and initial conditions will lead to an ensemble of different outputs. Event- driven approach is a method that require explicit consideration of events. Population forms that emerge from the irregular way of occasions at level of the individual or otherwise called as transition rates is portrayed as demography stochastic (Keeling & Rohani, 2008). The transition probabilities can be perform with individuals experience different rates due to each events (Bloomfield, 2014).

## 1.4 Common cold disease

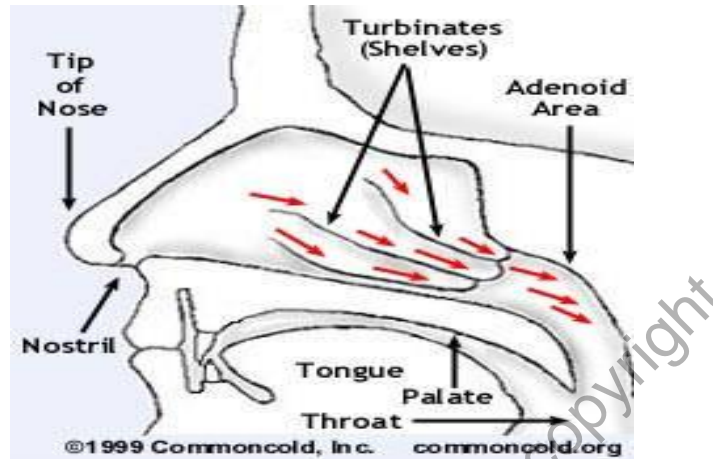


Figure 1.1: An illustration anatomy of the nose.

Infectious disease is defined as a disease caused by an infectious agent and have been characterized by their biological properties. It can be difficult to distinguish between the common cold or influenza. The differences between these diseases are the type of pathogen involved in the disease. For common cold, pathogen involved were rhinoviruses while influenza were influenza viruses A or B. This pathogen can be transmitted by an infected individual and this epidemiology is deal with populations (Krämer & Krickberg, 2010). Common cold can be categorize as SIS model. Common cold is a sickness brought about by virus infection situated in the nose and Figure 1.1 shows an anatomy of the nose. It is because of infection by an extensive variety of respiratory infections, of which the rhinoviruses are the most widely recognized (Kumar et al., 2007).

An illustration about the cold virus infection can be seen in Figure 1.2 and Figure 1.3. Rhinoviruses likewise cause some sore throats, ear infections, sinus infections, and to a lesser degree, pneumonia and bronchiolitis. For the most part, people endure a few colds for each year, yet the rate decreases with age, likely as an after effect of amassing

insusceptibility to various infection strains. Rhinoviruses are spread effortlessly through individual to- individual contact because there are no less than 100 different antigenic strains of rhinovirus, making it troublesome for the immune system to confer protection (Kumar & Clark, 2009).

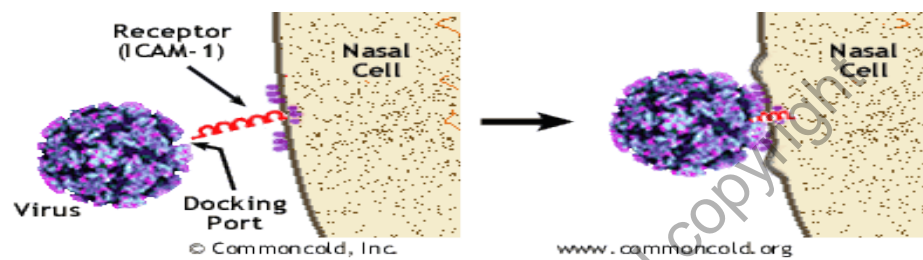


Figure 1.2: An illustration about the cold virus infection occurs. (Source: <http://www.commoncold.org/understand.htm>)

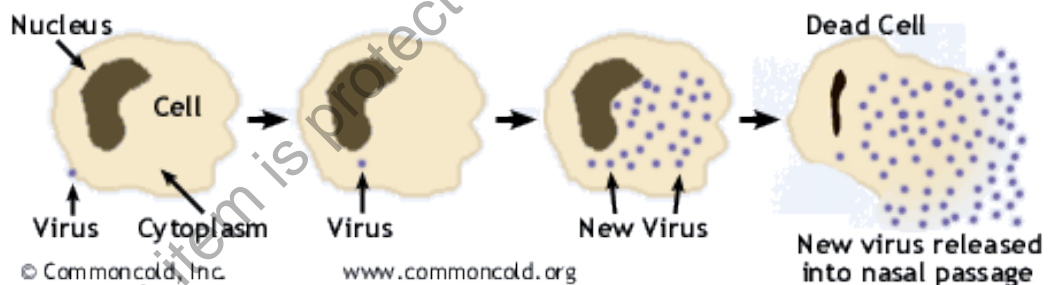


Figure 1.3: An illustration about the cold virus infection occurs. (Source: <http://www.commoncold.org/understand.htm>)

## 1.5 Problem statements

For many years, people have debated about common cold that occur in Malaysia. Common cold is part and parcel of childhood. Despite common cold is occurring every years, average Malaysian does not take this matter seriously. This problem has negatively



impacted the society because the disease spreads quickly and easily through person-to-person contact. The virus is transmitted through droplets when sneezing or coughing and it will be passed from one person to another. A possible cause of this problem is the individuals will recover with no immunity to the common cold and immediately susceptible once they have recovered. This infectious disease is categorized as SIS model. Perhaps a study which investigates the SIS model with deterministic model and stochastic model could help the situation better.

## **1.6 Objectives**

The specific objectives are as follows:

- I. To compare between the deterministic and stochastic SIS model with demography and without demography (presence of births and deaths).
- II. To derive the reproductive number,  $R_0$  between the models.
- III. To compare the SIS models demography without pharmacological treatment and with pharmacological treatment.

## **1.7 Scope of study**

In this study, deterministic and stochastic modelling will be used in SIS models. Gillespie algorithm will be used to simulate stochastic model in R by drawing a process randomly from all events in process according to their respective probabilities. There are two groups tested in SIS models which are UniMAP's students and UniMAP's staffs. These data were taken from UniMAP's university health center for the month of September 2015.

## CHAPTER 2

### LITERATURE REVIEW

#### 2.1 Introduction

A review of the published literature covering the topic of mathematical modeling, deterministic modeling, stochastic modeling, reproductive number,  $R_0$  in SIS model and common cold are discussed. There are variations of adding demography into the populations and have been analyzed in this SIS model.

#### 2.2 Mathematical modelling

Mathematical models have ended as helpful devices in society and help to decide whether the infectious disease is spread or in control into the populations. The use of mathematical modelling is to characterize and define real world phenomena, test ideas and make forecasts about this present reality (Hethcote, 2000). In recent years, there has been a great deal of eagerness to formulate the idea of mathematical modelling especially for SIS model and portrayed the mathematical model for epidemic models. By using Kermack- McKendrick (KMK) method, the number of susceptible will never stop for lacks of susceptible as the number of susceptible is greater than zero compared to the number of infected which always tend to zero.

The SIS model is the explanation of the population dynamics for bacterial and other diseases. It means that an infected individual recovers from the disease after treatment and susceptible again to infection as there is no long lasting immunity towards the disease.

### 2.3 Deterministic modelling

Allen and Burgin (2000) recommended that the value of the basic reproductive number,  $R_0$  can decide the eradication of the infection in the populations. The infection is wiped out when the  $R_0 < 1$  while the disease holds on in population if  $R_0 > 1$ . Driessche and Watmough (2002) gives the definition of the basic reproduction number,  $R_0$  as a threshold parameter of the models and demonstrated that, if  $R_0 < 1$ , then disease free equilibrium is locally asymptotically steady while if  $R_0 > 1$ , then it is unstable. They outlined together with treatment, multigroup, staged progression, multistrain and vector-host models and can be applied to more complex models and they gave the significant results for disease control.

Likewise, Hethcote (2000) additionally explored dynamics behaviour and basic reproductive,  $R_0$ . He expressed that if  $R_0 > 1$ , the disease free intermittent arrangement is unsteady. This statement had been proved by Wu and Weng (2010) saying that the reproductive number,  $R_0$  gives a role to represent the elimination of the disease in the populations.

Later, the thought has been extended by Chitnis (2011) and Zhou et al. (2016) demonstrated that if  $R_0 > 1$ , the number of infected individuals will be slowly to decrease and pathogen starts to spread out in the population. While if  $R_0 < 1$  the disease will not persist.

Recently, Andersson and Lindenstrand (2011) demonstrated that as the population turn out to be extensive, the procedure can be inexact by a deterministic process. Chitnis (2011) investigated the motion of SIS model and proposed a derivation of threshold criterion for epidemic invasion within the populations.

## 2.4 Stochastic modelling

Stochastic models include an element of randomness in the process. Allen and Burgin (2000) conducted a study on stochastic SIS models in discrete time. The results of their analysis showed that all stochastic models are considered to have finite state spaces and ultimate disease extinction with the value of  $R_0$ . Sometimes, the time until disease extinction may be taken very long because of the population size increases. Hence, there are differences between population sizes and the model towards the behaviour of SIS stochastic model because it is a process of random variable.

Andersson (2009) looked at a stochastic SIS epidemic with demography for initial stages and time to extinction. The results showed that the number of susceptible and number of infected had been analyzed for an exponentially distributed time before going extinction in the populations. Event-driven approach is a method that requires explicit consideration of events. It had been displayed that the discrete time Markov Chain (DTMC) relies upon the exponential distribution and the independence of the involved random events (contact periods and recovery times) by Artalejo et al. (2010). Allen and Glenn (2012) also stated that threshold can predict a major outbreak in stochastic theory.

Allen and Driessche (2013) conducted a study in which they relate the stochastic threshold in discrete time infectious disease models. The main findings in this analysis was the threshold extinction gave a prediction on what will happen in the populations. Fortunately, there are effective algorithms to help these problems by using Gillespie algorithm. By then, Artalejo et al. (2010) stated that Gillespie calculation makes sense of what happens next and wrapped up by drawing a random process from all events according to their respective probabilities. This should be possible effortlessly in R by drawing the index of the next process with a weighted sample command.

Allen and Driessche (2013) stated that the fundamental information for control, eradication or management of diseases are obtained from threshold for disease extinction. The deterministic and stochastic threshold are in agreement for discrete time and continuous time infectious disease model with large infectious group. Branching process theory can be connected in conjunction with the deterministic model to give extra information about disease extinction.

Zhao and Jiang (2014) considered the threshold of a stochastic SIS epidemic model with vaccination. They found the threshold of the stochastic model to know the outcome of the disease in the populations. This situation is similar to the threshold of the deterministic model. Zhao et al. (2015) conducted a study on the threshold behaviour of a stochastic model. It is very useful to determine the forecasting epidemic dynamics and treatment strategies. The extinction of the disease depends on the value of  $R_0$  and the disease will die out when  $R_0 < 1$ .

Economou et al. (2015) developed on the number of recovered individuals in the SIS stochastic epidemic models. They expressed  $R_0$  as a random variable rather than an expected value. Stochastic SIS models with nonlinear incidence rate is set up by perturbing transmission coefficient (Teng & Wang, 2016). Elimination and powerless permanence of the disease in probability was attained by using threshold value,  $R_0$ . The parameters (transmission rate, recovery rate and initial conditions) are considered to be random variables and provides complete probabilistic portrayal of SIS epidemiological models by Casabán et al. (2016).

## 2.5 Common cold disease

Respiratory infections are the prevailing reasons for respiratory sickness throughout the world. The models foresee that the infection may not repopulate the population but rather return gradually after recovery because of the no long lasting immunity. There are intervention methods to help the infected individuals in population (Knipl & Röst, 2009). Pappas and Hendley (2011) stated that symptoms persist for at least 10 days and with treatment, usually take only 5 to 7 days to recover. Common cold transmitted virus and this will lead to appearance of common cold symptom within 1 to 2 days after getting infected. Common cold season usually begin in September after children are back in school. So, the epidemic results are not from a single common cold virus only but from variety type of viruses having through populations during the break.

Zoorob et al. (2012) used the blood-spectrum antibiotic in the study and they do not recommend using the antibiotic for common cold. They proposed another treatment which is symptomatic treatment. Allan and Arroll (2014) stated that the common cold symptoms usually peak at 1-3 days and last about 7- 10 days, although the disease can persists for three weeks. The type of symptoms will be different among individuals because of the factor of age as there are different level of immune system in our body.

## CHAPTER 3

### METHODOLOGY

#### 3.1 Introduction

##### 3.1.1 Deterministic, reproduction number and stochastic of the SIS models.

In this chapter, a brief description of some details on how to implement the SIS models using deterministic ordinary differential equations (ODE) and a discrete time Markov chain (DTMC) process in stochastic simulation is discussed. Then, differential equations will be constructed in this model. Derivation of reproductive number,  $R_0$  will be obtained and defined as ‘the expected number of secondary cases produced, in a completely susceptible population, by a typical infective individual’. The SIS models were tested on two groups which are UniMAP’s students and UniMAP’s staffs. Hence, there are two different population size as there are tested on two different groups. The solution to the mathematical models were obtained with the help of the computer program R. To obtain the numerical solution, the ordinary differential equations for this study were programmed into R and solved using the deSolve package. Figure 3.1 and Figure 3.2 are illustration about SIS model of common cold within the population. Table 3.1 shows the variables and parameters used in this model. Figure 3.3 are the flowchart of research work involved in common cold.

Table 3.1: Description of variables and parameters used in the model.

Variable	Interpretation
$S(t)$	Number of susceptible individuals at time $t$
$I(t)$	Number of infected individuals at time $t$
Parameter	Interpretation
$\mu$	Natural births and deaths rate
$\beta$	Transmission rate
$\gamma$	Recovery rate
$p$	Recovery rate from pharmacological treatment
$N$	Total population size (constant)

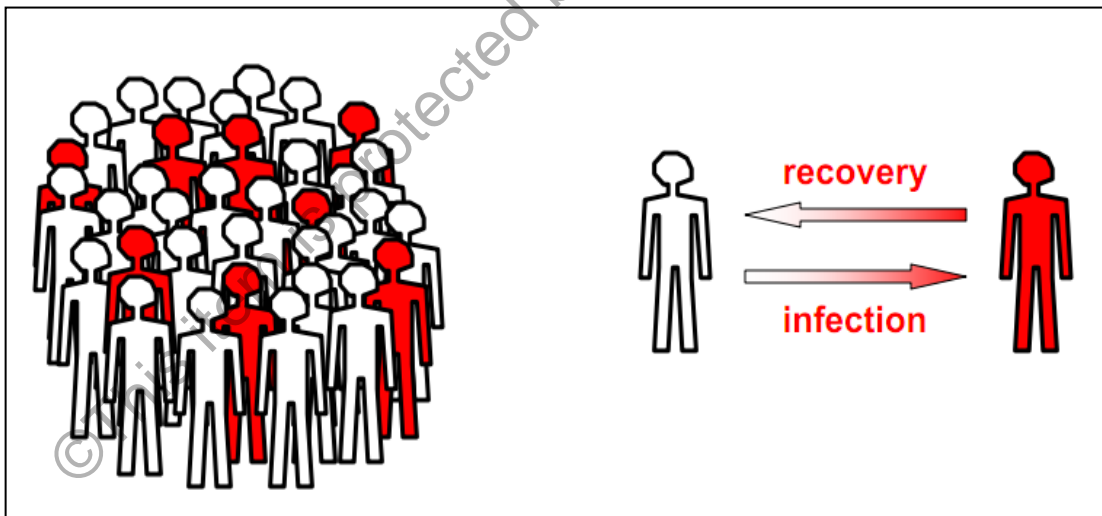


Figure 3.1: An illustration about SIS model within the population. (Source: [http://www.cim.pt/files/CIM\\_Course\\_Epidemiology](http://www.cim.pt/files/CIM_Course_Epidemiology))