Faculty of Computer Science and Information Technology

Mathematical Modelling of the Geographic Spread of Rabies Epidemic

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Bachelor of Computer Science with Honours (Computational Science)

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Pemodelan matematik mengenai penyebaran epedemik rabies berdasarkan geografi

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ABSTRACT

Zoonotic disease is infectious disease of animals that can cause diseases when transmitted to human. Rabies is a deadly disease that can be spread through bite or scratch or through contact with saliva from the infected animal. Since 1884, rabies has been known to occur in Malaysia. Recent outbreak was occurred in Sarawak started July 2017 with 21 deaths cases recorded. In order to investigate the immigration of dog affects the geographically spread of rabies in Sarawak, mathematical patchy model is used to describe the transmission dynamic of rabies between dogs and human. In each patch the submodel consists of susceptible, vaccinated, exposed and infected subpopulation of both dog and human (SEIV model). Mathematical modelling was proposed to provide a scientific basic for public health authorities in Malaysia and particularly in Sarawak to reduce and prevent the geographic spread of rabies. The control measure includes the vaccinating the dogs, culling stray dogs and transportation of dogs need to be monitored and under constant surveillance.

ABSTRAK

Penyakit zoonotic adalah penyakit berjangkit yang berpunca dari haiwan dan boleh menyebabkan penyakit apabila merebak kepada manusia. Rabies adalah penyakit yang berbahaya dan boleh menyebabkan kematian apabila tersebar mealui gigitan atau sentuhan dengan air liur dari haiwan yang dijangkiti. Sejak tahun 1884, penyakit rabies terlah merebak di Malaysia. Penularan wabak rabies yang terkini berlaku di Sarawak bermula pada bulan Julai 2017 dengan mencatat sebanyak 18 kematian yang dilaporkan. Untuk mengkaji penyebaran geografi penyakit rabies di Sarawak melalui immigrasi anjing, matematik model tampalan digunakan untuk menggambarkan dinamik penyebaran penyakit rabies antara anjing dan manusia. Di dalam setiap kawasan mengandungi sebatian matematik model berpotensi dijangkiti-terdedah-berjangkit-vaksinasi (SEIV). Model matematik relevan untuk memberi asas saintifik bagi pihak berkuasa kesihatan awam di Malaysia khusunya di Sarawak untuk mengurangkan dan mencegah penyebaran geografi penyakit rabies. Langkah kawalan melibatkan vaksinasi kepada anjing yang berpotensi untuk dijangkiti, pembunuhan anjing-anjing liar dan juga pengangkutan anjing perlu di pantau dan di bawah pengawasan yang berterusan.

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CHAPTER 1: INTRODUCTION

1.1 Project Title

Mathematical modelling of the geographic spread of rabies epidemic.

1.2 Introduction

Infectious diseases are diseases that caused by the spread of microorganism (bacteria, viruses, fungi, or parasite) that can be spread directly or indirectly from one person to others. As for rabies disease, it is a type of zoonotic disease. Zoonotic disease is infectious disease of animals that can cause disease when transmitted to humans. Rabies is a deadly disease that can be spread through the bite or scratch of an animal and can be transmitted between animal and human through contacts with saliva from the infected animal. The fatal virus will spread to the nervous system and causing severe inflammation in the brain and death.

Rabies has been known to occur in Malaysia since 1884. Since 1924 only the records of human cases have been kept. Highly endemic for rabies occurred is in Malaysian states bordering Thailand, which has the most number of cases occurred. Sarawak have been recorded 21 deaths caused by this deadly disease which reputedly has 99 per cent mortality rate since its outbreak started July 2017.

There is some possible mode that can contribute to the spread of rabies geographically. For example, the construction of Pan Borneo Highway and the opening up more for oil palm plantations that has high possibility the foreign labourers could bring their animals with them from Kalimantan Barat. Other than that, the movement of stray dogs that infected with rabies virus (under incubation period from the border town along the highway). Adoption of stray dogs and irresponsible owner dog left their own pets at other towns when they noticed the pets were ill. From all of the possible spread mode mentioned as above, this study is to describe the geographical spread of rabies caused by the immigration of the dogs.

To model the transmission of dynamics of rabies, we use compartmental model which consists of susceptible, exposed, infectious and vaccinated classes (i.e. SEIV model) for both dogs and human. As the movement of dogs has a great impact on the spread of rabies, we use an epidemic patchy model to investigate the geographically spread of rabies. The mathematical will be developed respectively in R programming language.

1.3 Problem Statement

In this 21st century, even with the advanced medical technologies, rabies remains as one of the most feared fatal zoonotic disease which almost 60 000 human deaths occur globally per year (Fooks et al., 2014).

Rabies is a deadly disease that can be spread through the bite or scratch of an animal and can be transmitted between animal and human through contacts with saliva from the infected animal. The fatal virus will spread to the nervous system and causing severe inflammation in the brain and death.

Infective mammals, especially dogs can bite other dogs and humans to spread the rabies virus from dogs into human population. The rabies virus infects the central nervous system and causes disease in the brain. Once symptoms of the disease develop, its mortality is 100%.

Even though rabies has been controlled or eliminated for decades in Malaysia, in July 2017, the death cases from human rabies around Serian District in Sarawak became the country's first such deaths in almost two decades.

A test conducted by the Virology Unit of Institute of Medical Research has shown there is a link between the rabies cases in Serian and that in Kalimantan (Goh Pei Pei, 2017). Therefore, there is an urgent need to study the geographical spread of rabies diseases theoretically through mathematical modelling.

1.4 Objective

There are three main objectives for this research:

i. To investigate the dynamics of geographic spread of rabies diseases theoretically using mathematical patchy model.
ii. To carry out numerical solution of the mathematical model to determine how the movement of dogs affects the geographic spread of rabies.
iii. To develop a user interface that enable better understanding on how the dynamics of geographic spread of rabies disease.

1.5 Research Methodology

The methodology of this project is the mathematical modelling process. By justifying the assumptions, the mathematical compartmental model will be constructed in the system of non-linear differential equations which subdivided the human and dog population into SEIV (susceptible, exposed, infectious, vaccinated) compartments. Since the rabies epidemic model has large number of equations and the parameters involved, the equations will be solved by numerical simulation using R programming. Figure 1 shows the common methodology of the modelling process.

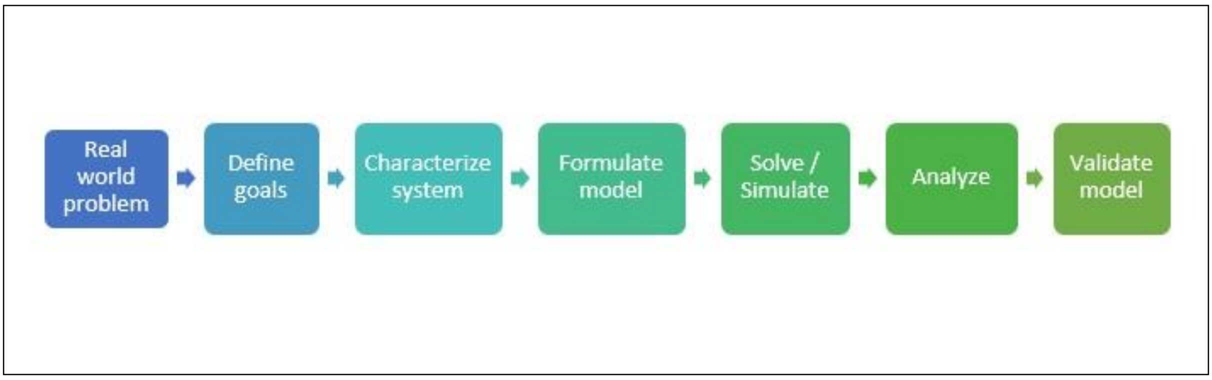

Figure 1.1 Methodology of the modelling process.

1.6 Scope

To model the geographic spread of rabies that caused by the movement of dog in system of ordinary differential equations (ODEs), we use epidemic patchy model in which each patch of the submodel consists of susceptible, exposed, infectious and vaccinated subpopulations of dogs and humans, respectively. SEIV model describes the spread of rabies among dogs and from infectious dogs to humans. The mathematical model is solved numerically and study how the movement of dog effect the spread of rabies by performing sensitive analysis. The numerical simulation will be carried out by using numerical solver in R programming.

1.7 Significance Project

This project can contribute to the already existing research knowledge on rabies disease. The information and findings of this project will give benefit to the society to create awareness on the risk of rabies epidemic and the spread of rabies epidemic caused by the movement of dogs. It is hoped that people will be more aware on the importance of treatment in case of suffering from dog bite and also will vaccinate their pets to control the disease.

Meanwhile, by carrying out the numerical simulation on the rabies epidemic, it will help to determine the best possible control measure to reduce the diseases. Hence, an interactive website application can be used to visualize how the dynamics of geographic spread of rabies disease and the dynamics of human rabies epidemic.

1.8 Project Schedule

The project schedule is a guidance for the progression of the final year project. The project began on 29th September 2019. This final year project will be carried out throughout first and second semester of the academic year of 2019/2020 and expected to end on 29th May 2020. The detailed of project schedule shown in Appendix A.

1.9 Expected Outcome

The expected outcome for this project is to produce the detailed mathematical analysis and simulation on the geographic spread of rabies and also to produce an interactive user-friendly interface to present the spread of rabies epidemics.

1.10 Project Outline

1.10.1 Chapter 1: Introduction

In chapter 1, briefly introduce the proposed research project. Chapter 1 contains introduction, problem statement, objectives, methodology, project scope, significance of project, project schedule, expected outcome, and summary. In introduction section, describes the background and some useful information related to the project. For the problem statement, it describes the problems that occur and the current cases in Sarawak. Methodology briefly describe what method to be used in order to achieve the objectives. The scope project is the limitation of the proposed research to be developed. Next, the significance of project is the importance of doing this research project and give benefit to the community. The expected outcome is the final achievement of the research project.

1.10.2 Chapter 2: Literature Review

Chapter 2, discuses about the literature review done by other researches based on journal, articles research paper, book and other reliable resources. This chapter is review on existing technique and methods similar to the proposed project. Comparison between proposed project research and existing project is been carried out to review on the existing technique and method. At the end of this chapter, a brief description of mathematical model used is state.

1.10.3 Chapter 3: Research Methodology

This chapter explain the methodology to be used in this project. The mathematical modelling is being used as a guideline to carry out the proposed project. The justifying assumptions, model formulation, identify all the parameters involve in the equations will be discussed in this chapter. This proposed project is using complex differential equation and numerical solutions will be used to solved the solution.

1.10.4 Chapter 4: Result and Discussion

In chapter 4, the numerical solution, and the discussion of results will be shown. It will discuss further in this chapter.

1.10.5 Chapter 5: Conclusion and Future Work

Chapter 5 is the final phase to complete the entire project and suggest some future work. The conclusion is comprising of awareness and improvement throughout this research. The lesson learned throughout the entire project is discuss. Future enhancement on the purposed developed model is being outlined.

1.11 Summary

In this project, a mathematical model will formulate the geographic spread of rabies epidemic. The numerical simulation on the rabies epidemic will help to determine the best possible control measure to reduce the diseases and also to predict the human rabies infectious case in Sarawak. The sensitive analysis is further use to study how the movement of dog effect the spread of rabies. In a nutshell, this proposed project is expected to give better understanding about the spread of rabies by visualize how the dynamics of geographic spread of rabies disease and the dynamics of human rabies epidemic.

CHAPTER 2: LITERATURE REVIEW

2.1 Overview

In this chapter, we review existing research on the transmission dynamics of the rabies epidemic based on selected research papers and other reliable sources. The literature review contains review of related methods and techniques as well as a brief explanation to the related research work. Four related research articles will be reviewed. At the end of this chapter, a brief description of mathematical model for each research article is given. The deterministic compartmental model consists of susceptible, exposed, infectious, and vaccinated subpopulations of both dogs and humans and describes the spread of rabies among dogs and from infectious dogs to humans.

2.2 Epidemiological Modelling

The study of disease occurrence and its control measures is called epidemiology. Epidemiology is the study of the distribution and determinants of health-related states or events (including disease). Various method can be used to carry epidemiological investigation; surveillance and descriptive studies can be used to study distribution; analytical studies are used to study determinants. (WHO, 2019). Epidemic is an unusually large, short term outbreak of disease. The spread of an infectious disease is not only determined by disease - related factors such as the infectious agent, mode of transmission, latent period, infectious period, susceptibility and resistance, but also social, cultural, demographic, economic and geographic factors.

In this project, we focus on the geographic spread of rabies epidemics that caused by immigration of dogs between multi-patch. We consider a four-dimensional model consists of the susceptible(S), exposed(E), infectious(I) and vaccinate(V). of both subpopulation dogs and humans. The immigration of dogs between two patches could be categorized into dynamic deterministic modelling which indicates the movement of the infectious dogs to human between the patches.

Similar to other infectious diseases, rabies should also be controlled through vaccination program. WHO recommended that 70% of dogs should be immunized to eliminate the rabies (WHO, 2004). Unfortunately, the rate of vaccination for dogs in most regions is lower than 10%. The vaccine of dogs is less expensive than that for human, but the dog vaccination requires continuously human material and financial resources (Chen et al., 2015).

Mathematical models and the numerical solutions serve as useful experimental tools for developing and testing the theories, whereas sensitive analysis is used to observe the effect of changes in parameter values on the disease dynamics in the real world problem situations. The mathematical descriptions of disease epidemics lead to several useful findings including the expected size of epidemic and the critical level that is needed to achieve effective disease control measure. The transmission of infectious epidemic can be reduced by understanding the major factors affecting the spread of disease, apart from creating awareness and lead to effective ways of prevention.

2.3 Review of Related Research Work

2.3.1 Modelling the Geographic Spread of Rabies in China.

Chen et al. (2015) focuses on how the movements of dogs affect the geographically inter-provincial spread of rabies in Mainland China. Multi-patch model is used to describe the transmission dynamics of rabies between dog and human, in which each province is regarded as a patch. The submodel for each patch consists of susceptible(S), exposed(E), infectious(I) and vaccinated(V) subpopulations of both human and dogs which describes the transmission of rabies among dogs and from infectious dogs to humans.

The basic reproduction number R_0 is defined as the susceptible number of secondary cases produced by a typical infection in a completely susceptible population. The R_0 of rabies which shows the expected number of dogs infected by a single infected dog, derived from the SEIV model that describes the transmission dynamics of rabies. The value of R_0 gives an important threshold that determines if the disease will die out or not. If $R_0 > 1$ the disease will persist as each primary infected dog will produce more than one secondary infected dog. The disease will die out if $R_0 < 1$.

From the sensitive analysis we can obtain the relationship between the epidemiological parameters and R_0 for a two-patch model. Furthermore, by sensitive analysis the study on how the immigration rate affects the R_0 of the whole system and the isolated patches can be carried out. In order to control and prevent geographical spread of rabies, the results suggest that the management of dog markets and trades need to be regulated and dogs transportation needs to be monitored. Other than that reducing dog birth rate and increasing dog immunization coverage rate are two most effective controlling measures on the spread of rabies.

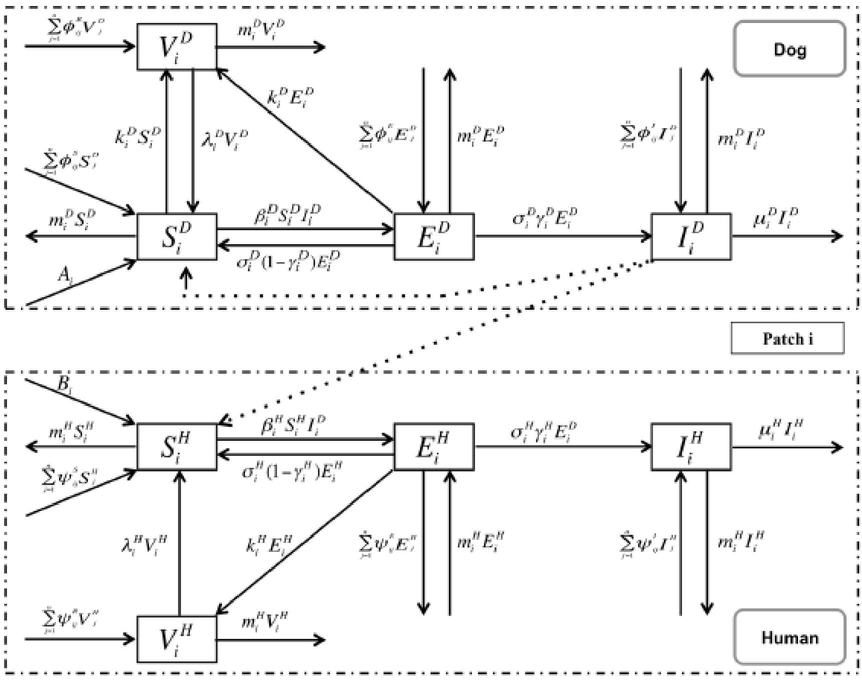

Figure 2.1 Compartmental diagram related work A.

Parameter	Description	Reference
A_i	the annual birth rate of dogs in patch *i*	estimation
λ_i^D	the loss rate of vaccination immunity for dogs in patch *i*	[19]
$\frac{1}{\sigma_i^D}$	the time duration in which infected dogs in patch *i* remain infectious	[18]
γ_i^D	the risk factor of clinical outcome of exposed dogs in patch *i*	[5]
m_i^D	the non-disease related death rate for dogs in patch *i*	[24]
k_i^D	the vaccination rate of dogs in patch *i*	[5]
μ_i^D	the disease-related death rate for dogs in patch *i*	[5]
β_i^D	the transmission coefficient of infectious dogs to susceptible dogs in patch *i*	fitting
B_i	the annual birth rate of humans in patch *i*	[17]
λ_i^H	the loss rate of vaccination immunity of humans in patch *i*	[25]
$\frac{1}{\sigma_i^H}$	the time duration of infectiousness of infected humans in patch *i*	[2]
γ_i^H	the risk factor of clinical outcome of exposed humans in patch *i*	[20]
m_i^H	the natural death rate of humans in patch *i*	[17]
k_i^H	the vaccination rate of humans in patch *i*	[5]
μ_i^H	the disease-related death rate of humans in patch *i*	[5]
β_i^H	the transmission coefficient of infectious dogs to susceptible humans in patch *i*	fitting
$\phi_{ij}^K \geq 0$ ($K = S, E, I, V$)	the immigration rate from patch *j* to patch *i* for $i \neq j$ of susceptible (exposed, infectious, and vaccinated) dogs	fitting
$\psi_{ij}^K \geq 0$ ($K = S, E, I, V$)	the immigration rate from patch *j* to patch *i* for $i \neq j$ of susceptible (exposed, infectious, and vaccinated) humans	fitting

Figure 2.2 List of Parameters related to work A.

2.3.2 Analysis of Rabies in China: Transmission Dynamics and Control.

Zhang et al. (2011) focuses on a deterministic model to study the transmission dynamic of rabies in China, in order to explore the effective control and prevention measures.

In this work, their model simulations agree with the human rabies data reported whereby the basic reproduction number is known to be $R_0 = 2$ for the rabies transmission. Zhang et al. (2011) demonstrates that (i) reducing dog birth rate and increasing dog immunization coverage rate are the most effective methods for controlling rabies in China; and (ii) large scale culling of susceptible dogs can be replaced by immunization them. However, they also claimed that the annual crop of newborn puppies can exceed 5 million and the proportion of immunized dogs is only about 10% which is too low.

As for the mathematical model, this research proposed a susceptible, exposed, infectious, and recovered compartmental model to determine the transmission dynamics of rabies in China. Even though this model does not include culling of dogs, it provides a good match to the reported data. Zhang et al. (2011) conducted some sensitive analysis and suggested the strategies to control the transmission of rabies epidemic. The first strategy is to decrease the dog birth rate in order to reduce the dog population and the second, stop culling dogs by increasing the dog immunization rate.

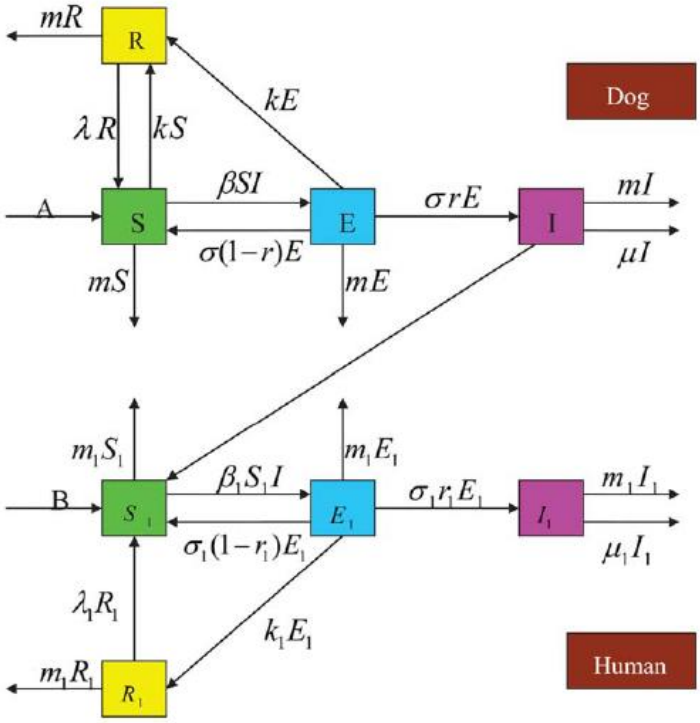

Figure 2.3 Compartmental diagram of related work B.