Modelling the Spread of Zika Virus on a Small World Network

By

Obvious Nchimunya Chilyabanyama (obvious.chilyabanyama@aims.ac.rw)

June 2017

AN ESSAY PRESENTED TO AIMS RWANDA IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE AWARD OF MASTER OF SCIENCE IN MATHEMATICAL SCIENCES

DECLARATION

This work was carried out at AIMS Rwanda in partial fulfilment of the requirements for a Master of Science Degree.

I hereby declare that except where due acknowledgement is made, this work has never been presented wholly or in part for the award of a degree at AIMS Rwanda or any other University.

Scan your signature

Student: Obvious Nchimunya Chilyabanyama

Scan your signature

Supervisor:Professor Nancy Ann Neudauer

ACKNOWLEDGEMENTS

Sincere gratitude to the African Institute of Mathematical Sciences for giving me an opportunity such as this.

I would like to sincerely thank My supervisor and Tutor , Professor Nancy Ann Neudauer and Jan Hazla respectively, for their tireless support and guidance thought this research.

DEDICATION

This is optional.

Abstract

Recently there has been outbreaks of Zika virus which has [Jan: s/has/have] lead to epidemics. Not much work has been [Jan: done] over the years to model the spread of the [Jan: s/the/this] infection. Since its emergence Zika virus has been modelled with traditional compartmental models,where [Jan: Space after comma] the population is assumed to be well mixed. We study a different approach based on small world networks.We [Jan: Space after period.] build a Zika virus model on a small world network, to describe the behaviour and course of Zika virus.

Small world networks, introduced by Strogatz and Watts, on the other hand [Jan: Delete "on the other hand".] assume that one is more likely to spread the disease to someone in their family, someone who lives near them, or someone they know.

The Smallworld [Jan: s/Smallworld/small world] model of infectious disease combines this sort of clustering in the graph with a probability [Jan: s/a probability to model/modelling] to model the spread of disease as a dynamical system.

Contents

1. Introduction

Mathematical models have been used to describe the course of infectious disease for a long time. The most commonly used models are the compartmental models, which are identified by acronyms that indicate the compartments in the model, such as SIR (susceptible, infectious and recovered), SIS (susceptible, infected and susceptible), SEIR (susceptible, exposed, infected and recovered) and variants of them. These models can be described using a system of differential equations with the number of equations equal to the number of compartments in the model. [Jan: Maybe a reference somewhere here?] When studying infectious disease propagation using these models an assumption of uniform mixing is made; that is any individual in the population has the same probability of contacting any other individual.

However the uniform mixing approach has been found to be unrealistic for a long time [Jan: Too strong. Say it is unrealistic in some cases.] and spatial effect and heterogeneity have shown to have an impact on the spread of infections. Instead of relying on this kind of models and due to recent advances in the research of complex networks, there has been increased interest in trying to capture the effects of contact patterns between individuals. These patterns can be described by contact networks, where the vertices correspond to individuals and the edges to contacts between them (Wallinga et al., 1999). One of the main motivations for studying complex networks has been to better understand the structure of social networks, which without a doubt has to be reflected in contact networks. Thus, there is a natural link between epidemic modelling and research on complex networks (Kaski et al., 2005)

Small world network model have been more realistic in capturing the spread patterns of some infectious diseases. The small world models have been built on the assumption that infected individuals will spread the infection among their close contacts with a higher probability compared to their random acquaintances. They where first introduced by Watts and Strogatz (Watts and Strogatz, 1998).

Since the emergence of Zika virus epidemic, there has been several studies to model the spread of the virus. Most research on Zika has been modelling the propagation of the infection using compartmental models as can be seen in the work of Kucharski et al. (2016), Dantas et al. (2017) and Bonyah and Okosun (2016), where they used the SEIR compartmental model with vector to model the propagation of Zika.

In this research, we model the spread of Zika virus on a small world network and investigate the effects of small work parameters on the spread of the infection. We assume there is no perfect mixing in the population, but the contact patterns can be described using a small world network. This is a much more realistic assumption as it captures the contact patterns of individuals in the community or network. We build a network that models the contact patterns of individuals in a city. Zika virus is mainly transmitted through a vector (mosquito)contact and transmission is in reference to mosquito bite. The dynamics of transmission through a mosquito are represented in a small world network.

The aim of the study is to broaden the understanding of the spread of Zika virus. This might lead to new disease control measures and research topics in the field.

This paper is arranged in as follow: In chapter 2 we review some related works . In chapter 3 we it give some background knowledge of networks and compartmental models. In chapter 4 we give a description of deterministic and stochastic compartmental models. Lastly in chapter 5 it gives the Zika model and results from simulations based on a small world network.

2. Literature Review

2.1 Zika Virus

Zika virus is a member of the Flaviridae family and the Flavivirus genus. It is related to other mosquito borne viruses such as Dengue virus, Yellow-fever virus (YFV) and West Nile virus (Dick et al., 1952). The virus originates from the Zika forest of Uganda and the first case was isolated in 1947 from a rhesus monkey in the forest. Then later in 1954 a human was diagnosed with the virus in Nigeria (Junior et al., 2015). Since then the virus has spread to different parts of the world.

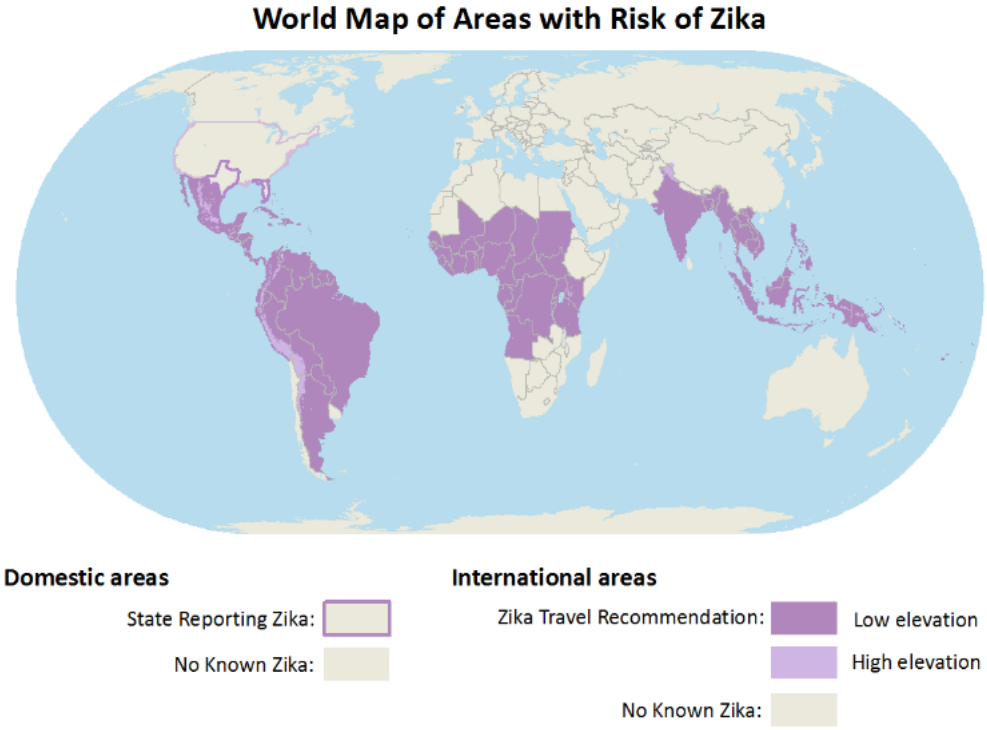


Figure 2.1: Countries with Zika Virus: Source CDC

Zika virus is mainly spread by Aedes mosquitoes. When a pathogen carrying mosquito bites an uninfected individual it infects them with the virus. Other ways by which the virus spreads include, blood transfusion, unprotected sex with an infected person and from mother to child, infected mothers can pass on the virus to their unborn children (Musso et al., 2014).

Some of the symptoms of Zika virus are papular rash,fever, arthritis or arthralgia Musso et al. (2015). Papular rash is characterized by a flat, red area on the skin that is covered with small confluent bumps and arthralgia is characterised by pain or aching in the joints without pain.

In addition, headache and red eyes are common symptoms of Zika virus. Simões et al. (2016) adds that the extent of the risk that Zika infection will result in birth defects still remains unknown. For expecting mothers, Zika virus affects their foetus and development of the baby. Babies can face a range of neurologic sequelae such as intellectual disability, hearing loss, vision loss, and seizures. These problems can range from mild to severe and are often life-long (Rasmussen et al., 2016).

There is no known vaccination to prevent or treat the Zika virus. Prevention measures can be taken to prevent the spread of the virus. This can done by preventing mosquito bites. Measures such as sleeping under a mosquito net, using mosquito repellent and fumigating mosquito breeding areas in the vicinity among others can be taken. Another measure of prevention of Zika virus is practising safe sex and avoiding travel to areas with high prevalence of Zika.

Drugs for the symptoms of Zika are administered to patients as a way of treating Zika patients because of the lack of a vaccine for the virus.

The spread of Zika virus has resulted in Zika epidemics in some part of the world as can be seen in figure 2.1 above as of April 2017. This causes a worry as the effects of the epidemic are more devastating and if not controlled can affect the whole country, region and World at large.

2.2 Epidemiology

Epidemiology is the study of the origin and course of diseases in a community. The goal of epidemiologist is to understand the cause of a disease, then to predict its course, and come up with methods to control the disease. This involves collaborative work of statisticians, mathematicians, physicians and various health specialists (Brauer, 2017).

The knowledge about infectious diseases has been built up by the method of experience, by observation and analysis of particular conditions associated with occurrence of the disease in nature (Frost, 1923).

The first step in epidemiology was the collection and analysis of data on causes of death in London parishes in the early 1660s by Graunt. He gave a method of estimating the comparative risks of dying from various diseases, giving the first approach to a theory of competing risks (Brauer, 2017).

Mathematical models of disease transmission have been used to link biological processes of disease transmission and emergence of dynamics of infections at population level. Researchers try to understand the environmental, biological and behavioural infectiousness of a disease.

Environmental infectiousness depends on geographical conditions of the area in which, an infected person resides. Some pathogens cannot survive inside or outside a host in given geographical conditions. Thus, some diseases or infections spread faster in certain weather conditions (Grassly and Fraser, 2006). Understanding the timing and causes of seasonality offers important insights on how parasite–host systems interact. How and when parasite control measures can be applied, and how disease risks will respond to anthropogenic climate change and altered patterns of

seasonality (Altizer et al., 2006). These factors must be captured in the models.

Biological infectiousness depends on the pathogen's life cycle and the individual's or host's immune system. Some individuals have a strong immunity against certain infections, this may slow down the propagation the infection. On the other hand the life cycle of pathogens also affects the transmission dynamics of the infection. Some pathogens can only survive in the host while the other can survive outside the host, this will play a major role in the spread of the infection. The interaction of the genetic determinant of disease propagation in the pathogen and host is important in building models for the transmission dynamics of infectious diseases.

Behavioural infectiousness depends on the interaction behaviour of an individual. The contact pattern of the person affects how the individual is likely to propagate the disease. Depending on the nature of disease transmission, a person who has a lot of contacts is are more likely to spread the disease to more people compared to one who has fewer contacts (Johnson et al., 2001). Contact in this context implies any interaction likely to result in transmission of an infection.

The susceptibility of an individual largely depends on the biological, environmental and behavioural factors of an individual. For example, one's contact pattern, immunity and the environmental conditions will highly affect the probability of contracting an infection.

For over a century, mathematical representation and analysis of infectious diseases has been the centre of infectious disease epidemiology (Beisner, 2005).

Mathematical modelling of infections diseases, started by the works of Daniel Bernoulli in Bernoulli (1760), in the quest to model the spread of small box and possible eradication. A century later the modelling become well established. The modelling of infectious disease dynamics is important for science and public policy among others. There are three main aims of infectious disease modelling; to understand the how the spreading mechanism of the disease, to predict how the disease will progress among the population and to understand how the disease can be controlled. They provide tools for investigating and quantifying the spread of disease. Conducting experimental research on the spread of infectious disease raises a lot of ethical issues and therefore can not be conducted on humans. Mathematical simulations and modelling the disease has helped in providing understanding of the impact of the infectious disease on the population and give a guide for new control measures (Ming et al., 2016).

2.3 Modelling Infectious Disease with Compartmental Models

Differential equations have been used in the modelling of the dynamics of the spread of infectious diseases. They are based on the assumption of uniform mixing, that is, everyone in the population has an equal probability of contracting an infectious disease (Kaplan et al., 2002). Compartmental Mathematical models have been used to describe the transmission dynamic of Zika Virus (Gao et al., 2016). Infectious diseases are transmitted indirectly or directly by contact between the infected and those who are not infected thus these models try to capture these interactions (Sattenspiel, 1990).

In compartmental models of infectious disease individuals are divided into several compartments such as; Susceptible (S) , latent (E) , infected (I), vaccinated (V) and recovered or removed (R). Depending on the on the propagation of the disease, compartmental models are built by combining these different classes or creating new ones (Li and Muldowney, 1995).

Deterministic models also known as compartmental describe and explains what happens on average of the population. They assume that the population is homogeneous, that is, everyone in the population reacts the same risks of exposure and infection. This assumption does not capture biological, environmental and geographical factors that effect susceptibility of individuals. Hence, the introduction of stochastic models. Stochastic models introduce the idea of randomness in the reaction to risk and infection by individuals in the population (Ming et al., 2016). The main advantage of the stochastic models is they take into consideration each individual, but the major drawback is that it is laborious to model them as they require a lot of stimulation and sometimes become mathematically complex.

Deterministic models are built on theories of ordinary differential equations, partial differential equations and difference equations (Keeling and Rohani, 2008). The trends in these research areas are for higher model dimension and deeper and more refined analysis. Unlike for stochastic models where the trends of research are toward specific diseases and toward deterministic and stochastic mixed models (Fu et al., 2013).

To build models that incorporate contact patterns of the individuals, Mathematicians have resolved to use results from the work of Moreno (1945), where he analysed contact patterns of prisoners. This work has given basis for understanding or building models based on the contact patterns of individuals in the population (Sattenspiel, 1990). Freeman (2004) characterizes the analysis of social networks by four properties. First, it involves the intuition that links between social actors are important. Second, it is based on the collection and analysis of data about social relations that link actors. Third, it draws heavily on graphic imagery to reveal and display the patterning of those links and lastly, it develops mathematical and computational models to describe and explain those patterns. A number of disease propagation models have been built for various infectious diseases among others Malaria, Zika, HIV -AIDS, Smallpox and Chickenpox (Ding et al., 2016).

2.4 Modelling Infectious Diseases on Graphs

Graph theory has over the years grown and has found its application in many fields. A graph also known as a network can be defined as a pair $G = (V, E)$ where V is a finite set of nodes $E \subset V \oplus V = \{e_1, e_2, \ldots, e_m\}$ is a set (Estrada, 2012).

Over the years contemporary science, has had challenges in describing complex networks. This posed limits in the advancement of many disciplines. However, with the advancement of computerization, there is a raise in the possibility of understanding the stability of large networks Barabási and Albert (1999).

For many complex networks vertices are described as elements of the system and edges represent

the interaction between them. Similarly, in modelling the spread of infectious diseases on networks, individuals or populations are represented by nodes of the network, contacts likely to result in the transmission of disease are represented by edges. Modelling of infectious disease on networks give better models for heterogeneous populations (Ming et al., 2016). One of the major challenges in modelling the spread of infectious diseases on networks, is capturing the contact patterns of individuals. The non availability of such data has lead to mathematicians modelling the spread of infectious diseases on various simulated network structures (Pastor-Satorras and Vespignani, 2001).

Random network models of infectious disease do not take into account spatial position of individuals and connections are made at random (Keeling and Eames, 2005). The growth rate and and final epidemic size of a disease on a random network are reduced compared with a random mix model. Growth rate in random network is $\tau(n-2)-g$ and the growth rate with random mixing is $\beta - g = \tau\widehat{n} - g$, where τ is the transmission rate across a contact, n and $\widehat{n}$, is the number of contacts in a network and the unit number of contact per unit time in a random mixing model respectively. g is the probability of recovery.

The reduction in the growth rate is due to two reasons; each infectious individual has been infected by one of its contacts, reducing the number of susceptible $n-1$ and as an infectious individual starts to infect its susceptible contacts it depletes its local environment, regardless of the population prevalence rate, hence limits the rate of disease spread (Keeling and Eames, 2005).

Lattice based epidemic models are used to study the spatial and temporal rates of the disease spread in a spatially distributed host populations (Rhodes and Anderson, 1997). Models built on latices assume that individuals are located as nodes on a regular lattice and connections are made to a collection of near neighbours or each node. For example people may be spread out such that connections are made to their four nearest neighbours, one on the left,right, up and down. (Lloyd et al., 2006). To avoid the effect of the nodes at the end not being connected the last and first neighbours are made neighbours. The spread of influenza is one of the infectious disease that have been modelled based on lattice models (Liccardo and Fierro, 2013).

Another kind of network epidemic model has been the small world network. Disease spread through small-world networks has received considerable attention from both a theoretical and more applied context. The high level of clustering means that most infection occurs locally, but short path lengths mean that epidemic spread through the net-work is rapid and disease is unlikely to be contained within small regions of the population (Watts and Strogatz, 1998).

The spread of infectious diseases on network has also has also been modelled on scale free networks. Infectious disease like Ebola, SARS and HIV-AIDS have been modelled on scale free networks. A scale free network is a network whose degree distribution follows a the power that is $P(k) \approx ck^{-\lambda}$ (Morita, 2016)

Simulated network models have been used to model the spread of disease, whose network data is difficult to collect. Various infectious diseases have been modelled on simulated networks (Keeling and Eames, 2005). Networks that are based on simulation are limited because they are no ways to test the sensitivity of the epidemiological results to the details of the network structure. Nevertheless, a range of idealized networks and analytical tools that can reveal elements of network structure that are important determinants of epidemic dynamics, have been developed (Keeling

and Eames, 2005).

A number of infectious disease models have been built on various network structures. This is so because networks capture the contact patterns in a community. The networks are either social networks or simulated networks. Many real world and social networks in which infectious diseases propagate is either small world or scale free networks and not random or regular as earlier assumed Watts and Strogatz (1998). The underlying structure of a network influences the effect of that the dynamics of epidemics will have on a population. For example in a small world network, where the network has a high clustering coefficient a shorter average distance. A disease is more likely to spread faster than in a random network or a regular network (Watts and Strogatz, 1998).

3. Background

3.1 Definitions

3.1.1 Epidemic and Pandemic . An infectious disease is a disease that is caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi; these diseases can be spread, directly or indirectly, from one person to another. An epidemic is a situation where an infectious disease is affecting many people at a particular time and spread at a very high rate. A pandemic on the other hand is an epidemic over a large area (Morens et al., 2009).

3.1.2 Deterministic and Stochastic Infectious Disease Models. The dynamics of infectious disease propagation are modelled as a dynamical system. A dynamical system is a system that evolves with time over a state space according to a fixed rule. Thus, let $\mathbb{X}$ be a state space $\mathbb{T}$ set of times and $\mathbb{R}$ rule that specifies how the state evolves with time. the rule is a function whose domain is $\mathbb{X} \times \mathbb{T}$ and co-domain $\mathbb{X}$ that is,

$$\mathbb{R} : \mathbb{X} \times \mathbb{T} \longrightarrow \mathbb{X}.$$

This means that $\mathbb{R}$ takes two arguments $(\mathbf{x}, t)$ where $\mathbf{x} \in \mathbb{X}$ is the initial state and $t \in \mathbb{T}$ the future time. That is $\mathbb{R}(\mathbf{x}, t)$ gives the state of the system at time t given the initial state of the system was $\mathbf{x}$ (Nykamp, 2017).

The population can be partitioned into different disease states and the movement of individuals from one state to another is tracked over time. Compartmental models are built to tract the flow of individuals in each state at time t.

The SIS model, are built to model disease transmission in the case were the population has only two compartments susceptible and infected. The number of people susceptible at time t is denoted by $S(t)$ and that of infected people is denoted by $I(t)$. The SIS model assumes that there is no immunity after recovery. It is used to model infections were once a person recovers from the infection, they become susceptible again. An example of such an infections disease is flu.

If people have immunity after an infection another compartment $R(t)$, for the number revered people people who recover is added to the SI model. This leads to Susceptible, Infected and Recovered SIR models. For example a person who recovers from Chickenpox develops immunity against it.

In the case where there is a latent period between when one gets infected and when they become infectious. An intermediate compartment for the number of people who are exposed $E(t)$ is added to the SIR model to make a susceptible, exposed infected and recovered (SEIR) model.

The independent variable in the compartmental models is the time t. The rates of transfer between compartments are expressed mathematically as a result models are formulated initially as differential equations. Most epidemic models are built on the SIR model (M'Kendrick, 1925). The system can be written as;

$$\begin{aligned}\frac{dS}{dt} &= -\alpha S(t)I(t),\\ \frac{dI}{dt} &= \alpha S(t)I(t) - \gamma I(t),\\ \frac{dR}{dt} &= \gamma I(t),\end{aligned} \tag{3.1.1}$$

where, α and γ are parameters of the model and with assumptions that there is homogeneous mixing in the population. That is the rate of new infections is proportional to the current numbers of susceptibles and infectives in the population. This is the main assumption deterministic models are built on. Deterministic population models are models where the behaviour of the population of determined completely by history and the rules which govern the model.

In formulating these models, in terms of derivatives of the sizes of the compartments it is assumed that the number of members in each compartment is differentiable with time. This assumption is tenable only when the disease outbreak has been established, but not valid at the beginning of a disease outbreak, when they are few infectives. When they are a few infectives, the number of infectious depends on random contacts of between a small number of individuals (Brauer and Castillo-Chavez, 2012).

On the other hand, life phenomena are in general stochastic in nature and the dynamics cannot be well captured by deterministic models hence a need for stochastic models. Stochastic models take into account random variations associated with environmental and biological fluctuations of the factors that affect disease propagation. These random fluctuations may impact the evolution of the infection. Unlike deterministic models which assume homogeneous mix, an assumption which only holds in small populations. It is quite unlikely that all people will be equally susceptible to the disease and effective in spreading it (Ball, 1985).

There are a number of different stochastic modelling processes, such as discrete time Markov chain model, continuous time Markov chain models and stochastic differential equation models. These models differ in underlying assumptions regarding the time and variables.

For example, let us take an SIR compartmental model. S, I and R represent compartments as well as the number of individuals in each compartment and we assume that $S(t)+I(t)+R(t) = N$ is constant. Time $t > 0$ is continuous for each state $S(t)$, $I(t)$ and $R(t)$. Let β to be the average number of contacts an infectious person makes per unit of time that take leads to infection. The probability of a susceptible individual moving from compartment S to compartment I in the time interval $[t, \triangle t]$ that is S $\to S-1$ and I $\to I+1$ is β S I $\triangle t + o(\triangle t)$.

Assuming that an infected person recovers at the rate γ hence the probability of an infected person moving from infected to recovered over an interval $[t, \triangle t]$ is given by $\gamma I_{t+\triangle t} - o(\triangle t)$. Since,

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

which implies that knowing $S(t), I(t)$ is knowing $R(t)$. Hence the model becomes an $S(t), I(t)$

model and thus the stochastic dynamical system can be written as;

$$P((S(t+\triangle t), I(t+\triangle t) - (S(t), I(t)) = (-1, 1)) = \beta S(t) I(t) \triangle t + o(\triangle t). \quad (3.1.2)$$

$$P((S(t+\triangle t), I(t+\triangle t) - (S(t), I(t)) = (0, -1)) = \gamma I(t+\triangle t) - o(\triangle t). \quad (3.1.3)$$

With a complementary equation,

$$P((S(t) + \triangle t, I(t) + \triangle t) - S(t), I(t)) = (0, 1)) = -\left(\beta \frac{S(t)}{N}\right) I(t) \triangle t + o \triangle t \quad (3.1.4)$$

[Jan: Fix typos in equation above.] which is refereed to as the general stochastic epidemic model (Greenwood and Gordillo, 2009).

3.1.3 Network. A graph also known as a network can be defined as a couple $G = (V, E)$ where V is a finite set of nodes $E \subset V \oplus V = \{e_1, e_2, \ldots, e_m\}$ is a set (Estrada, 2012). Nodes can be human beings, cities or houses while edges could be any connection such as friendship, physical connection or road.

A network is said to be connected if there exists a path between any two nodes in the network. Distance between any two nodes in a network is defined as the length of the shortest path between them.

This can be summed up as the average distance taken over all pairs of vertices, which give the idea of the typical distance between nodes in a network. The diameter of the graph is the largest distance taken over all pairs.

3.1.4 Statistical Characterization. Networks can be characterized by the following statistical properties.

i **Degree distribution:** The degree of a node is the number of connections to other nodes, a particular node has and is denoted by k and the average degree of a network of a network is denoted by $\langle k \rangle$. Looking at the entire space or network one can obtain a distribution for the degree. Let $n(k)$ be the number of nodes of degree k in a network of size n, $p(k) = \frac{n(k)}{n}$. Where $p(k)$ represents the probability that a node selected uniformly at random has degree k. The degree distribution is obtained by plotting $p(k)$ against k (Estrada et al., 2015). The common distribution found in the network are normal distribution, exponential, power law distribution and Poisson distribution(Chung and Lu, 2002).

ii **Clustering:** A cluster in a network is a collection of nodes which are similar among them and are dissimilar to other nodes belonging to other clusters. Clustering in friendship network may signify friends people have in common. Local clustering in a network is measured by the Watts-Stogatz coefficient and the global clustering by Newman clustering coefficients.

Watts-Strogatz average clustering coefficient is given by

$$\overline{C} = \frac{1}{n}\sum_{i} c_i \tag{3.1.5}$$
$$c_i = \frac{2t_i}{k_i(k_i-1)}$$

where t_i is the number of triangles attached to node i of degree k_i. The Watts-Strogatz clustering coefficient of a node quantifies how close its neighbours are close to making a clique. In terms of friends it quantifies how one's friends are friends with each other. The clustering coefficient lies between 0 and 1, if its zero, then no two nodes of a node's neighbours are connected and if it is 1 then all the neighbours of a node are connected to connected to each other.

The Newman clustering coefficient is given by

$$c = \frac{3t}{p_2} = \frac{3|c_3|}{p_2} \tag{3.1.6}$$

where $t = c_3$ number of triangle in the network and $|p_2|$ the number of closed paths of length 2. The Newman clustering coefficient quantifies how clustered a network is as a whole. Nodes with less than two neighbours are given 0 as the clustering coefficient.

In a social network if a person A is friends with person B and B friends with C it is most likely that A will be introduced to C and the two will know each other. This will result in the three forming a triangle. The clustering coefficient either global or local gives a proportion of how many such triangles are there and how many are likely to exist. The local clustering coefficient will give this value in relation to a particular node while the global clustering coefficient will give the value over the entire network (Estrada et al., 2015).

A network is said to be small world or to exhibit small world properties if its Newman clustering coefficient is greater than the Watts-Strogatz clustering coefficient. That is a small world network has a high clustering coefficient and a low average distance (Estrada, 2012). A small world property can be defined as let D be the average distance between any pair of vertices in a network, if D increase proportionally to the logarithm of the size of the network$N$ (Newman and Watts, 1999). That is,

$$D \propto \log N \tag{3.1.7}$$

A high clustering coefficients represents local connectivity and results in near cliques and the short average distance represents global connectivity of nodes in a graph citepMehlhorn2013.

3.1.5 Random Graphs. A random graph $G(N,p)$ can be defined as, given N number of vertices, edges between them are drown such that between any pair i,j there is an edge with uncorrelated probability p.

Let z be the average degree. The probability p of an edge being present between any two vertices is given by $p = \frac{z}{N-1}$, for large N it can be approximated by $\frac{z}{N}$ (Newman et al., 2002). The degree

k of a vertex has a probability distribution p_k given by;

$$p_k = \binom{N}{k} p^k (1-p)^{N-k} \approx \frac{z^k e^{-z}}{k!}, \tag{3.1.8}$$

for a constant k and large N.

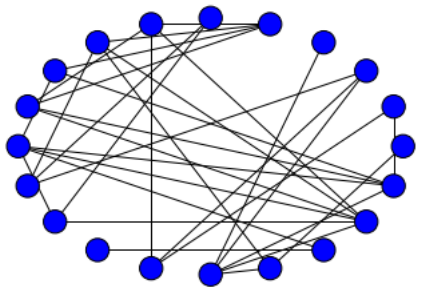
For example, let us take 20 vertices draw an edge between any vertices with probability $p = 0.2$ We can get a random network shown in figure 3.1 below.

It can be shown that a random graph can exhibit small world effects. Assuming that person A, represents a node on a network such as figure 3.1. A has z neighbours and about z^2, z^3 second and third neighbours respectively, and so on. Then the diameter of the network D is given by $z^D = N$. Thus

$$D = \frac{\log N}{\log z}$$

The logarithmic increase in the diameter of the network and the distance between nodes is typical of a small world effect. Since $\log N$ increases slowly with N it allows the distance to be quite small in very large systems (Newman, 2000). Random networks have a low clustering coefficient $c = \frac{z}{N}$ (Newman, 2003).

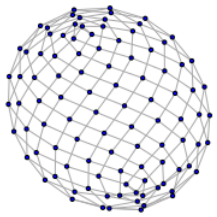
Figure 3.1: Random Graph with N =20 and p = 0.2



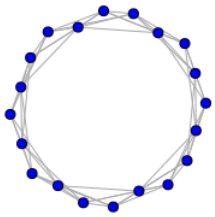
However, random networks are not a good model of social networks. People's circles of acquaintances tend to overlap to a great extent. Random models have a very low clustering coefficient.

3.1.6 Ordered Lattice:. In order to deal with real world networks, graphs must have both high clustering and small world effect properties.Random graphs as discussed earlier show a small world effect. Their average vertex to vertex distance increase only logarithmically with N but they do not show low clustering (Newman, 2000). This leads us to another graph model which is an ordered lattice.

The opposite of a random graph is a completely ordered lattice. An ordered lattice is a graph where each vertex is connected to its z neighbours. A lattice can be drawn in many dimensions. For example, figure 3.2 shows two lattices drawn in different dimensions.



(a) A square lattice, with z =4



(b) A ring lattice, with $z = 3$

Figure 3.2: Different types of regular lattices

Regular lattices and random graphs have a long history of use in network theory and modelling of population structures, Harris (1974) gives an example of a classic lattice.

The clustering coefficient of a lattice is given as

$$C = \frac{3(z-d)}{4(z-2)} \tag{3.1.9}$$

where d is the dimension of the lattice. For a large z, C tends to $\frac{3}{4}$.

However, regular lattices do not show the small world effect of vertex to vertex distances which increase slowly with size. For a regular lattice of higher dimensions such as the shape of a square or hypercube of size L with $N = L^d$ vertices, the average vertex to vertex distance increases linearly with the system size, which is not typical of the small world behaviour.

Models built on latices assume that individuals are nodes on a regular lattice and connections are made of some collection of near neighbours or each node. For example, people may be spread out such that connections are made to their four nearest neighbours, one on the left, right, up and down or eight neighbours including the four diagonal elements (Lloyd et al., 2006).

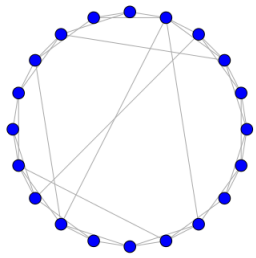
The main difference between a random graph and lattice is that, in lattice networks interactions are local, that is individuals are only related to their neighbours. Where as in random networks the connections made are global, that is, connections are made without taking spatial locations of an individual into consideration.

3.1.7 Watts - Strogats Small World Networks. We have shown that lattices are characterised by high clustering coefficients but long path lengths or vertex to vertex distances. That is, it takes many steps to move between any two randomly selected vertices, whereas random networks have shorter vertex to vertex distances, since there are many long range links, but low clustering (Keeling and Eames, 2005).

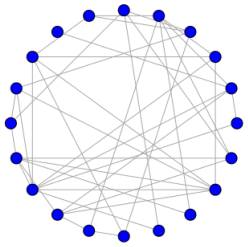
Small world networks were first introduced by Watts and Strogatz as an intermediate between a regular lattice and a complete graph. They are built by randomly rewiring certain proportions

of the network links with a probability p (Watts and Strogatz, 1998). The small world networks allow for random contacts across the network. That is in addition to near neighbours as a regular lattice, each node has a random distant neighbour connected to it (Watts and Strogatz, 1998).

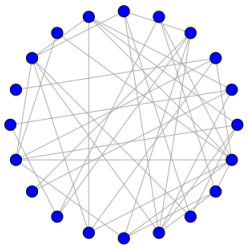
The Watts-Strogatz network is essentially a regular lattice with some degree of randomness in the connectivity of vertices. Take for example in figure 3.2b above and we rewire some edges with a some probability p, that is one of its ends is moved into a randomly chosen position on the lattice. For a small p this produces mostly a regular graph, but with a few connections stretched along distances across the lattice and for $p = 1$ it produced a complete graph. Figure 3.3c below shows Watts- Strogats networks with different probabilities.



(a) A Small world, with p =4



(b) A Small world network, with $p = 0.5$



(c) A Small world network, with $p = 0.8$

Figure 3.3: Watts- Strogatz

4. Compartmental and Stochastic Models

4.1 Deterministic Models

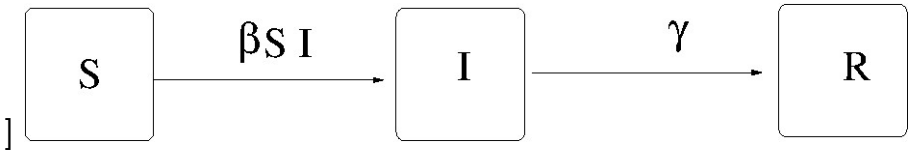
4.2 SIR Model

In the SIR model the population is partitioned into three compartments susceptible, infected and recovered. This is the basis for most epidemiological models (M'Kendrick, 1925). In building the model the number of individuals susceptible, infected and recovered is assumed to be differentiable over time. The simple epidemic model is given by.

$$\frac{dS}{dt} = -\beta SI, \tag{4.2.1}$$
$$\frac{dI}{dt} = \beta SI - \gamma I, \tag{4.2.2}$$
$$\frac{dR}{dt} = \gamma I, \tag{4.2.3}$$

$N = S + I + R$ The model is based on the assumption that susceptible individuals become infected at a rate β proportional to the number of people infected and susceptible at time t and infected people recover at γ rate. The reciprocal $\frac{1}{\gamma}$ is referred to as the average infectious period . Another assumption in this model is that the population remains constant, thus it does not take int account the demographic changes of the population. Figure 4.1 shows the compartmental diagram for an SIR model without demographic dynamics.

Figure 4.1: SIR compartmental diagram



4.2.1 Model Analysis. We determine the equilibrium and the stability of 4.2.1, but since $N = S + I + R$ knowing S and I implies that we can solve for R. Hence our system of equations can be reduced to

$$\frac{dS}{dt} = -\beta SI. \tag{4.2.4}$$
$$\frac{dI}{dt} = \beta SI - \gamma I. \tag{4.2.5}$$

With $S(0) > 0$, $I(0) > 0$ and $R(0) = 0$ as the initial conditions for the model. We now calculate the disease free equilibrium and endemic equilibrium by equating 4.2.4 and 4.2.5 to zero then solving them. Despite its extreme simplicity, this model 4.2.1 cannot be solved explicitly.That is, we cannot obtain an exact analytical expression for the dynamics of S and I though time, instead the model has to be solved numerically.

The equation 4.2.4 gives two import insights in understanding the spread of disease and has since been used in infectious disease modelling for a long time.

4.2.2 Threshold Phenomenon. It is important to determine whether the infection will result in an epidemic or not and what factors could determine this. Consider the initial stage after $I(0)$ individuals have been infected in a population with $S(0)$ susceptible. Equation 4.2.5 can be rewritten as,

$$\frac{dI}{dt} = I\left(\beta S - \gamma\right) \tag{4.2.6}$$

In equation 4.2.6 if the initial susceptible (S(0)) is less than $\frac{\gamma}{\beta}$, then $\frac{dI}{dt} < 0$. This means that there will be no epidemic in this case.

This result was coined by M'Kendrick (1925) and is refereed to as the threshold phenomenon. The initial S(0) must exceed the threshold $\frac{\gamma}{\beta}$ for an epidemic occur.In other words the relative removal rate $\frac{\gamma}{\beta}$ must be small enough to allow the occurrence of the epidemic.

The reciprocal of the of relative removal rate is called the basic reproductive ratio and is one of the most important quantities in epidemiology. The basic reproduction ratio is defined as the average number of secondary cases arising from an average primary case in an entirely susceptible population. It measures measures the maximum reproductive potential for an infection. For the our SIR model in equation 4.2.1 it is given by:

$$R_0 = \frac{\beta}{\gamma} \tag{4.2.7}$$

For initial susceptible $S(0) = 1$, if $R_0 > 1$ then there will be an outbreak and if $R_0 < 1$ the will be no outbreak. It can be noted that every disease has a different R_0 value and also depending on the population's contact pattern the R_0 value will differ.

4.2.3 Epidemic Burnout. The threshold phenomena gives a description of what happens in the initial stages after introduction of an infection. Another important quantity we get from the SIR model is the long term state infection. From they system in equation 4.2.1 we take

$$\frac{dS}{dt} = -\beta SI \tag{4.2.8}$$

$$\frac{dR}{dt} = \gamma I \tag{4.2.9}$$

dividing equation 4.2.6 by equation 4.2.9 we get

$$\frac{dS}{dR} = \frac{-\beta S}{\gamma} = R_0 S \tag{4.2.10}$$

Integrating equation 4.2.10 with respect to R, we get;

$$\int \frac{dS}{S} = \int R_o dR \tag{4.2.11}$$
$$lnS = -R_0 R + k \tag{4.2.12}$$
$$e^{lnS} = e^{-R_0 R + k} \tag{4.2.13}$$
$$S(t) = e^{-R_0 R(t)} e^{k} \tag{4.2.14}$$

assuming R(0) = 0

$$S(t) = S(0) e^{-R_0 R(t)} \tag{4.2.15}$$

Hence, as the epidemic develops, the number of susceptibles reduce. The numbered of recovered does not start increasing immediately because of infectious period, but eventually it does. Their number of susceptibility in the population will always be above zero as can be seen in equation 4.2.15.

From equation 4.2.15, $s(t) \geq e^{-R_o}$ since $R(t) < 1$. Thus, there will always be a proportion of susceptibles in the population. The epidemic burnout gives the intuitive idea that the chain of transmission eventually breaks due to the decline in infectives not due to lack of susceptibles (Haran, 2009).

4.2.4 Disease free equilibrium. Adding demographic parameters to 4.2.1 we get a new system of equations. That is, adding a parameter for birth rate and death rate, hence the population is no longer closed in this case.

$$\frac{dS}{dt} = \mu - \beta SI - \mu S \tag{4.2.16}$$
$$\frac{dI}{dt} = \beta SI - \gamma I - \mu I \tag{4.2.17}$$
$$\frac{dR}{dt} = \gamma I - \mu R \tag{4.2.18}$$

Using the same procedure we used to get the equation 4.2.7 it can be shown that the R_0 for this model is

$$R_0 = \frac{\beta}{\mu + \gamma} \tag{4.2.19}$$

Now we calculate the equilibria of the model by setting equation 4.2.16, 4.2.17 and 4.2.18 to zero, that is $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$ and denote by $S^*, I^* and R^*$ values of S, I and R that satisfy this condition. From equation 4.2.16 we get

$$\mu - \beta SI - \mu S = 0 \tag{4.2.20}$$
$$\mu - S(\beta I + \mu) = 0 \tag{4.2.21}$$
$$S = \frac{\mu}{\beta I + \mu} \tag{4.2.22}$$

It can be shown that $S^*I^*R^* = (1, 0, 0)$ is the epidemic free equilibrium.

To establish the endemic equilibrium , we factorize I in equation 4.2.17 and we get,

$$I(\beta S - (\gamma + \mu)) = 0 \tag{4.2.23}$$

thus we get

$$I = 0 \rightarrow S = \frac{\gamma + \mu}{\beta} \tag{4.2.24}$$

Therefore, $I^* = 0$ and $S^* = \frac{\gamma+\mu}{\beta}$, but since $I^* = 0$ is a disease free equilibrium. We concentrate on $S^* = \frac{\gamma+\mu}{\beta} = \frac{1}{R_0}$ see 4.2.19

Now, we take $I \neq 0$ and solve (4.2.18). Since $S + R + I = 1$

$$\gamma I - \mu(1 - S - I) = 0 \tag{4.2.25}$$
$$\gamma I - \mu I - \mu(1 - S) = 0 \tag{4.2.26}$$
$$I = \frac{\mu}{\beta} R_0 \left(1 - \frac{1}{R_0}\right) \tag{4.2.27}$$
$$I = \frac{\mu}{\beta}(R_0 - 1) \tag{4.2.28}$$

Thus the endemic equilibrium point (S^*, I^*, R^*) is $\left(\frac{1}{R_0}, \frac{\mu}{\beta}(R_0 - 1), 1 - \frac{1}{R_0}\frac{\mu}{\beta}(R_0 - 1) - \frac{1}{R_0}\right)$

4.2.5 stability of the model. Once an outbreak occurs, its important to understand the long term behaviour of the outbreak and finding the stability of the model gives an insight on this. In other words, calculating the stability of the model is establishing at which point the epidemic burn out will occur.

4.3 SEIR Model

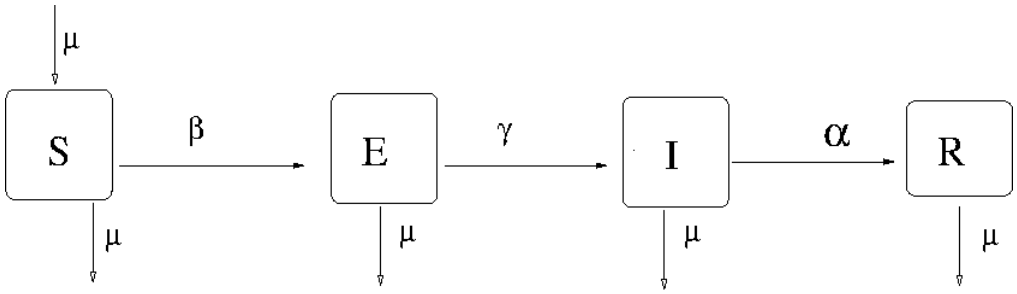
The susceptible, Exposed, Infected and Recovered models add a new comportment to the previously discussed SIR Model. The earlier models assume that once a person is infected, they become infectious immediately. In this model an assumption is made that once a person is infected there

is an intermediate stage between the time of infection and when they become infectious, this may be refereed to as the latent or incubation period of the infection. The system of equations will be;

$$S' = \mu - \beta SI - \mu S \tag{4.3.1}$$
$$E' = \beta SI - (\mu + \gamma)E \tag{4.3.2}$$
$$I' = \gamma E - (\alpha + \mu I) \tag{4.3.3}$$
$$R' = \alpha I - \mu R \tag{4.3.4}$$

where β is the rate at which susceptible individuals become infectious, γ the rate at which infected individual become infection. The quantity $\frac{1}{\gamma}$ is called the latent period of the infection. α is the recovery rate. In this model the total number of infected individuals is given by $E + I$ and we assume that our system is density dependant thus $S + E + I + R = 1$ and that the population is constant implying that the birth rate (μ) = death rate (μ). Figure 4.2 shows the compartmental diagram of an SEIR model.

Figure 4.2: SEIR compartmental model



Since $R = 1 - S - E - I$ we can be drop equation 4.3.4 from the system and calculate equilibrium point by equating equations 4.3.1 to 4.3.3 to zero and solving the system of equations.

From equation (4.3.1) we get $S = \dfrac{\mu}{\beta I - \mu}$ and from equation 4.3.3 we get $I = \frac{\gamma E}{(\alpha+\mu)}$ and from equation 4.3.3 we get $E = \dfrac{\beta SI}{(\mu + \gamma)}$. Thus, for I = 0, E =0 and S = 1 hence, the disease free equilibrium of the system $S^*, E^*, I^* = (1, 0, 0)$.

When $I^* \neq 0$ we find the disease pandemic equilibrium, which is given by

$$S^*, E^*, I^* = \left(\frac{(\alpha + \mu)(\gamma + \mu)}{\beta\gamma}, \frac{\alpha + \mu}{\gamma} I^*, \frac{\mu}{\beta S*} \frac{\mu}{\beta} \right).$$

The reproductive number R_0 will be calculated using the new generation matrix method. Let F and V be non negative matrices,

$$F = \left[\frac{\partial F_i(x^*)}{\partial j} \right] \tag{4.3.5}$$

Where $F_i(x^*)$ are the rates of new infections in compartment i and

$$V = \left[\frac{\partial V_i(x*}{\partial j}\right] \tag{4.3.6}$$

Where $V_i(x^*)$ are the rates of transfer of infection from one compartment to another (Van den Driessche and Watmough, 2002). $F = \begin{pmatrix} 0 & 0 \\ \beta & 0 \end{pmatrix}$ and $V = \begin{pmatrix} \gamma+\mu & \gamma \\ 0 & \alpha+\mu \end{pmatrix}$

Therefore,

$$FV^{-1} = \begin{pmatrix} 0 & 0 \\ \beta & 0 \end{pmatrix} \begin{pmatrix} \frac{1}{(\gamma+\mu)} & \frac{-\gamma}{(\alpha+\mu)+(\gamma+\mu)} \\ 0 & \frac{1}{\alpha+\mu} \end{pmatrix} = \begin{pmatrix} 0 & 0 \\ \frac{\beta}{(\gamma+\mu)} & \frac{-\beta\gamma}{(\alpha+\mu)+(\gamma+\mu)} \end{pmatrix} \tag{4.3.7}$$

The equation 4.3.7 has eigenvalue values λ_1 , λ_2 as 0 and $\frac{-\beta\gamma}{(\alpha+\mu)+(\gamma+\mu)}$ respectively.

$$R_0 = max|\lambda_1||\lambda_2| \tag{4.3.8}$$

Thus the R_0 for the system will be $\frac{\beta\gamma}{(\alpha+\mu)+(\gamma+\mu)}$.

For the disease free equilibrium (1,0,0)is asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$ (Van den Driessche and Watmough, 2002). That is the solutions of the systems of equations 4.3.1 4.3.3 move towards the disease free equilibrium when $R_0 < 1$.

4.4 Stochastic Models

4.4.1 Stochastic SIR Model. We will only consider an SIR model for the stochastic models. The total population $N(t) = S(t) + I(t) + R(t)$ just as in deterministic models. Where

$$S(t), I(t), R(t) \in \{0, 1, 2, \dots, N\} \tag{4.4.1}$$

and $t \in \{0, \triangle t, 2 \triangle t, \dots\}$. There are two independent discrete random variables S, E and I because $R(t) = N(t) - S(t) - I(t)$. Therefore the stochastic process for the SIR model is a bivariate process $\{S(t), I(t)\}_{t=0}^{\inf}$ ha has a joint probability

$$p_{(s+k,i+j),(s,i)}(\triangle t) = \Pr\{(\triangle S, \triangle I) = (k, j) \mid (S(t), I(t)) = (s, i)\} \tag{4.4.2}$$

where $\triangle S = S(t + \triangle t) - S(t)$. Hence the transition probability of the SIR model is a follows;

$$p_{(s+k,i+j),(s,i)}(\triangle t) = \begin{cases} \beta is/N \triangle t & (k, j) = (-1, 1) \\ \gamma i \triangle t, & (k, j) = (0, -1) \\ b(N - s - i) \triangle t & (k, j) = (1, -1) \\ 1 - \beta is/N \triangle t - [\gamma i + b(N - s)] n \triangle t, & (k, j) = (0, 0) \\ 0, otherwise \end{cases} \tag{4.4.3}$$

The time step $\triangle t$t must be chosen small enough such that each transition probabilities lie in the interval [0,1]. Applying the Markov property, the difference equation satisfied by the probability $p_{(s,i)}(t+\triangle t)$ can be expressed in terms of the transition probabilities.

$$\begin{aligned} p_{(s,i)}(t+\triangle t) = {} & p_{(s+1,i-1)}(t)(t)+\triangle t) rac\beta N(i-1)(s+1)\triangle t + p_{(s,i+1)}(t)\gamma(i+1)\triangle t \\ & + p_{(s-1,i+1)}(t)b(i+1)\triangle t + p_{(s-1,i)}(t)b(N-s+1-i)\triangle t \\ & + p_(s,i)(t)\left(1-\left[\frac{\beta}{N}is+\gamma i+b(N-s)\right]\triangle t\right) \end{aligned}$$

The difference equations can be written as in matrix form as

$$p_{(s,i)}(t+\triangle t) = P(\triangle t)p(t),$$

where $P(\triangle t)$ is the transition matrix and $p(t)$ is the probability distribution vector for the stochastic process.The state set is divided into two classes; the current and the transient.(N,0) is an adsorbing recurrent state while all other states are transient. The probability of an out break is given given as $1-\frac{1}{R_0}$ when $R_0 > 1$ (Brauer, 2017).

One the main aspects in which deterministic and stochastic models differ is extinction. In deterministic SIR model an epidemic never goes to extinction in a limited time frame because the number of infectives declines exponentially and only reaches zero at infinity. In a deterministic framework an epidemic is said to go into extinction if it has a negative growth rate. Where as in the stochastic SIR model an epidemic is the epidemic becomes extinct in a more direct sense, the number of infects can go to zero without waiting forever.

5. Spread of Zika Virus on a Small World Network

The deterministic models discussed in the chapters above assume that all individuals have an equally small probability of being infected. In this section we build a model for the propagation of Zika virus based on a small world network.

Traditional models of infectious disease dynamics have a long, successful history of describing and modelling infectious disease spread of many diseases. They are quite simple and tractable (Fu et al., 2013).

There are certain specific and common situations when the structure of social connectivity is at least as important as the activity of the underlying infectious agents for the study of transmission of infection and control. This is one among the major reasons that has motivated the modelling of infectious diseases on social networks Fu et al. (2013).

5.1 Vector Borne Disease Propagation on a Small World Network

[Jan: Summarize what you are doing in this section: You give a heuristic argument why we consider only people in our model instead of both people and vectors.]

We assume that there is a lattice with two layers.One for mosquitoes, another for human beings. We assume mosquitoes are stationary and that people have close and remote links. That is mosquitoes do not cover long distances, but just hover around a specific location. On the other hand, people can travel to distant locations. Close links refer to individual's close acquaintances while distant links refer to and individuals random acquaintances.

A mosquito M_1 bites a Zika infected person h_1 with probability α_1. Then transmits the virus to person h_2, with a probability of α_2. Thus, person h_1 is connected to person h_2 through M_1. It can then be said that h_2 can be infected by h_1 with probability p_1. Assuming that α_1 and α_2 are independent $p_1 = \alpha_1\alpha_2$.

If person h_3 travels to the place where h_1 lives or gets close enough that he gets bitten by mosquito M_1 can be infected probability α_3. Thus, α_3 is the probability that person h_3 travels and get bitten by mosquito M_1. It can be said that h_1 infects h_3 with probability p_2, because h_1 is connected to h_3 through M_1. Assuming α_1 and α_3 are independent, $p_2 = \alpha_1\alpha_3$. The phenomenon of infecting a close like or distant link can be expressed in 4 cases.

i). h_2 may get infected by h_1 through M_1. In this case h_1 and h_2 are referred to as near neighbours.

ii). h_4 may travel to a place close enough to get the infection from h_1 through M_1. In this case h_3 referred to as a distant neighbour.

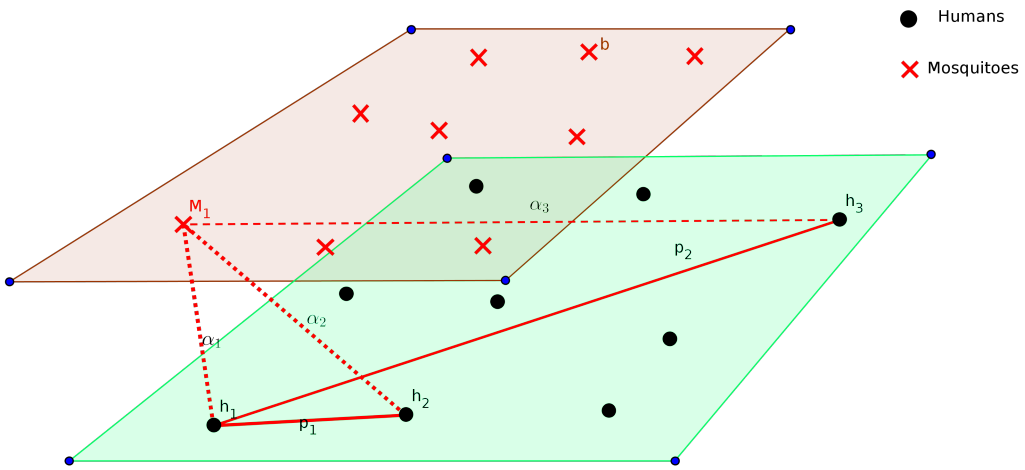


Figure 5.1: Disease transmission through a vector

iii). h_1 may travel to a place close enough to infect h_4 through another mosquito in that vicinity.In this case h_3 is referred to as a distant neighbour.

iv). h_1 and h_3 may both travel to some place at the same time and h_1 transmits the infection to h_3 and this case is neglected. Thus, in the this case h_1 and h_3 would not be referred to as near or distant neighbours.

The probabilities of cases (ii) and (iii) might be different but we assume that we can average them out and use single value for p_2. We neglect probability in case (iv), since we consider it to be small compared to case (ii) and case(iii). We then assume that a mosquito can only transmit an infection once. Therefore, M_1 is a scourge of mosquitoes. [Jan: scourge? Which word do you mean?]

The existence of near and distant neighbours in the disease infection dynamics of Zika virus on a lattice with two layers in 5.1 makes it possible to represent the dynamics of disease spread on a small world network in figure 5.3. Thus, in modelling the spread of Zika virus on a small world network, the dynamics of transmission through mosquitoes are represented by the edges of the graph. An edge is drawn between two vertices, whenever there is a likelihood of transmission from one to another via a mosquito bite as can be seen in figure 5.1.

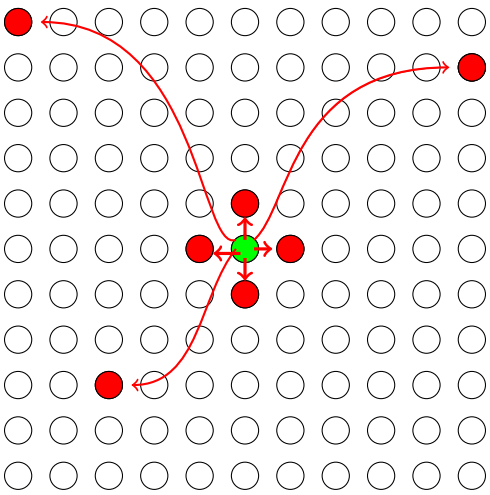


Figure 5.2: Smallworld network structure

5.2 Small World Methodology

We can now suppose that the population is arranged on a regular 2-dimensional square grid. Where each vertex can infect its 4 nearest neighbours and a number of distant neighbours. Near neighbours in this case refers to individuals that one spends most of their time with, could be colleagues at work or school, people in the same house and distant neighbours refers to random individuals that one is likely to transmit the infection to.

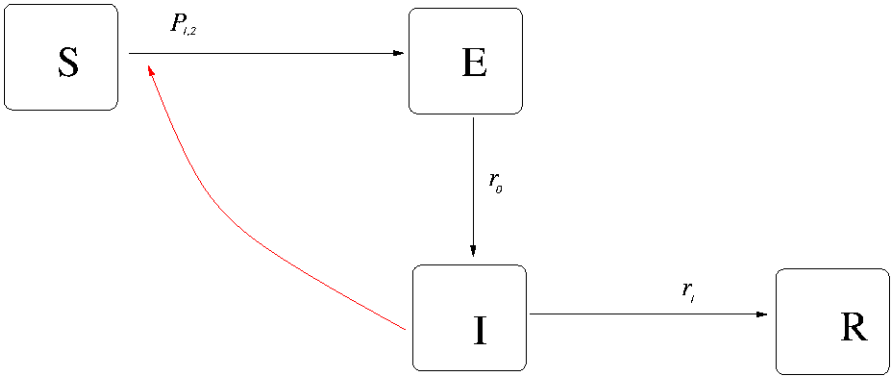


Figure 5.3: State transition diagram

Figure 5.2 shows the arrangement of nodes in a small world network and figure 5.3 shows the transmission state diagram. The probabilities of transition from one compartment to another are per day and each day we assume that the given transition occur independently. Transition from :S to E [Jan: occurs] with infection probabilities $p_{1,2}$ based on the small world network structure and: E to I with probability r_0 and I to R with probability r_1. In figure 5.2, the infected green node may infect its four near neighbours, with probability p_1 and its three remote neighbours with probability p_2. By infection we mean transition from susceptible to exposed state.

Infected individuals can cause susceptible individuals, whom they are linked [Jan: to], to becomes

exposed with with probability p_1 or p_2. Infected individuals can infect their close neighbours with probability p_1 and infect their distant neighbours with probability p_2. p_1 and p_2 are probabilities of infection per day. Exposed individuals become infected with probability r_0 and infected individuals become recover with probability r_1.

The number of near neighbours $n_1 = 4$ or less, taking into account the boundary cases. The number of distant neighbours n_2 for each node is independent and identically distributed. That is for each node u there are $n_2^{(u)}$ distant neighbours. $n_2^{(u)}$ is chosen to follow a discrete exponentially decaying distribution

$$\Pr[n_2^{(u)} = k] = c \cdot e^{-\mu k} \tag{5.2.1}$$

where $c \approx \dfrac{1}{1 - e^{-\mu}}$ and $\mu > 0$ (Fu et al., 2013). The degree distribution in most social networks is exponential because of the celebrity effect (Estrada et al., 2015). In social networks, there are few people who have a high number of connections and many others with a few number of connections. In modelling infectious diseases these individuals are referred to as super spreaders. [Jan: Would be good to include formula for expectation of n_2 as function of μ.]

The transition probability r_0, the number of days an individual is in the exposed state is as a result of a series of Bernoulli trials with mean $\frac{1}{r_0}$, follows a geometric distribution $f_X(x) = (1-p)^{x-1}p$. [Jan: Write this formula in terms of r_0.] Similarly the infectious period follows a geometric distribution with mean $\dfrac{1}{r_1}$ (Fu et al., 2013).

5.3 Model

The model has 6 parameters, they are N, p_1, p_2, n_2, r_0 and r_1. We let N be the population size of a city or country and is arranged in a regular grid of side length l such that $l^2 = N$. The rest of the parameters have been described above.

A thorough review of literature in Lessler et al. (2016) indicates that the incubation or latent period for Zika virus infection is 11.2 days after infection ,with [Jan: Comma: space after, not before.] a 95% confidence interval of $7.6 - 18$. Further the center for disease control and prevention (CDC) [Jan: Capitalize CDC name properly.] indicate that the incubation period for the Zika virus ranges from 3 days to 14 days from infection (Krow-Lucal et al., 2017). Therefore we estimate r_o with $\frac{1}{11.2}$ [Jan: These are the values before you exhibit symptoms. Are they the same for becoming infective?] [Jan: Consider adding some days to allow time for a mosquito to transmit the virus.]

95% of the of Zika patients will still have detectable virus infectiousness 18.9 days after infection with a confidence interval of 13.6 -79.4 (Lessler et al., 2016).The infectiousness in Zika infection ends 1.5 - 2 days before the virus becomes undetectable (Funk et al., 2016). Thus the chosen value of the infectious period is $18.9 - 1.5 = 17.4$ days. Therefore r_1 is estimated to be $\dfrac{1}{17.4}$.

Hence, we have μ, p_1 and p_2 as free parameters. Without active control, the average number of secondary infections resulting from a primary Zika virus infectious is between 3 and 6. Therefore,

we choose 4.5 as the R_0. [Jan: Say what is R_0.] Since the number of remote neighbours is random and fixed for each, we estimate $E(n_2^{(u)}) = \widehat{n_2}$. [Jan: We don't "estimate", we define.]

In this state each infectious individual will infect on average $n_1kp_1 + E[n_2^{(u)}]p_2$ new individuals everyday.Where k is the average number of near neighbours' links that support possible infection and [Jan: s/and/since] near neighbours are arranged in clusters, therefore $0.5 < k < 1$. In our computation we will use $k = 0.5$. [Jan: You say $k > 0.5$ and then $k = 0.5$.] The average number of individuals infected each day can be estimated by the number of secondary infections each day of an individuals infectious period. [Jan: I don't get this sentence, correct.] Thus ;

$$n_1kp_1 + \widehat{n_2}p_2 \approx \frac{R_0}{r_1} \tag{5.3.1}$$

$$n_1kp_1 + \widehat{n_2}p_2 \approx 0.2586 \tag{5.3.2}$$

thus, $p_1 \approx 0.1293 - 0.5\widehat{n_2}p_2$, in terms of small world parameters $\widehat{n_2}$ and p_2.

Now n_1 and n_2 represent the number of interactions an individual has each day. Hence the $n_1 + n_2$ is the lower bound is a lower bound of the number of active acquaintances because it is a number of links that are sufficiently intimate to support transmission of the virus. In reality some links would be closer than others and more likely to lead to transmission. We assume that all n_1 links are infected with probability p_1 and n_2 with probability p_2 each day. The probabilities p_1 and p_2 are not necessarily the same.

Note that the choice of n_1 and n_2 is not critical; what is more important is the infection probability $n_1kp_1 + n_2p_1$.

We can summarize the parameters of the models as;

$$n_1 = 4 \tag{5.3.3}$$

$$\widehat{n_2} = 8 \tag{5.3.4}$$

$$r_0 = \frac{1}{11.2} \approx 0.089 \tag{5.3.5}$$

$$r_1 = \frac{1}{17.4} \approx 0.057 \tag{5.3.6}$$

$$p_1 = 0.1293 - 4p_2 \tag{5.3.7}$$

Now we have one free parameter p_2. We can now estimate the number of new infections by;

$$E(-\Delta S) = (n_1kp_1 + \widehat{n_2}p_2 - r_1)I \tag{5.3.8}$$

[Jan: You never explain your choice of $\widehat{n_2}$. Since you don't vary it in simulations, wouldn't it be better to fix it in the beginning and then make calculation for p_1 and p_2 with one free parameter less?]

From equation 5.3.8 we can estimate the number of new infections as;

$$E(-\Delta S) = (2p_1 + 8p_2 - 0.057)I \tag{5.3.9}$$

From equation 5.3.2, it can be shown that p_1 and p_2 have natural bounds. That is taking $p_2 = 0$, implies that $p_1 \leq 0.1293$. For $p_1 = 0$, we get $p_2 \leq 0.03232$.

Further, the rate of spread of infection is given by ;

$$1 - \frac{r_o + r_1}{2} + \sqrt{\frac{1}{4}(r_o - r_1)^2 + n_k r_o}, \tag{5.3.10}$$

where as before $n_k = n_1 k p_1 + \widehat{n}_2 p_2$ (Fu et al., 2013). From equations 5.3.8, it can be seen that the disease will be contained if $n_k < r_1$. If $n_k < r_1$ there will be a negative the increase in the number of infected individuals thus, the disease will be contained. When the probability of recovery is greater than the probability of infection. individuals will recover before they can infect others, this will result in the out break being contained. [Jan: Mention that this comes from eigvalue analysis.]

5.4 Simulation

To investigate how disease propagation varies depending on p_1, p_2, and r_1 we ran a couple of simulations on a small work network. The code for the simulation is attached in the appendix.

We initiate the model with one infected individual and an r_1 which is relatively small .We simulated our models with various parameters and observe they dynamics of the infection.

We ran simulations for 5 cases;

1. $p_1 = 0.129$, $p_2 = 0$ and $r_1 = 1/17.4$
2. $p_1 = p_2 = 0.02580$ and $r_1 = 1/17.4$
3. $p_1 = 0$,$p_2 = 0.0323$ and $r_1 = 1/17.4$
4. $p_1 = 0.0693$,$p_2 = 0.0173$ and $r_1 = 1/17.4$
5. $p_1 = 0.045$,$p_2 = 0.01125$ and $r_1 = 1/50$

In the first and third cases we investigate the boundary cases, when$p_1 = 0$ and $p_2 = 0$ respectively. In the second case we investigate a case where $p_1 = p_2$. In the fourth case we investigate and intermediate, where p_1 is greater than p_2. Lastly we investigate the case where we increase the infectious rate from the initial 17.4 days to 50 days and look at the intermediate case where $p_1 > p_2$.

5.5 Results

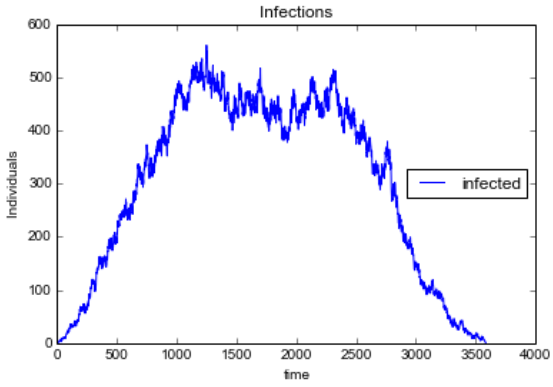
[Jan: Make clear that you are comparing your simulation to determinstic SEIR. Also, what are your parameters for SEIR? Shouldn't they be the same for the first four cases?]

From our simulated model for the transmission dynamics of Zika virus the following results were obtained. In figure 5.7 we depict the evolution of infected individuals at 20 day intervals in all the cases starting from day 60 to day 120 of the infection.

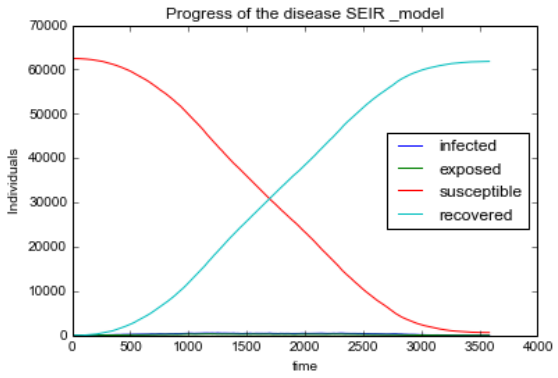
Case 1

It can be observed that the increase in the number of infected individuals overtime is stochastic in figure 5.4a. From figure 5.4a it be seen that the outbreak takes a long time before it dies off. When p_0 it implies that the spread of the infection is local. In the first row of figure 5.7, at different time steps infected nodes can be seen in clumps. There are few infections in the first 80 days of the infection as can be seen in figure 5.7, this implies that the infection does not spread rapidly when the spread is only via local links. In figure 5.4b, we observe that there few infected and exposed individuals over time. There is a steady decrease in the number of susceptibles and a gradual increase in the number of individuals recovering over time.

[Jan: Comment on the fact that in our model it's not really an epidemic (look at y axes).]



(a) progression of infections over time



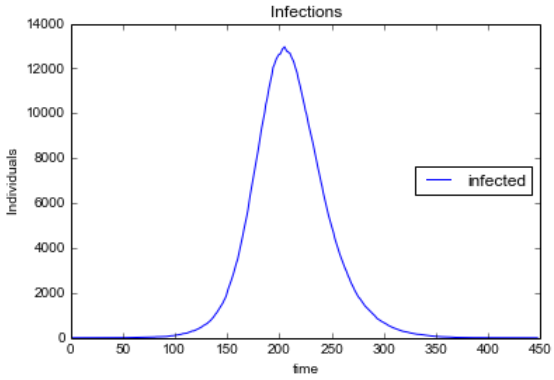
(b) Flow of individuals in compartments of the infection over time

Figure 5.4: Infection dynamics for $p_1 = 0.129$, $p = 0$ and $r_1 = 1/17.4$

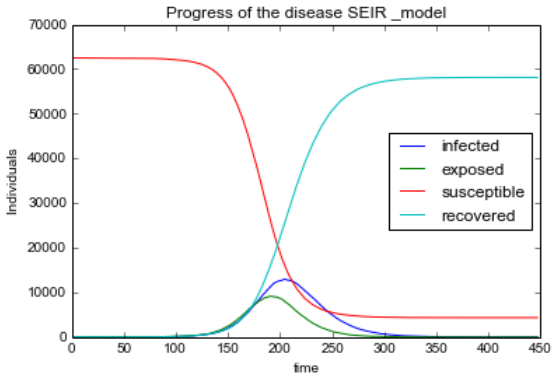
Case 2

In this case we observe that the number of infected individuals over time increases sharply and when it reaches the peaks decreases sharply as can be seen in figure 5.5a. In this case there are both local and distant transmissions of the infections. From 5.5a the infection takes a short time to reach its peak and to die off. A lot of people are infected throughout the course of the infection. In figure 5.5b we see that number of susceptible individuals decreases slowly up to some point then decrease sharply. The infection does not die out completely, but the epidemic does. Despite there still being individuals who are infected, they cannot spread the virus further as everyone else has developed immunity against it. In the second row of figure 5.7, a few clumps

716 can be seen and some random infections on different days of the infection, representing local
717 transmission and distant transmissions respectively.



(a) Infections over time



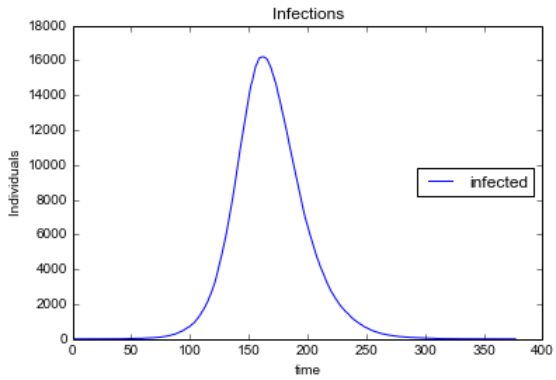
(b) Flow of individuals in compartments of the infection over time

Figure 5.5: Infection dynamics for $p_1 = p_2 = 0.02586$ and $r_1 = 1/17.4$

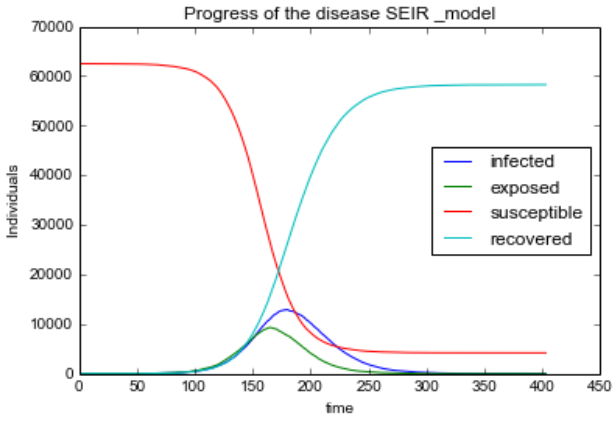
[Jan: Don't use \newpage]

Case 3

In this case the spread will only be through distant links. The infection will increase sharply, but not as much as in case 2 and will have a lower peak than in case 2 as can be seen in figure 5.6a. In figure 5.6b, it can be observed that the number of susceptible individuals decreases gradually for a time then decrease sharply. Similar to case 2, the number of infected individuals does not drop to zero. Thus, the curve for susceptible will not go to zero. Some individuals will still be infected, but because most people will develop immunity hence there will no longer be spread of the infection. In the third row of figure 5.7, we can observe that on each day of the infection, there are spatially uncorrelated infectious because there are no local infections.



(a) Progression of the infection overtime



(b) Flow of individuals in compartments of the infection over time

Figure 5.6: Infection dynamics for $p_1 = 0$, $p_2 = 0.0323$ and $r_1 = 1/17.4$

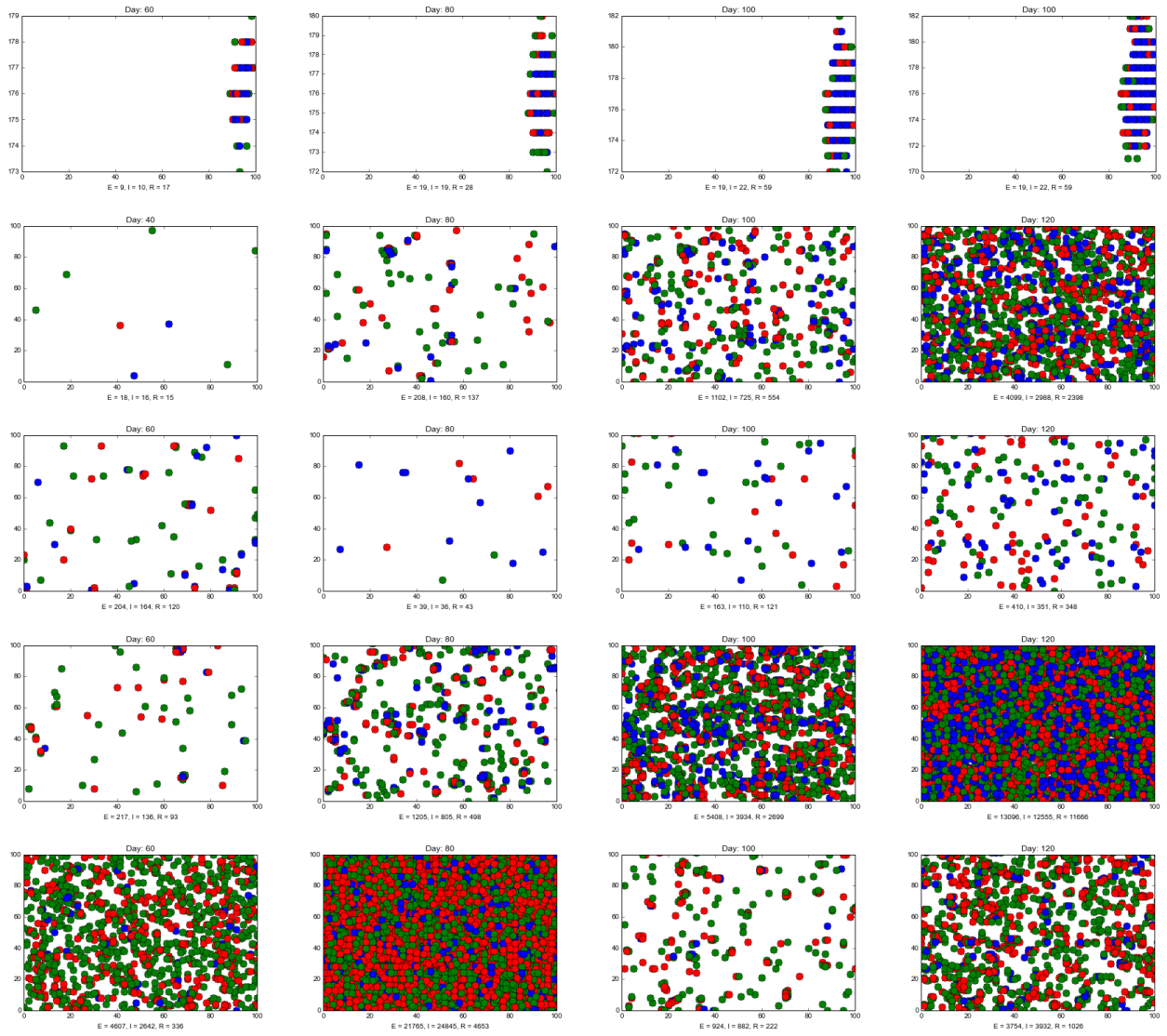
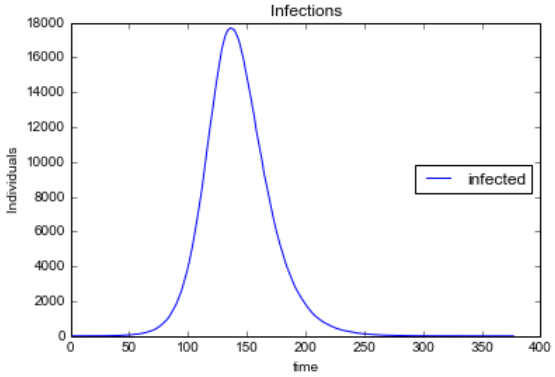


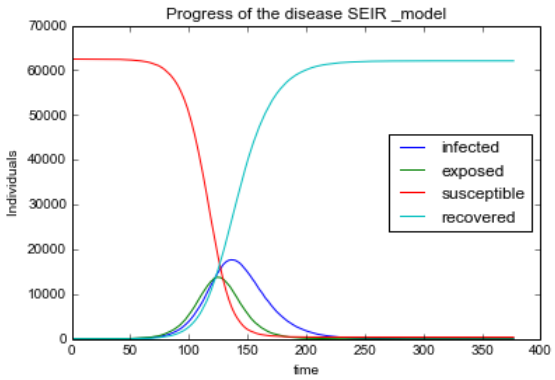
Figure 5.7: Each row depicts the evolution at 20 days interval of infection. Infected nodes are shown in red, exposed nodes in blue and recovered nodes in green.

[Jan: Please check again your code. From the figure in the top row it is clear that close links work only left-right. Also case 4 looks suspicious to me, though I'm not sure about that.]

Case 4 In this case infection spreads across all links. The probability of of infecting distant neighbour is lower than that of infecting near neighbours. The infection in this case spread similar to cases 2 and 3, though the peak number of infected will be lager than in both cases. Comparing to cases 1 to 3 the infection reaches its peak in a shorter period of time than in the other model figure 5.8a. In the figure 5.8b the dynamics of the infection is similar to case 3. In the fourth row of figure 5.7, we can observe that the infection in this case will burst early than in all other cases.



(a) Progression of infection overtime

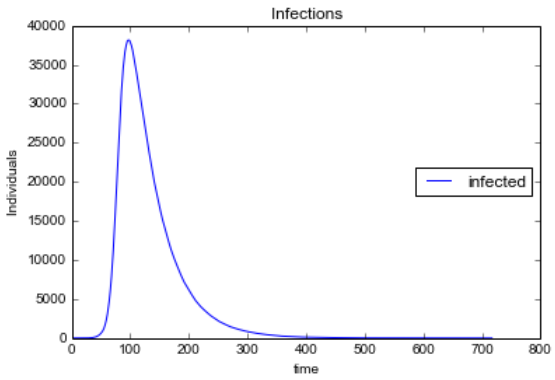


(b) Flow of individuals in compartments of the infection over time

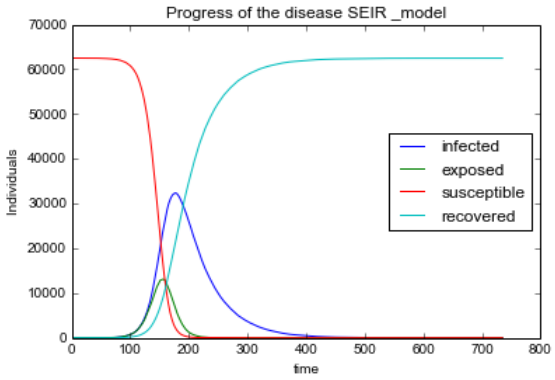
Figure 5.8: Infection dynamics for $p_1 = 0.0693$, $p_2 = 0.01173$ and $r_1 = 1/17.4$

Case 5

In all the previous cases we kept $r_1 = 1/17.4$, were 17.4 is the number of days an individual is infectious. Since r_1 has larger confidence interval (Lessler et al., 2016), we try $r_1 = 1/50$. In this case the infection grows slowly in the early days, but later increases rapidly in a short period of time. In figure 5.9a it can be observed that the number of individuals infected overtime growth [Jan: s/growth/grows] exponentially in a short period of time before it starts decreasing. In figure 5.9b it can be observed that the number of susceptibles falls drastically because of the rapid spread of the infection.



(a) Progression of infections over time.



(b) Flow of individuals in compartments of the infection over time

Figure 5.9: Infection dynamics for $p_1 = 0.045$, $p_2 = 0.01125$ and $r_1 = 1/50$

From the first four cases, we can observe that the infections along the distant links (small world parameters), have a significant effect on the spread of the infection. In case 1 where $p_2 = 0$ the infection does not spread rapidly compared to case 3 , where $p_1 = 0$. The spread of the infection when $p_1 = p_2$ is quite similar to the spread to case 3 when there are only infections across distant neighbours. The infection spread the faster in case 4 in relation to cases 1 to 3.

Thus case 4 would be more appropriate to model the spread of Zika virus. [Jan: Why? We would have to see the data to conclude this.] In case 5, when the infectious period is increased the infection will spread slowly foe some time the later it will explored and spread rapidly because infected individuals will infect more people before they recover.

5.6 Conclusion

In conclusion from our our model it can be said that the small world phenomenon, could have contributed greatly to the spread of Zika virus across the world. Small world networks can be used to understand why infectious disease that start at a particular place or area is able to spread all over the world in a short period of time. With increase in people's mobility, there is need to raise awareness on transmission of various infectious diseases in order to reduce the probability of disease transmission across long distances neighbours as well as preventing local infections.

In coming up with intervention measures, medical specialists might want to put up measures that reduce the infectious period of Zika patients, that is increasing r_1. Improved health care is one the factors that can lead to lower r_1.

The major limitation of this research is the unavailability of time series data on Zika infections, on which the model can be fit and the parameters of the model tested.

In this study we modelled the spread of Zika virus on a rewired 2 dimensional square grid. We would suggest as an area for future research, to investigate the spread of Zika virus on a lattice of higher dimension. [Jan: Are you sure you mean higher dimension? This is not the same as more neighbors.] That is increasing the number of near neighbours. Another area for further research would be, comparing the spread of Zika virus on a random network model with the smallworld model. Further we would suggest modelling the spread of Zika virus by taking into account seasonality. That is building a model where the probabilities of infecting near and distant neighbours depends on the season.

[Jan: Please give it another pass for typos and grammar.]

References

Cheryl L Addy, Ira M Longini Jr, and Michael Haber. A generalized stochastic model for the analysis of infectious disease final size data. *Biometrics*, pages 961–974, 1991.

Sonia Altizer, Andrew Dobson, Parviez Hosseini, Peter Hudson, Mercedes Pascual, and Pejman Rohani. Seasonality and the dynamics of infectious diseases. *Ecology letters*, 9(4):467–484, 2006.

Frank Ball. Deterministic and stochastic epidemics with several kinds of susceptibles. *Advances in applied probability*, 17(01):1–22, 1985.

Albert-László Barabási and Réka Albert. Emergence of scaling in random networks. *science*, 286 (5439):509–512, 1999.

Beatrix Beisner. *Ecological Paradigms Lost: routes of theory change*, volume 2. Academic Press, 2005.

Daniel Bernoulli. Essai d'une nouvelle analyse de la mortalité causée par la petite vérole et des avantages de l'inoculation pour la prévenir. *Histoire de l'Acad. Roy. Sci.(Paris) avec Mém. des Math. et Phys. and Mém*, pages 1–45, 1760.

Ebenezer Bonyah and Kazeem Oare Okosun. Mathematical modeling of zika virus. *Asian Pacific Journal of Tropical Disease*, 6(9):673–679, 2016.

Fred Brauer. Mathematical epidemiology: Past, present, and future. *Infectious Disease Modelling*, pages –, 2017. ISSN 2468-0427. doi: https://doi.org/10.1016/j.idm.2017.02.001. URL http://www.sciencedirect.com/science/article/pii/S2468042716300367.

Fred Brauer and Carlos Castillo-Chavez. *Mathematical models for communicable diseases*. SIAM, 2012.

Fan Chung and Linyuan Lu. The average distances in random graphs with given expected degrees. *Proceedings of the National Academy of Sciences*, 99(25):15879–15882, 2002.

Gerda Claeskens. Statistical model choice. *Annual Review of Statistics and Its Application*, 3: 233–256, 2016.

Eber Dantas, Michel Tosin, and Americo Cunha Jr. Calibration of a seir epidemic model to describe zika virus outbreak in brazil. 2017.

G. W. A. Dick, S. F. Kitchen, and A. J. Haddow. Zika virus (i). isolations and serological specificity. *Transactions of The Royal Society of Tropical Medicine and Hygiene*, 46(5):509, 1952. doi: 10.1016/0035-9203(52)90042-4. URL +http://dx.doi.org/10.1016/0035-9203(52)90042-4.

Odo Diekmann and Johan Andre Peter Heesterbeek. *Mathematical epidemiology of infectious diseases: model building, analysis and interpretation*, volume 5. John Wiley & Sons, 2000.

Chunxiao Ding, Nana Tao, and Yuanguo Zhu. A mathematical model of zika virus and its optimal control. In *Control Conference (CCC), 2016 35th Chinese*, pages 2642–2645. IEEE, 2016.

David JD Earn, Pejman Rohani, Benjamin M Bolker, and Bryan T Grenfell. A simple model for complex dynamical transitions in epidemics. *Science*, 287(5453):667–670, 2000.

P Erdodblac; s and A Reacute; nyi. ldquo; on random graphs. irdquo. *Publ. Math. Debrecen*, 6: 290–297, 1959.

Ernesto Estrada. *The structure of complex networks: theory and applications*. Oxford University Press, 2012.

Ernesto Estrada, Philip A Knight, and Philip Knight. *A first course in network theory*. Oxford University Press, USA, 2015.

Linton Freeman. The development of social network analysis. *A Study in the Sociology of Science*, 2004.

Wade H Frost. The importance of epidemiology as a function of health departments. *American Journal of Public Health*, 13(1):33–37, 1923.

Xinchu Fu, Michael Small, and Guanrong Chen. *Propagation dynamics on complex networks: models, methods and stability analysis*. John Wiley & Sons, 2013.

Sebastian Funk, Adam J Kucharski, Anton Camacho, Rosalind M Eggo, Laith Yakob, Lawrence M Murray, and W John Edmunds. Comparative analysis of dengue and zika outbreaks reveals differences by setting and virus. *PLoS neglected tropical diseases*, 10(12):e0005173, 2016.

Daozhou Gao, Yijun Lou, Daihai He, Travis C Porco, Yang Kuang, Gerardo Chowell, and Shigui Ruan. Prevention and control of zika as a mosquito-borne and sexually transmitted disease: a mathematical modeling analysis. *Scientific reports*, 6, 2016.

Peter Grassberger. On the critical behavior of the general epidemic process and dynamical percolation. *Mathematical Biosciences*, 63(2):157–172, 1983.

Nicholas C Grassly and Christophe Fraser. Seasonal infectious disease epidemiology. *Proceedings of the Royal Society of London B: Biological Sciences*, 273(1600):2541–2550, 2006.

Priscilla E Greenwood and Luis F Gordillo. Stochastic epidemic modeling. In *Mathematical and Statistical Estimation Approaches in Epidemiology*, pages 31–52. Springer, 2009.

Murali Haran. An introduction to models for disease dynamics. *Spatial Epidemiology SAMSI*, 12: 19–23, 2009.

Theodore E Harris. Contact interactions on a lattice. *The Annals of Probability*, pages 969–988, 1974.

Anne M Johnson, Catherine H Mercer, Bob Erens, Andrew J Copas, Sally McManus, Kaye Wellings, Kevin A Fenton, Christos Korovessis, Wendy Macdowall, Kiran Nanchahal, et al. Sexual behaviour in britain: partnerships, practices, and hiv risk behaviours. *The Lancet*, 358 (9296):1835–1842, 2001.

Vitor Laerte Pinto Junior, Kleber Luz, Ricardo Parreira, and Paulo Ferrinho. Zika virus: a review to clinicians. *Acta medica portuguesa*, 28(6):760–765, 2015.

Edward H Kaplan, David L Craft, and Lawrence M Wein. Emergency response to a smallpox attack: the case for mass vaccination. *Proceedings of the National Academy of Sciences*, 99 (16):10935–10940, 2002.

Kimmo Kaski, Jari Saramäki, José FF Mendes, SN Dorogovtsev, A Povolotsky, FV Abreu, and JG Oliveira. Modeling epidemics with dynamic small-world networks. In *AIP Conference Proceedings*, volume 776, pages 252–262. AIP, 2005.

Matt J Keeling and Ken TD Eames. Networks and epidemic models. *Journal of the Royal Society Interface*, 2(4):295–307, 2005.

Matt J Keeling and Pejman Rohani. *Modeling infectious diseases in humans and animals*. Princeton University Press, 2008.

Elisabeth R Krow-Lucal, Brad J Biggerstaff, and J Erin Staples. Estimated incubation period for zika virus disease. *Emerging Infectious Diseases*, 23(5):841, 2017.

Adam J Kucharski, Sebastian Funk, Rosalind M Eggo, Henri-Pierre Mallet, W John Edmunds, and Eric J Nilles. Transmission dynamics of zika virus in island populations: a modelling analysis of the 2013–14 french polynesia outbreak. *PLoS Negl Trop Dis*, 10(5):e0004726, 2016.

Justin Lessler, Cassandra T Ott, Andrea C Carcelen, Jacob M Konikoff, Joe Williamson, Qifang Bi, Lauren M Kucirka, Derek AT Cummings, Nicholas G Reich, and Lelia H Chaisson. Times to key events in zika virus infection and implications for blood donation: a systematic review. *Bulletin of the World Health Organization*, 94(11):841–849, 2016.

Michael Y Li and James S Muldowney. Global stability for the seir model in epidemiology. *Mathematical biosciences*, 125(2):155–164, 1995.

Antonella Liccardo and Annalisa Fierro. A lattice model for influenza spreading. *PloS one*, 8(5): e63935, 2013.

Alun L Lloyd, Steve Valeika, and Ariel Cintrón-Arias. Infection dynamics on small-world networks. *Contemporary Mathematics*, 410:209–234, 2006.

Robert M. May and Alun L. Lloyd. Infection dynamics on scale-free networks. *Phys. Rev. E*, 64:066112, Nov 2001. doi: 10.1103/PhysRevE.64.066112. URL https://link.aps.org/doi/10.1103/PhysRevE.64.066112.

Hendrik Mehlhorn and Falk Schreiber. *Small-World Property*, pages 1957–1959. Springer New York, New York, NY, 2013. ISBN 978-1-4419-9863-7. doi: 10.1007/978-1-4419-9863-7_2. URL http://dx.doi.org/10.1007/978-1-4419-9863-7_2.

Rui-Xing Ming, Jiming Liu, William KW Cheung, and Xiang Wan. Stochastic modelling of infectious diseases for heterogeneous populations. *Infectious diseases of poverty*, 5(1):107, 2016.

882 AG M'Kendrick. Applications of mathematics to medical problems. *Proceedings of the Edinburgh*
883 *Mathematical Society*, 44:98–130, 1925.

884 JL Moreno. The application of the group method to the classification of prisoners. In *Group*
885 *Psychotherapy: A Symposium. New York: Beacon House*, 1945.

886 David M Morens, Gregory K Folkers, and Anthony S Fauci. What is a pandemic? *Journal of*
887 *Infectious Diseases*, 200(7):1018–1021, 2009.

888 Satoru Morita. Six susceptible-infected-susceptible models on scale-free networks. *Scientific*
889 *reports*, 6, 2016.

890 D Musso, T Nhan, E Robin, C Roche, D Bierlaire, K Zisou, A Shan Yan, VM Cao-Lormeau, and
891 J Broult. Potential for zika virus transmission through blood transfusion demonstrated during
892 an outbreak in french polynesia, november 2013 to february 2014. *Euro Surveill*, 19(14):20761,
893 2014.

894 Didier Musso, Claudine Roche, Emilie Robin, Tuxuan Nhan, Anita Teissier, Van-Mai Cao-
895 Lormeau, et al. Potential sexual transmission of zika virus. *Emerg Infect Dis*, 21(2):359–61,
896 2015.

897 Mark EJ Newman. Models of the small world. *Journal of Statistical Physics*, 101(3):819–841,
898 2000.

899 Mark EJ Newman. The structure and function of complex networks. *SIAM review*, 45(2):167–256,
900 2003.

901 Mark EJ Newman and Duncan J Watts. Scaling and percolation in the small-world network
902 model. *Physical Review E*, 60(6):7332, 1999.

903 Mark EJ Newman, Steven H Strogatz, and Duncan J Watts. Random graphs with arbitrary
904 degree distributions and their applications. *Physical review E*, 64(2):026118, 2001.

905 Mark EJ Newman, Duncan J Watts, and Steven H Strogatz. Random graph models of social
906 networks. *Proceedings of the National Academy of Sciences*, 99(suppl 1):2566–2572, 2002.

907 Duane Q. Nykamp. "dynamical system definition.", 2017. URL http://mathinsight.org/
908 definition/dynamical_system.

909 Romualdo Pastor-Satorras and Alessandro Vespignani. Epidemic dynamics and endemic states in
910 complex networks. *Physical Review E*, 63(6):066117, 2001.

911 Yu. A. Kuznetsov; C. Piccardi. Bifurcation analysis of periodic seir and sir epidemic models.
912 *Journal of Mathematical Biology*, 32, 01 1994. doi: 10.1007/bf00163027.

913 H Joshua Posen, Jay S Keystone, Jonathan B Gubbay, and Shaun K Morris. Epidemiology of
914 zika virus, 1947–2007. *BMJ Global Health*, 1(2):e000087, 2016.

915 Sonja A Rasmussen, Denise J Jamieson, Margaret A Honein, and Lyle R Petersen. Zika virus
916 and birth defects—reviewing the evidence for causality. *New England Journal of Medicine*, 374
917 (20):1981–1987, 2016.

918 Robert C Reiner, T Alex Perkins, Christopher M Barker, Tianchan Niu, Luis Fernando Chaves,
919 Alicia M Ellis, Dylan B George, Arnaud Le Menach, Juliet RC Pulliam, Donal Bisanzio, et al.
920 A systematic review of mathematical models of mosquito-borne pathogen transmission: 1970–
921 2010. *Journal of The Royal Society Interface*, 10(81):20120921, 2013.

922 CJ Rhodes and Roy M Anderson. Epidemic thresholds and vaccination in a lattice model of
923 disease spread. *Theoretical Population Biology*, 52(2):101–118, 1997.

924 Lisa Sattenspiel. Modeling the spread of infectious disease in human populations. *American*
925 *Journal of Physical Anthropology*, 33(S11):245–276, 1990.

926 Lisa Sattenspiel and Carl P Simon. The spread and persistence of infectious diseases in structured
927 populations. *Mathematical Biosciences*, 90(1-2):341–366, 1988.

928 Ricardo Simões, Renata Buzzini, Wanderley Bernardo, Florentino Cardoso, Antônio Salomão, and
929 Giovanni Cerri. Zika virus infection and pregnancy. *Revista da Associação Médica Brasileira*,
930 62(2):108–115, 2016.

931 Jeffrey Travers and Stanley Milgram. The small world problem. *Phychology Today*, 1:61–67,
932 1967.

933 Pauline Van den Driessche and James Watmough. Reproduction numbers and sub-threshold
934 endemic equilibria for compartmental models of disease transmission. *Mathematical biosciences*,
935 180(1):29–48, 2002.

936 Jacco Wallinga, W John Edmunds, and Mirjam Kretzschmar. Perspective: human contact pat-
937 terns and the spread of airborne infectious diseases. *Trends in microbiology*, 7(9):372–377,
938 1999.

939 Duncan J Watts and Steven H Strogatz. Collective dynamics of 'small-world'networks. *nature*,
940 393(6684):440–442, 1998.

941 G Witten and G Poulter. Simulations of infectious diseases on networks. *Computers in Biology*
942 *and Medicine*, 37(2):195–205, 2007.