Modelling Infectious Diseases on Small World Network

By

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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: Firstname Middlename Surname

Scan your signature

Supervisor: Firstname Middlename Surname

ACKNOWLEDGEMENTS

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

DEDICATION

This is optional.

Abstract

A short, abstracted description of your essay goes here. It should be about 100 words long. But write it last.

An abstract is not a summary of your essay: it's an abstraction of that. It tells the readers why they should be interested in your essay but summarises all they need to know if they read no further.

The writing style used in an abstract is like the style used in the rest of your essay: concise, clear and direct. In the rest of the essay, however, you will introduce and use technical terms. In the abstract you should avoid them in order to make the result comprehensible to all.

You may like to repeat the abstract in your mother tongue.

Contents

1. Introduction

2. Literature Review

[Jan: It is better, but you should still read through it several times and correct typos.]

[Jan: Each paragraph should convey a specific piece of information and paragraphs should be ordered in a logical way. Especially the graph modelling section still feels disorganized (you are repeating same stuff over and over).]

[Jan: Clean up your bibliography (duplicates, broken names and titles).]

2.1 Zika Virus

Zika virus is a member of the flaviridae family and the flavivirus genus, [Jan: Flaviridae and Flavivirus should be capitalized.] [Jan: The first sentence should stop here.] it is related to other mosquito borne viruses such as dengue virus, yellow-fever virus (YFV) and west nile virus (Dick et al., 1952). [Jan: Dengue and West Nile should be capitalized.] 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.

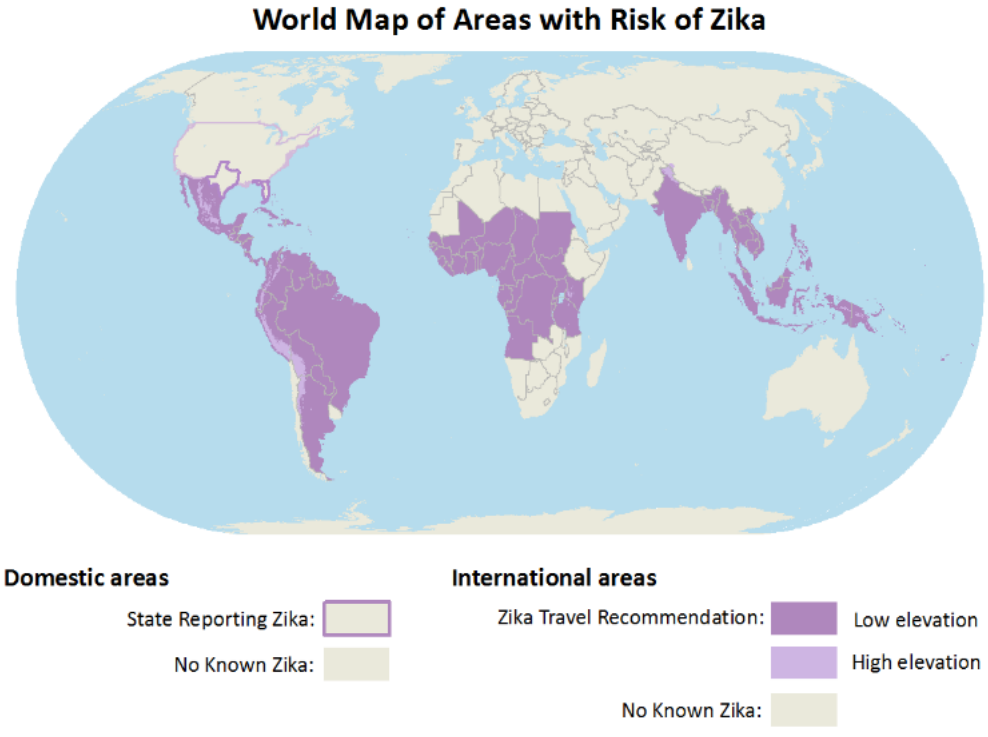


Figure 2.1: Countries with Zika Virus: Source CDC

Zika Virus is mainly spread by Aedes mosquitoes. When a pathogen carrying mosquito bites an no infected individual it leaves the pathogen in them. [Jan: bites an no infected individual?] Other ways of by which the virus spreads include, [Jan: s/ways of by/ways by] 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 are popular rash,fever,arthritis or arthralgia Musso et al. (2015). [Jan: "Popular" is probably a typo. Put space after comma.] [Jan: Maybe explain what is papular rash and arthralgia?] In addition, headache, joint pain and red eyes are common symptoms of Zika virus. Simões et al. (2016) adds that pregnant mothers who are infected with Zika during pregnancy usually have child bearing defects. [Jan: Why "usually"? The paper you are citing says: "The magnitude of the risk that infection with Zika virus occurred during pregnancy will result in birth defects remains unknown to date."] The 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 Zika virus. Prevention measures can be taken to prevent the spread of the virus.This done by preventing mosquito bites. [Jan: Space after full stop. s/This done/This is done] Measures such as sleeping under a mosquito net, using mosquito repellent, spraying mosquitoes [Jan: What is "spraying mosquitoes"?] inside and outside 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 . [Jan: No space before full stop.] Drugs for the symptoms of Zika are administered to patients as a way of treating Zika infected people because of the luck of a vaccination for the virus. [Jan: s/luck/lack I am pretty sure I marked this error before, why is it still here?]

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 an 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 [Jan: Space after full stop. Spellchecker should catch this, have you tried?] involves collaborative work by statisticians, mathematicians,physicians and various health specialist (Brauer, 2017). [Jan: s/specialist/specialists] The knowledge about infectious diseases has been built up by the method of experience, by [Jan: s/method of experience/experience] observation and analysis of particular conditions associated with occurrence of disease in nature (Frost, 1923).

The first step in epidemiology was collection and analysis of data on causes of death in London parishes in the late 1960s by Graunt. [Jan: Is 1960s a typo?] 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 for 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 factors of an infected person. Some pathogens cannot survive inside or outside in given conditions. Thus some diseases or infections spread faster in certain weather conditions(Grassly and Fraser, 2006). [Jan: Put space before opening parenthesis.] 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 strong immunity against certain infections, this may slow down the propagation the infection. On the other hand the life cycle of pathogens also affect [Jan: s/affect/affects] the transmission dynamics of the infection.Some pathogens can only survive in the host while 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 model for the transmission dynamics of infectious diseases.

Behavioural infectiousness depends on the interaction behaviour of an individual. The contact pattern of the person affect 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 depend 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.

Epidemiologist together with mathematicians have for years been involved in infectious disease modelling to understand the dynamics of the spread of the disease and to come with measures of how the spread can be controls. Recently there has been a growing interest in modelling the spread of Zika virus (Kucharski et al., 2016b). [Jan: This is general section on epidemiology, is Zika relevant here?]

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 is 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 dynamics. Conducting experimental research on the spread of infectious disease raises a lot of ethical issue and therefore can not be conducted on humans. Mathematical simulations and modelling the disease has helped in providing understanding the impact of the infectious disease on the population and give a guide

to new control measures (Ming et al., 2016).

Over a century, Mathematical representation and analysis of infectious diseases has been the centre of infectious disease epidemiology (Beisner, 2005). [Jan: This paragraph should be before the previous one.]

2.3 Modelling with Compartmental Models

Differential equation have been used in the modelling of the dynamics of the spread of infectious diseases. They are base 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 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, compartment models are built by combining these different classes or creating new ones (Li and Muldowney, 1995).

Deterministic models also know 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 to risks of exposure and infection. This assumption in some cases has proved not to realist [Jan: not to realist?] and hence the introduction of stochastic models. Stochastic models introduce the idea of randomness in the reaction to risk and infection by individual in the population (Ming et al., 2016). The main advantage of the stochastic model is they take into consideration each individual but the major draw back is that it is laborious to model them as they require a lot of simulation and sometimes become mathematically complex.

Deterministic models are studied either by theory or methods. [Jan: I don't understand sentence above.] Ordinary differential equations, partial differential equations and differential equations (Keeling and Rohani, 2008). [Jan: You listed ODEs and PDEs, what are differential equations?] 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 in these models 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 use to use results from the work of Moreno (1945) where he analysed contact patterns of prisoners. This work give 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 among social actors are important. Second, it is based on the data 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 model have being built for various infectious disease among others Malaria, Zika, HIV , Small pox chicken pox (Ding et al., 2016) [Jan: Correct capitalization above.]

2.4 Modelling with Graph

Graph theory has over the years grown and has found its application many fields. A graph also known as a network can be defined as triple $G = (V, E)$ 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). [Jan: Triple?]

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 systems 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 is to capture 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).

Studying the dynamics of epidemiological models on social networks is currently an active area of research. Many model have been developed on to understand how the structure of networks affects disease spread (Keeling and Eames, 2005). [Jan: This paragraph does not say anything interesting.]

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 disease propagate are either small world or scale free networks and not random or regular as earlier assumed Watts and Strogatz (1998).

Random network models of infectious disease do nit 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 $\widehat{n}$, the number of contacts in a network and the unit number of contact per unit time in a random mixing model. [Jan: Is it necessary to give detailed formulas here? What is g? Why do you claim network rate is smaller, they look similar to me.] 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 this is called a Neumann [Jan: It's "von Neumann". Actually, I don't think it's necessary to include those names here, just explanation is enough.] neighbours or eight neighbours where four diagonal elements are added to the Neuman neighbours and this is called the Moore neighbourhood (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 on 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. (Morita, 2016) [Jan: Explain what "scale-free" means.]

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).

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).

Since the emergence of Zika virus epidemic, there have several studies to model the spread of the virus. Most research on Zika has been modelling the propagation of the infectious using compartmental models as can be seen in the work of Kucharski et al. (2016a), Dantas et al. (2017a) and Bonyah and Okosun (2016), where they used the SEIR compartmental model with vector to model the propagation of Zika. Their main assumption is a well mixed population. That is the population is assumed to be homogeneous.

In this research we will compare the traditional epidemiological model based on the assumption of a well mixed or homogeneous population and the Small world networks to model the population Dynamics in the spread of Zika Virus. The tradition compartmental models assumes that everyone

in the population has the same probability of catching the infection. While the model built on a small world network assumes that one infects his close neighbours with a higher probability compared to any other random person in the network (Newman et al., 2002). This is a much more realistic assumption as it captures the contact patterns of individual in the community or network. Zika virus is mainly transmitted through a vector (Mosquito) contact and transmission is in reference to mosquito bite. [Jan: You should have separate section explaining what your work does and what your results are (once you have them...).]

3. Background

3.1 Definitions

3.1.1 Epidemic and Pandemic . An infectious disease is a disease that is caused by pathogenic micro organisms, such as bacteria, viruses, parasites or fungi; the 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 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 $t \in \mathbb{T}$. That is $\mathbb{R}(\mathbf{x}, t)$ give the state of the system at t given the initial state of the system was $\mathbf{x}$ (Nykamp, 2017).

The population can be characterized as $S(t)$, $E(t)$,$I(t)$ and $R(t)$. Where $S(t)$ is the number of individuals susceptible but not infected at time t, $E(t)$ is the number of people exposed or infected but not infectious at time t, $I(t)$ is the number of infected and infectious people at time t and $R(t)$ is the number of people whose ability to be infected is removed, by either immunization, death or recovery from the disease. The epidemiological models can be classified as Susceptible,Infected and Recovered (SIR) , Susceptible Infected (SIS or SIS) , Susceptible -Exposed - Infectious and Removed (SEIR) and by any other states the population may be partitioned into. [Jan: It feels to me you are contradicting yourself. If you assume continuous time, I don't think it is accurate to represent the disease evolution as "rule" $\mathbb{R}$.] !

The SIS model assumes that there is no immunity after recovery. It is used to model infections where once a person recovers they become susceptible again.For example infections like flue. SIR model assumes that once a person recovers they become immune to the infection for example chicken pox. The SEIR assumes that once a person becomes infected they do not become infectious immediately hence the intermediate compartment for exposed.

The independent variable in the compartmental model 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;

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

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. Which 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 and 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 small number of individuals (Brauer and Castillo-Chavez, 2012).

On the other hand Stochastic models are obtained by setting by adding a random variable called noise to the transmission dynamics of deterministic models.These random fluctuations may impact the evolution of the infection. Unlike deterministic model which assume homogeneous mix , an assumption which only holds in small populations. It is quiet unlikely that all people in will be equally susceptible to the disease and effective in spreading it (Ball, 1985). A stochastic model can be further be described as a model in which the distribution of the length of the infectious period as allowed to have any distribution that can be describe by its Laplace transform (Addy et al., 1991). [Jan: This description is vague. Can you give a minimal example of a stochastic model?]

Lets takes an SIR compartmental model, for $t > 0$, $S(t), I(t), R(t)$ is the number of individuals in susceptible, infectious and removed. $N(t)$ the total number of particles at time t. The Poisson process, which is the underlying structure basic to the class of stochastic models and all Markov chain processes(Greenwood and Gordillo, 2009). [Jan: It is not clear to me what is the relation of Poisson process to the rest. Explain better.] The individuals enter each compartment at random times [Jan: Why random times? I thought it is $t = 0$?] and the initial fixed values , $S(0)$,$I(0)$ and $R(0)$ are fixed for some $\lambda > 0$. [Jan: What is λ?] Letting 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 $\triangle t + o(\triangle t)$. If it is assumed the an infected person recovers at the rate γ hence the probability of an infected person moving from infected to recovered over an interval $[t, \triangle t]$ given by $\gamma I_{t+\triangle t} - o(\triangle t)$ .It is known that,

$$\begin{aligned} N_t &= S_t + I_t + R_t \\ \Rightarrow R_t &= N_t - S_t - I_t \end{aligned}$$

Which implies that knowing S_t, I_t is knowing R_t. Hence the model becomes an S_t, I_t and thus the stochastic dynamical system can be written as;

$$P((S_{t+\triangle t}, I_{t+\triangle t} - (S_t, I_t) = (-1, 1)) = \beta SI\triangle t + o(\triangle t). \tag{3.1.2}$$

$$P(((S_{t+\triangle t}, I_{t+\triangle t} - (S_t, I_t) = (0, -1)) = \gamma I_{t+\triangle t} - o(\triangle t). \tag{3.1.3}$$

[Jan: I think you are trying to give an example of a stochastic model, but I realized that only at the end of the paragraph. You should rewrite it. Also give more details about this model. Most important: is time discrete or continuouos?]

3.1.3 Network. A graph also known as a network can be defined as triple $G = (V, E)$ where V is a finite set of nodes $E \subset V \oplus V = \{e_1, e_2, \ldots, e_m\}$ is a set and f is a mapping which associates some elements of E to a pair of elements of V (Estrada, 2012). Nodes can be human beings, cities or houses while edges could be any connection such as friendship, physical connection or road. [Jan: I don't get this definition. Since $E \subseteq V \times V$, what is f for?] A network is said to be connected if there exist 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 by each a node can be reached. This can be summed up as the average distance taken over all, pairs of individuals , which gives the idea of the typical distance between nodes in a network or the diameter of the graph which is the largest distance taken over all pairs. [Jan: Please fix the preceding sentence.]

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 a particular node has and is denoted as k and the average distribution of a network is denoted by $\langle k \rangle$. [Jan: In this context use \langle and \rangle instead of $<$ and $>$.] 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, $p(k) = \frac{n(k)}{n}$. $p(k)$ 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 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 mean friends people have in common. Local clustering in a network is measured by the Watts -stoggatz coefficient and the global clustering by Newman clustering coefficients.

Watts -strogatz average clustering coefficient is given by

$$\overline{C} = \frac{1}{n} \sum_i c_i \tag{3.1.4}$$

$$c_i = \frac{2t_i}{k_i(k_i - 1)}$$

where t_i 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 ones friends are friends with each other. The clustering coefficient lies between 0 and 1, if it zero then node of a nodes neighbours are connected and if it is 1 then then all the neighbours of a node are connected to connected to each other. [Jan: Mixing formulas and text is bad style. So s/t_i = e number of/t_i is a number of]

The Newman clustering coefficient is given by

$$c = \frac{3t}{p_2} = \frac{3|c_3|}{p_2} \tag{3.1.5}$$

where $t = c_3$ number of triangle in the network and $|p_2|$ the number of closed paths of length 2.

[Jan: Please give intuitions behind those coefficients as in Phil's lecture.]

The Newman clustering coefficient or so know as the network clustering coefficient, gives the average clustering for the whole network. Node with less than two neighbours are given 0 as the clustering coefficient. 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 network has small world properties it has high clustering coefficent and low average distance (Estrada, 2012).

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.

Taking z to be the average degree. The probability p of and edge being present between any two vertices is given by $p = \frac{z}{n-1}$, for large n can be approximated $\frac{z}{n}$ (Newman et al., 2002). The number of nodes connected to any particular vertex, the degree k of that vertex has a probability distribution p_k given by;

$$p_k = \binom{n}{k} p^k (1-p)^{n-k} \approx \frac{z^k e^{-z}}{k!}. \tag{3.1.6}$$

For example let us take 20 vertices draw and edge between with probability $p = 0.2$ We can get a random network presented in 3.1 below. A random network model can exhibit the small world network property. It can be shown that a random graph can exhibit small world effects. Assuming that person A, represents a node on 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

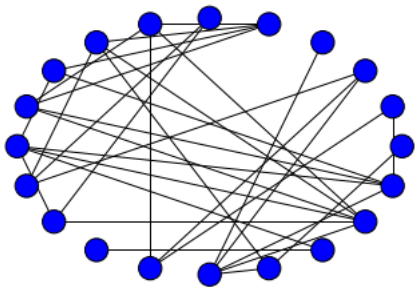
$$D = \frac{\log n}{\log z}$$

The logarithmic increase in the diameter of the network and the distance between node 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). A random graph has an average degree $z = pN$. Random networks have a low clustering coefficient $c = \frac{z}{N}$ (Newman, 2003).

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 Odered Lattice. In order to deal with real work networks, graphs mus have both clustering and small work effect property. Random graphs as discussed earlier show a small work effect. The average vertex to vertex distances increase only logarithmically with n but does not show clustering (Newman, 2000). This leads us to another graph model which is an ordered lattice.

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



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 to model population structures, gives an example of classic lattice (Harris, 1974).

The clustering coefficient for a lattice is given as

$$C = \frac{3(z-d)}{4(2-z)} \tag{3.1.7}$$

where d is the dimension of the lattice.

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 dimensions with 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 to the small world behaviour.

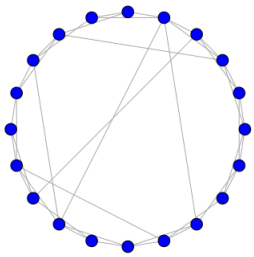
Models built on latices assume that individuals are located as nodes on a regular lattice and connections are made of some collection of near neighbours or each node. For example people may be spread out such that connections are made to their four nearest neighbours, one on the left,right, up and down this is called a Neumann neighbours or eight neighbours where four diagonal elements are added to the Neuman neighbours and this is called the Moore neighbour hood (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 main difference between a random graph and lattices is that interactions are local, that is individuals are only related to their neighbours. Where as in random networks the connections are made are global, that is connections are made without taking spatial locations of an individual into consideration.

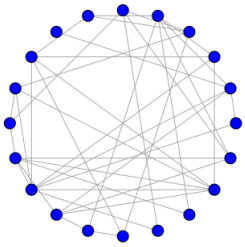
3.1.7 Watts - Strogats Small World Networks. We have shown that lattices are characterised by high clustering coefficients but long path lengths or vertex to vertex distances. That is it takes many steps to move between any two randomly selected vertices, where as random networks have shorter vertex 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 the regular lattice and randomly rewiring certain proportions p of the network links(Watts and Strogatz, 1998). The small world networks allows for random contacts across the network. That is in addition to near neighbours as in a regular lattice, each node has a random distant neighbour connected to it (Watts and Strogatz, 1998). [Jan: Give more precise definition and/or add an example.]

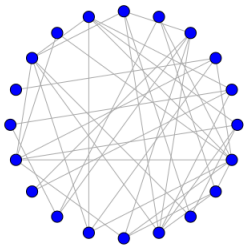
The Watts-Strogatz network is essentially a regular lattice with some degree of randomness in the connectivity of vertices. Take for example figure 3.2b above and we rewire some edges with a some probability p, that is one of its ends is moved into a randomly chosen position in the lattice. For a small p this produces mostly a regular graph but with a few connections stretch along distances across the lattice and for $p1$ it produced a complete graph. Figure **??**elow 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

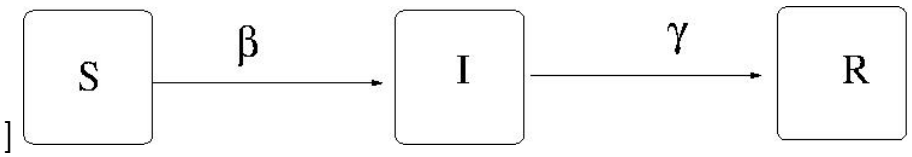
4.2 SIR Model

In the 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.

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI, \\ \frac{dI}{dt} &= \beta SI - \gamma I, \\ \frac{dR}{dt} &= \gamma I, \end{aligned} \tag{4.2.1}$$

$N = S + I + R$ 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

$$\frac{dS}{dt} = -\beta SI. \tag{4.2.2}$$

$$\frac{dI}{dt} = \beta SI - \gamma I. \tag{4.2.3}$$

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 4.2.2 and 4.2.3 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 4.2.2 gives two import insights in understanding the spread of disease and has since been used in infectious disease modelling for along time.

4.2.2 Threshold Phenomenon. Its is important to determine whether the infection will result into 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 4.2.3 can be rewritten as,

$$\frac{dI}{dt} = I\left(\beta S - \gamma\right) \tag{4.2.4}$$

In equation 4.2.4 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 what 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 . 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:

$$R_0 = \frac{\beta}{\gamma} \tag{4.2.5}$$

For initial susceptible $S(0) = 1$, if $R_0 > 1$ then there will be an outbreak 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 give 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

$$\frac{dS}{dt} = -\beta SI \tag{4.2.6}$$

$$\frac{dR}{dt} = \gamma I \tag{4.2.7}$$

dividing equation 4.2.4 by equation 4.2.7 we get

$$\frac{dS}{dR} = \frac{-\beta S}{\gamma} = R_0 S \tag{4.2.8}$$

Integrating equation 4.2.8 with respect to R, we get;

$$\int \frac{dS}{S} = \int R_o dR \tag{4.2.9}$$

$$lnS = -R_0 R + k \tag{4.2.10}$$

$$e^{lnS} = e^{-R_0 R + k} \tag{4.2.11}$$

$$S(t) = e^{-R_0 R(t)} e^{k} \tag{4.2.12}$$

assuming R(0) = 0

$$S(t) = S(0) e^{-R_0 R(t)} \tag{4.2.13}$$

Hence as the epidemic develops the number of susceptible reduce, taking into consideration the infectious period there is a lag but eventually the number of recovered start to increase. There number of susceptible in the population will always be above zero as can be seen in equation 4.2.13.

From equation 4.2.13, $s(t) \geq e^{-R_o}$ 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.

$$\frac{dS}{dt} = \mu - \beta SI - \mu S \tag{4.2.14}$$

$$\frac{dI}{dt} = \beta SI - \gamma I - \mu I \tag{4.2.15}$$

$$\frac{dR}{dt} = \gamma I - \mu R \tag{4.2.16}$$

Using the procedure we used to get equation 4.2.5 it can be shown that the R_0 for this model is

$$R_0 = \frac{\beta}{\mu + \gamma} \tag{4.2.17}$$

Now we calculate the equilibria of the model by setting equation 4.2.14, 4.2.15 and 4.2.16 to zero, that is $\frac{dS}{dt} = \frac{dI}{dt} = \frac{dR}{dt} = 0$ and denote by $S^*, I^* and R^*$ values of I,S and R that satisfy

the condition ,that this satisfy the condition. From equation 4.2.14 we get

$$\mu - \beta SI - \mu S = 0 \tag{4.2.18}$$
$$\mu - S(\beta I + \mu) = 0 \tag{4.2.19}$$
$$S = \frac{\mu}{\beta I + \mu} \tag{4.2.20}$$

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

To establish the endemic equilibrium , we factorize I in equation 4.2.15 and we get,

$$I(\beta S - (\gamma + \mu)) = 0 \tag{4.2.21}$$

thus we get

$$I = 0 \rightarrow S = \frac{\gamma + \mu}{\beta} \tag{4.2.22}$$

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 4.2.17

Now, we take $I \neq 0$ and solve (4.2.16). Since $S + R + I = 1$

$$\gamma I - \mu(1 - S - I) = 0 \tag{4.2.23}$$
$$\gamma I - \mu I - \mu(1 - S) = 0 \tag{4.2.24}$$
$$I = \frac{\mu}{\beta} R_0 \left(1 - \frac{1}{R_0}\right) \tag{4.2.25}$$
$$I = \frac{\mu}{\beta}(R_0 - 1) \tag{4.2.26}$$

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 out break occurs its important to understand the long term behaviour of the out break 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 epedemic burn out will occur.

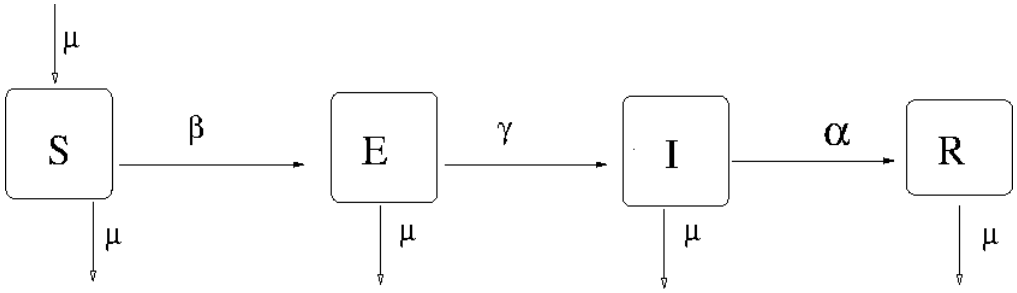
4.3 SEIR Model

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 one a person is exposed there is an intermediate stage between the time of infection and when they become infectious, this maybe refereed to as the latent or incubation period of the infection. The will 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 exposed people 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 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 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 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 $R_0 < 1$.

4.3.1 Other Compartmental Models.. There are several other types of compartmental model and epidemiologist tend to include additional components. Here are some of the models that can be used to model infectious diseases.

4.3.2 SI. The susceptible infected model assumes that once someone is infected there is no recovery. Hence it has only two components and it is used to model infectious like HIV and other incurable infectious diseases. The description of the short term and long term behaviour of the model can be calculated similar to the SIR model.

5. Spread of Zika virus on a small world network

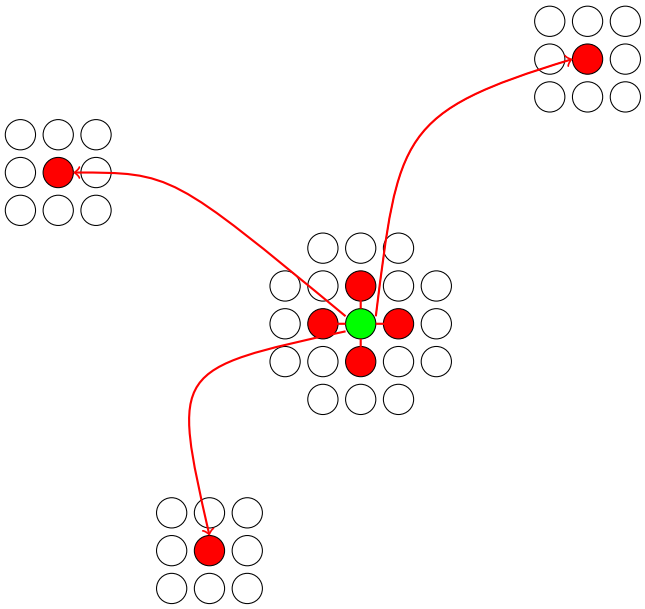


Figure 5.1: Smallworld network structure

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 disease. They are quiet simple and tractable (Fu et al., 2013).

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

We suppose that that the population is arrange in a regular grid. Where each vertex can infect its 4 near neighbours and a couple distant neighbours. Near neighbours in this case refers to individuals that one spends most of their time 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.

Transmission of Zika virus is mainly through mosquito bite, thus in modelling the spread its spread on a small world network the dynamics of transmission through mosquitoes is represented by edges of the graph. An edge is drawn when there between two vertices, whenever there is a likelihood of transmission from one to another via mosquito bite.

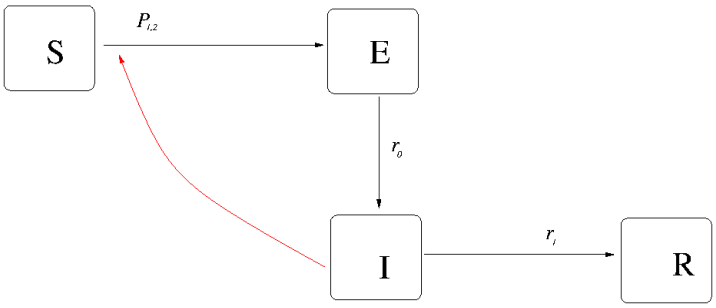


Figure 5.2: State transition diagram

Figure 5.1 shows the arrangement of nodes in a small world network and figure 5.2 show the transmission state diagram: S to E based on the small world network network structure and the infection probabilities $p_{1,2}$: E to I with probability r_0 and I to R with probability r_1. in figure 5.1, the infected green node may infect its four red 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.

Let p_1 be the probability of an infected individual causing their susceptible near neighbours to become infected and p_2 the probability of their distant or remote neighbours to be come infected. Exposed people become infectious with probability r_0 and recover or get removed with probability r_1. In addition n_1 and n_2 is number of close neighbours and near neighbours respectively.

The number of distant neighbours n_2 if fixed and random for each node. That is for node i there are $n_2^{(i)}$ distant neighbours. $n_2^{(i)}$ is chosen to follow a discrete exponentially decaying distribution

$$f_c(x) = \frac{1}{c} e^{\frac{-x}{\mu}} \tag{5.0.1}$$

with parameter μ proportional to the expected number of links to remote nodes and $c = \frac{1}{1-e^{frac-1\mu}}$ ensures that f_c is a probability distribution function (Fu et al., 2013). The degree distribution in most social networks are exponentially distributed because of the celebrity effect (Estrada et al., 2015). In social networks there are few people who are with high connections and many with an average number of connections. In modelling infectious diseases these individuals are referred to as supper spreaders.

The transition probability r_0, the number of days an individuals is in the exposed state is as a result of bernoulli trials with mean $\frac{1}{r_0}$, follows a geometric distribution $f_X(x) = (1-p)^{x-1}p$. Similarly the infectious period follows a geometric distribution with mean $\frac{1}{r_o}$ (Fu et al., 2013).

5.1 Model

The model has seven parameters, the are $N, p_1, p_2, n_1, n_2, r_0$ 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 95% of patients begin to exhibit symptoms of Zika infection after 11.2 days of infection with a 95% confidence interval of $7.6 - 18$. Further the center for disease control and prevention (CDC) indicate that the incubation period for Zika virus ranges for 3 day to 14 days from infection (Krow-Lucal et al., 2017). Therefore we estimate r_o with $\frac{1}{11.2}$

95% of the cases 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 for infectious period id $18.9 - 1.5 = 17.4$ days. Therefore r_1 is estimated to be $\frac{1}{17.4}$.

Hence we have n_1, μ, p_1 and p_2 free parameters. Without control the average number of secondary infection for Zika virus is between 3 and 6, therefore we choose 4.5 as the R_0. Since the number of remote neighbours is random and fixed for each, we estimate $E(n_2^{(i)}) = \mu$.

$$n_1 p_1 + \mu p_2 \approx \frac{R_0}{r_1} \tag{5.1.1}$$

$$n_1 p_1 + \mu p_2 \approx 0.2586 \tag{5.1.2}$$

thus, $p_1 \approx 0.0645 - 0.25\mu p_2$

We can summarize the parameters of the models as;

$$n_1 = 4 \tag{5.1.3}$$

$$\mu = 8 \tag{5.1.4}$$

$$r_0 = \frac{1}{11.2} \approx 0.089 \tag{5.1.5}$$

$$r_1 = \frac{1}{17.4} \approx 0.057 \tag{5.1.6}$$

$$p_1 = 0.0645 - 2p_2 \tag{5.1.7}$$

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

$$E(- \triangle S) = (n_1 k p_1 + \mu p_2 - r_1) I \tag{5.1.8}$$

Where k is the average number of near neighbours' links that support possible infection and near neighbours are arrange in clusters, therefore $0.5 < k < 1$. In all our computation we will take $k = 0.5$. From equation 5.1.8 we can estimate the number of new infections as;

$$E(- \triangle S) = (2p_1 + 8p_2 - 0.057) I \tag{5.1.9}$$

For each infected vertex the number of secondary infections per day is $(n_1 k p_1 + \mu p_2)$ the total will be;

$$n_k r_1 + n_k (1 - r_1) r_1 + n_k (1 - r)^2 r_1 + ... + n_k (1 - r_1)^n r_1 + ... \tag{5.1.10}$$

We let $(1-r) = X$ in equation 5.1.10 such that $0 \leq X \leq 1$ and $n_k = n_1 k p_1 + \mu p_2$, we can see that its a geometric progression and the sum is give by,

$$n_k r_1(1 + X + X^2 + ... + X^n + ...) = n_k r_1 \left(\frac{1 + X^n}{1 - X}\right) \tag{5.1.11}$$

as, $n \longrightarrow \infty$

$$n_k r_1(1 + X + X^2 + X^3 + X^n + ...) = n_k r_1 \left(\frac{1}{1 - X}\right) \tag{5.1.12}$$

$$n_k r_1 \frac{d}{dX}(1 + X + X^2 + X^3 + X^n + ...) = n_k r_1 \frac{d}{dX}\left(\frac{1}{1 - X}\right) \tag{5.1.13}$$

$$n_k r_1(1 + 2X + \cdots + nX^{n-1} + \dots) = n_k r_1 \frac{1}{1 - X^2} \tag{5.1.14}$$

$$n_k r_1(1 + 2(1 - r_1) + 3(1 - r_1) + \dots) = \frac{n_k}{r_1} \tag{5.1.15}$$

572 The average number of new infections is 4.5 hence;

$$2p_1 + 8p_2 = 0.2565 \tag{5.1.16}$$

From equation 5.1.7 and 5.1.16 we can estimate the value of p_2 as;

$$\begin{aligned} 2(0.0645 - 2p_2) + 8p_2 &= 0.2565 \\ p_2 &\approx 0.03187 \end{aligned}$$

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