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Mathematical Modeling of MERS-CoV Nosocomial Epidemic

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MATHEMATICAL MODELING OF MERS-COV NOSOCOMIAL EPIDEMIC

A Thesis

by

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ABSTRACT

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This thesis concerns about the analysis and modeling of spread of an infectious disease inside a hospital. We begin from the basic knowledge of the simple models: SIR and SEIR, to show an appropriate understanding of the epidemic dynamic process. We consider the Middle East Respiratory Syndrome Corona Virus (MERS-CoV), in Saudi Arabia, to introduce MERS-CoV SEIR ward model by developing different systems of equations in each ward (unit). We use the Next Generation Matrix method to calculate the basic reproduction number R_0. Simulations of different scenarios are done using different combination of parameters.

To model MERS-CoV we established a system of equations from sketch of wards model of a hospital. We divide it into five wards where individuals can travel from one unit to the other and interact with the environment. We consider the following units: Waiting room/Reception (WR), Intensive Care Unit (ICU), Hemodialysis (HD), and Hospital Wards. Each ward has its own carrying capacity which represents the maximum number of patients that can be admitted. We have three kinds of agents: Patients (P), Health Care Workers (HCW), and Mobile HCW.

Here, we study the disease free equilibrium and calculate their values by using *Matlab* codes to obtain the basic reproduction number.

DEDICATION

The research of this thesis could not have been performed without the assistance, patience, trust, and support of certain people.

I dedicate this work to my parents. They have been my main support throughout my life and in my education. Special feeling of gratitude to Emma Gaspar G. and Pablo Quiroz F. whose words of encouragement were the reason to continue with my goals. My brother and my sister, Antonio Quiroz G. and Carolina Quiroz G., to support me with their knowledge and time to correct me in my studies and presentations.

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TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER I

INTRODUCTION

1.1 Background of Mathematical Modeling

The study of mathematical epidemiology helps to understand the behavior of disease epidemics and to assess the effectiveness of surveillance and control measures to stop the spread of infection. In other words, it is a risk assessment tool using the language of mathematics by providing insights about an infections process. Diseases have different classifications. They can be either infectious or noninfectious and differ in their natural history.

Definition 1.1.1 An **infectious disease** is caused by a microorganism such as a virus that enters the body of another organism [8]. The disease can be passed down between individual organisms [8]. There are two modes of transmission. Direct and indirect. **Direct transmission** is passed by having close contact with an infectious individual. **Indirect transmission** is passed between hosts via the environment [8].

It all started in the eighteenth century when epidemiologists feel the need to study the behavior of diseases in a deeper way. This was done by constructing mathematical models and offering a prediction of changes of disease courses. Up to now, there has been many scientific papers that use the knowledge that provides us with a wide information of how those can be applied. We will start by formulating the model based on the famous Kermack and McKendrick systems of equations [8].

1.2 SIR Model

The model is divided into three compartments where individuals can be transferred from one compartment to another at certain rates. The first compartment that is represented by the

letter **S** stands for **S**usceptible compartnent. The second one, **I**, is for **I**nfected. At this point the person has the neccesary viral load to transmit the disease to another person. Lastly, the third compartment, **R**, stands for **R**emoved. In R, the individual is free from the disease and no longer infectious or dead. We assume the model is under a closed population without demographics [8]. This means that the population is constant and there is no immigration/emigration. There are two types of transitions; one transition is from S to I and the second is from I to R. For the first transition, from S to I: a susceptible person moves into the infected compartment at a disease transmission rate β and it can be written as $\beta = \lambda p$ where λ is the force of infection and p is the probability of transmission upon contact. Secondly, from I to R, an infected individual moves into the recovered compartment with another recovery rate γ. Moving from I to R at a rate of γ can be determined by how long on an average a person can stay in the I compartment. Its reciprocal of the recovery parameter $\frac{1}{\gamma}$ gives the average infectious period. The following descriptions are expressed in **Figure 1.1**

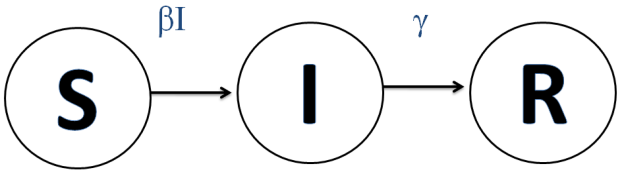


Figure 1.1: SIR Transfer Diagram.

The SIR flow can be depicted by the following system of differential equations,

$$\begin{aligned} \frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \gamma I \\ \frac{dR}{dt} &= \gamma I \end{aligned} \tag{1.1}$$

Where the likelihood of the transition βSI happening is proportional to number of S and number

of I. By adding the three variables we have $S+I+R=1$. If we take the derivative with respect to time to the sum of the sizes of the compartments we obtain the following identity $S'+I'+R'=0$. This makes the third equation of R' redundant. This system of equations have initial conditions: S(0) which is the initial proportion of susceptible population and I(0) is the initial proportion of infectious population. Then, $S(0)>0$, $I(0)>0$, and $R(0)=0$.

One of the most important feature in the process of modeling diseases is the reproduction number R_0.

Definition 1.3.3.1 The **basic reproductive ratio** is the average number of secondary cases arising from an average primary case in an entirely susceptible population [8].

This, will determine if the disease will turn out to be epidemic or not. If $R_0<1$ the disease will not spread into a large population. Otherwise, if $R_0>1$, an outbreak of the disease will become epidemic.

1.2.1 SIR Simulations

In this section, the SIR model is solved numerically using *ode45* in *Matlab* (see code in Appendix 1). We give values assigned to the parameters in Table 1.1. The numerical solutions are illustrated in Figure 1.2

Table 1.1: SIR Parameters.

Parameter	Description	Base Values	Reference
β	Transmission rate	1.42	[8]
γ	Recovery rate	0.1428	[8]

The model simulated at the values given in Table 1.1 suggests that susceptible individuals will decrease while the infected and recovered individuals will increase. At some point the epidemic will reach a peak and then decreases while R continues. This means that, from S, individuals will move to I and R at some time. Individuals in compartment R will not go back to S and I. In this model we assume, an average number of 520 contacts per year which means, the daily average is 520/365. We also assume probability 1 for transmission upon contact. For the mean infectious period we use 1/7 $days^{-1}$ [8].

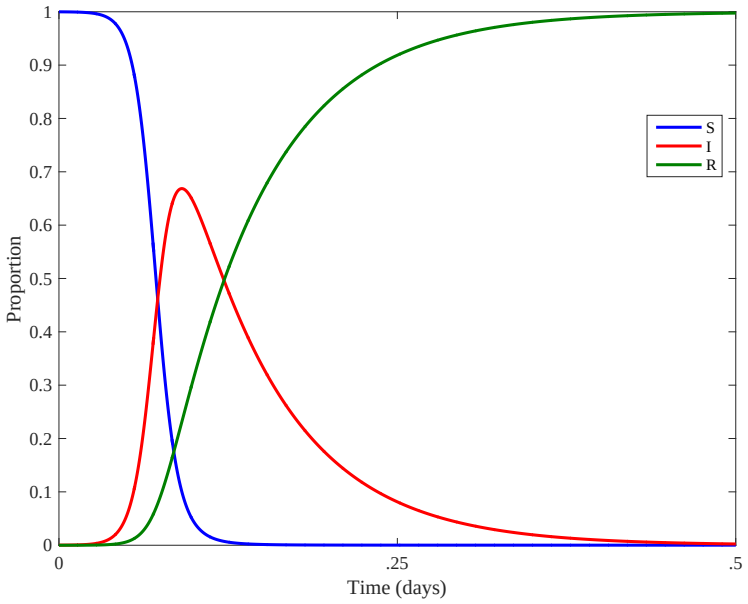


Figure 1.2: SIR Model simulation.

Since $S+I+R=1$ to change this into a disease free equilibrium we are going to add them so it can gives us 1. By adding them it should gives us 1 and not zero. Now, the disease free equilibrium (DFE) is $(S^*+I^*+R^*)=(1,0,0)$ where $S^*=1$, $I=0$, $R=0$. To find the points, we need to look at $\frac{dI}{dt}=\beta SI-\gamma I$ so we can do the following,

$$\frac{dI}{dt}=\beta SI-\gamma I$$
$$I'=\beta SI-\gamma I$$
$$0=\beta S^*I^*-\gamma I^*$$
$$0=(\beta S^*-\gamma)I^*$$
$$0=\beta S^*-\gamma$$
$$\gamma=\beta S^*$$
$$\frac{\gamma}{\beta}=S^*$$

To find I^* we do the following,

$$\frac{dS}{dt} = \beta SI$$
$$S' = \beta S^* I^*$$
$$0 = \beta(\frac{\gamma}{\beta})I^*$$
$$0 = -\gamma I^*$$
$$0 = I^*$$

And to find R^* we can do the following,

$$S' + I' + R' = 1$$
$$\frac{\gamma}{\beta} + 0 + R' = 1$$
$$R' = 1 - \frac{\gamma}{\beta}$$
$$R' = \frac{\beta - \gamma}{\beta}$$

If the ratio of the parameters β and γ is bigger than one, we expect the number of infected individuals to be large eventually and an epidemic to grow. If $S(0) < \frac{\gamma}{\beta}$ then $I' < 0$. This means the disease dies out [8]. Additionally, $\frac{\gamma}{\beta}$ is called the relative removal rate [8] and the inverse is the basic reproduction number which is $R_0 = \frac{\beta}{\gamma}$ and is solved in chapter 1.4.4 [8].

SIR models are useful to show the behavior of certain type of diseases such as, influenza, smallpox, and rubella (childhood infectious diseases). These diseases acts so fast that demography is ignored. However, this is not the only concern we have about SIR models. We may encounter a person who catches the disease, becomes infected but is not infectious. The person, in this case, is exposed and is better represented in the SEIR model.

1.3 SEIR Model

Many infectious diseases have an exposed period, also called the latent period, where the individual carries the disease, but is not yet infectious [8]. At this stage, the disease is barely growing over time and there are no visible symptoms. In this case, the viral load is so low that it

cannot be transmitted to another person. This means the person becomes exposed and goes from the Susceptible to the Exposed compartment and which is represented by the letter **E**.

To develop the model we consider four compartments S, E, I, and R. We will assume the model is closed (demography is neglected) and recovered individuals are not relapsing. We may consider the following figure 1.3 for a better graphic view.

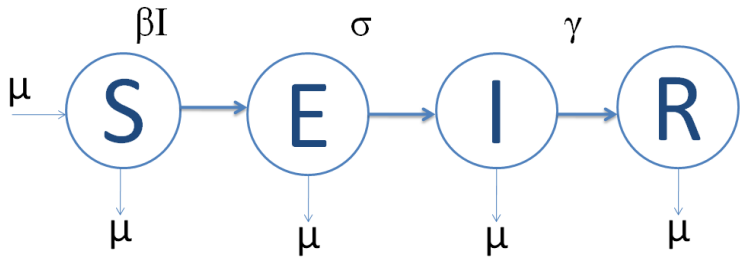


Figure 1.3: SEIR Transfer Diagram.

The SEIR system can be depicted by the following system of differential equations,

$$\begin{aligned}
\frac{dS}{dt} &= -\beta SI - \mu S + \mu \\
\frac{dE}{dt} &= \beta SI - \sigma E - \mu E \\
\frac{dI}{dt} &= \sigma E - \gamma I - \mu I \\
\frac{dR}{dt} &= \gamma I - \mu R
\end{aligned} \tag{1.2}$$

where the parameter σ stands for the rate of becoming infectious and μ is the natural death rate. Thus, the mean latent period is $\frac{1}{\sigma}\ days^{-1}$. Since we assume $S+E+I+R=1$ we may omit the last equation since $R^{'} = -S^{'} - E^{'} - I^{'}$ and is given by

$$\begin{aligned}
\frac{dS}{dt} &= -\beta SI - \mu S + \mu \\
\frac{dE}{dt} &= \beta SI - \sigma E - \mu E \\
\frac{dI}{dt} &= \sigma E - \gamma I - \mu I
\end{aligned} \tag{1.3}$$

1.3.1 SEIR Simulations

In this section, SEIR model is solved numerically using *ode45* in *Matlab* (see code in Appendix II). We give values assigned in Table 1.2 and the numerical simulations are illustrated in Figure 1.4

Table 1.2: SEIR Parameters.

Parameter	**Description**	**Base Values**	**References**
β	Transmission rate	1.42	[8]
σ	Infectious rate	0.07142	[8]
γ	Recovery rate	0.1428	[8]
μ	Natural death rate	$1/50$	[8]

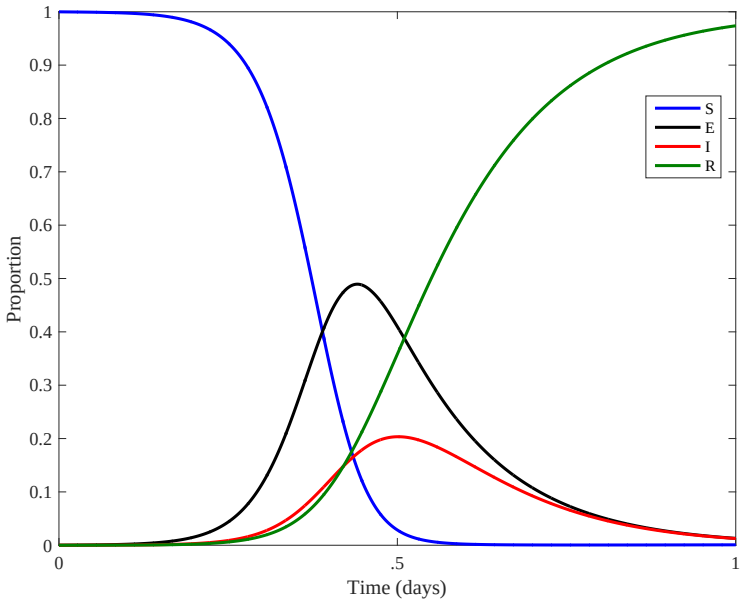


Figure 1.4: SEIR Model Simulation.

In Figure 1.4 the susceptible population will start decreasing at some point of time and will finally be stable. On the other hand, the recovered population will increase and will be stable after some point. Now, for the exposed and infected populations, they will first increase but for not too long and then will decrease to zero.

1.3.2 SEIR Stability Analysis of DFE

We may also consider how to determine if the infectious disease will be endemic or not. That is, we will study stability of the disease-free equilibrium where the number of infected is zero. Setting the SEIR model equal to zero and solving the equations we will be able to determine the disease-free equilibrium.

The disease free equilibrium (DFE) is (1,0,0,0) where S=1, E=0, I=0 R=0. If we let $S = S^*$ and $0 \leq S^* \leq 1$, then, we will obtain a situation where there will be no infection where one part of the population will be susceptible and the rest is recovered. It follows to have the disease free equilibrium point as $(S^*, 0, 0, 0)$. We will determine the stability of the DFE using the Jacobian matrix of the SEIR equation. Recall the SEIR model in (1.3) after omitting R' is,

$$\frac{dS}{dt} = -\beta SI - \mu S + \mu =: f_1(S,E,I)$$
$$\frac{dE}{dt} = \beta SI - \sigma E - \mu E =: f_2(S,E,I)$$
$$\frac{dI}{dt} = \sigma E - \gamma I - \mu I =: f_3(S,E,I)$$

Then, the Jacobian matrix of the system is given by,

$$J = \begin{bmatrix} \frac{\partial f_1}{\partial S} & \frac{\partial f_1}{\partial E} & \frac{\partial f_1}{\partial I} \\ \frac{\partial f_2}{\partial S} & \frac{\partial f_2}{\partial E} & \frac{\partial f_2}{\partial I} \\ \frac{\partial f_3}{\partial S} & \frac{\partial f_3}{\partial E} & \frac{\partial f_3}{\partial I} \end{bmatrix} = \begin{bmatrix} -\beta I - \mu & 0 & -\beta S \\ \beta I & -\sigma - \mu & \beta S \\ 0 & \sigma & -\gamma - \mu \end{bmatrix}$$

By applying the disease free equilibrium $(1,0,0,0)$ were $S^* = 1$, and $E^* = I^* = 0$, to the Jacobian matrix we have,

$$J = \begin{bmatrix} -\mu & 0 & -\beta \\ 0 & -\sigma - \mu & \beta \\ 0 & \sigma & -\gamma - \mu \end{bmatrix}$$

The eigenvalues are found by solving $det(J - \lambda I) = 0$ where,

$$det(J - \lambda I) = det\left(\begin{bmatrix} -\mu & 0 & -\beta \\ 0 & -\sigma - \mu & \beta \\ 0 & \sigma & -\gamma - \mu \end{bmatrix} - \begin{bmatrix} \lambda & 0 & 0 \\ 0 & \lambda & 0 \\ 0 & 0 & \lambda \end{bmatrix} \right)$$
$$= det\left(\begin{bmatrix} -\mu - \lambda & 0 & -\beta \\ 0 & -\sigma - \mu - \lambda & \beta \\ 0 & \sigma & -\gamma - \mu - \lambda \end{bmatrix} \right)$$

then,

$$det(J - \lambda I) = (-\mu - \lambda)[(-\sigma - \mu - \lambda)(-\gamma - \mu - \lambda) - \beta\sigma]$$
$$= (-\mu - \lambda)[\lambda^2 + \lambda(\sigma + \gamma + 2\mu) + \sigma(\gamma + \mu - \beta) + \mu(\gamma + \mu)]$$

Thus, the eigenvalues are the zeros of,

$$\lambda_1 = -\mu < 0$$

Solving the quadratic equation we have,

$$\lambda_{2,3} = \frac{-(\sigma+\gamma+2\mu) \pm \sqrt{(\sigma+\gamma+2\mu)^2 - 4(\sigma(\gamma+\mu-\beta)+\mu(\gamma+\mu))}}{2}.$$

$\lambda_2 > 0$, $\lambda_3 < 0$

The eigenvalues determine if the system has asymptotic stability or not and we take a decision, whether it is stable or not, based on their signs [3]. The properties of the eigenvalues are as follows, [3].

- Stable: If both eigenvalues have negative real part [3].
- Unstable: If at least one eigenvalue has a positive real part is unstable [3].

In this case, λ_2 and λ_3 are negative and λ_1 is a positive root. Since at least one eigenvalue has a positive real part [3] then the system is unstable. Substituting the values to the parameters we get, $\lambda_1 = -.0000391389$, $\lambda_2 = .213326$, and $\lambda_3 = -.427624$. The disease free equilibrium is unstable and there will be an epidemic in the population. If $\lambda_2 < 0$ then $R_0 < 1$ and no outbreak of the epidemic. Then, the next generation matrix will lead us to determine what is R_0. See Example 2 in section 1.4.1.

1.4 Next Generation Matrix and Examples

The Next Generation Matrix calculates and give the basic reproduction number R_0. In general, let us have a matrix with entries (i, j) where i is the secondary infection caused in the compartment by the infected individual in compartment j [2]. Then, if we let $x \in R^n$ and $y \in R^m$ to be the sub population in each respective compartment where n is the number of disease compartment and m the number of non-disease compartments. Moreover, denoting $\mathscr{F}_i$ to be the rate at which secondary infectious increase the $i-th$ compartment [2] and $\mathscr{V}_i$ is the rate at which disease progression decreases the ith compartment, [2]. We can denote a compartment model in

the form of [2]

$$x_i' = \mathscr{F}_i(x,y) - \mathscr{V}_i(x,y) \quad i = 1,...,n, \quad [2] \tag{1.4}$$
$$y_j' = p_j(x,y) \quad j = 1,...,m \quad [2]$$

Now, in order to obtain equilibrium from the susceptible population we need to assume two things,

I. Let $\mathscr{F}_i(0,y) = \mathscr{V}_i(0,y) = 0$ for all $y \geq 0$ [2]

In this assumption, we have all new infections to be secondary infections arising from an infected host [2]. At this point, there should not be any immigration of people into the compartment. It ensures that the disease free set consisting of all points of the form $(0,y)$ is invariant [2].

II. The disease free system $y_j' = p_j(x,y)$ has a unique equilibrium, that is asymptotically stable. Where the solutions with initial conditions of the form $(0,y)$ will approach a point $(0,y_0)$ as $t \to \infty$ [2]. This assumption helps us to ensure that the disease-free equilibrium is an equilibrium [2]. The point $(0,y_0)$ is the disease free equilibrium of the full system [2].

Secondly, let assume that

I. The matrix $\mathscr{F}_i(x,y) \geq 0$ for nonnegative x and y; $\quad i = 1,...,n \quad$ [2]

We denote $\mathscr{F}$ to be new infections and nonnegative [2].

II. The matrix $\mathscr{V}_i(x,y) \geq 0 \qquad x_i = 0, \quad i = 1,...,n \quad$ [2]

$\mathscr{V}_i$ is denoted to be the net outflow from compartment i and negative, whenever the compartment is empty [2].

III. For all nonnegative x and y we have $\quad \sum_{i=1}^{n} \mathscr{V}_i(x,y) \geq 0 \quad$ [2]

This sum has the representation of the total outflow from all infected compartments [2]

By all of this assumptions we can start deriving the Next Generation Matrix. First, as an example, if one individual is introduced to the hospital free of any disease [2], the initial ability to spread through the population is determined by the linearization of equations(1.4) at initial point $(0, y_0)$ (the disease equilibrium) [2]. Then we have,

$$\frac{\partial \mathscr{F}_i}{\partial y_j}(0, y_0) = 0, \quad \frac{\partial \mathscr{V}_i}{\partial y_j}(0, y_0) = 0 \qquad \text{for every} \quad (i, j) \quad [2]$$

where this linearized equations for the disease compartments, x, are departed from the remaining equations and it follows to be written as [2].

$$x' = (F - V)x \quad [2] \tag{1.5}$$

Where F and V are $n \times n$ matrices with the following entries:

$$\mathrm{F} = \frac{\partial \mathscr{F}_i}{\partial x_j}(0, y_0), \quad \mathrm{V} = \frac{\partial \mathscr{V}_i}{\partial x_j}(0, y_0) \quad [2]$$

Definition 1.4.1.1 **Endemic** is revalent in a particular locality, region, or population [6]. An endemic equilibrium is **(locally) asymptotically stable** if and only if it corresponds to a point on the bifurcation curve at which the curve is increasing..[2]. **Epidemic**, is affecting many persons at the same time, and spreading from person to person in a locality where the disease is not permanently prevalent [6].

Because it is a disease -free system, $y^{'} = p(0, y)$ that has a unique asymptotically stable equilibrium then (2.1) can be determined by the matirx $(F - V)$ in (1.5) [2]

If, we have a number of secondary infections produced by one individual that is infected then, we can denote it as the product of expected duration of the infections period and the rate of secondary infections occurred [2]. Moreover, we can define the expected time that is spent in each compartment by the following integral [2],

$$\int_0^\infty t\theta(t, x_0)dt \quad [2]$$

where $\theta(t, x_0)$ is the solution of (1.5)and by letting $F = 0$ and x_0 to be a nonnegative initial condi-

tion, we can represent an infected index case as [2]

$$x' = -Vx, \quad x(0) = x_0 \tag{1.6}$$

where we can solve it by using the integrating factor

$$x' + Vx = 0 \quad \text{with} \quad \mu(t) = e^{\int V dt} = e^{Vt}$$

$$\begin{aligned} e^{Vt}x' + e^{Vt}Vx &= 0 \\ (xe^{Vt})' &= 0 \\ xe^{Vt} &= c \\ x = \frac{c}{e^{Vt}} \Longrightarrow x &= ce^{-Vt} \end{aligned}$$

and by using the initial conditions we have $x(0) = ce^{-V0} \Longrightarrow x_0 = c$.

Thus, $\theta(t, x_0) = x_0 e^{-Vt}$ is the solution to (1.6) where it shows the path of an individual through a disease compartment from initial exposure through to recovery. Then, we can let the exponential of the solution (1.6) a matrix to be defined by the Taylor series,

$$e^M = I + M + \frac{M^2}{2} + ... + \frac{M^k}{k!} + ... \quad [2].$$

Then, $x_0 \int_0^\infty te^{-Vt}dt = x_0 V^{-1}$ where $x \geq 0$ [2] where $(i, j)th$ entries of the matrix V^{-1} is the expected time an individual is initially introduced to comparment j and spends time in compartment i [2] and by introducing matrix F we have the following,

$$x_0 \int_0^\infty Fe^{-Vt}dt = FV^{-1}x_0 \quad \text{where} \quad x \geq 0 \quad [2]$$

where $(i, j)th$ entries of the matrix F is the rate of secondary infections produced in compartment i by an index case in compartment j, [2]. Thus, we have the next generation matrix denoted by $K_L = FV^{-1}$ at disease free equilibrium, [2]. Up to now, let us define some properties of K_L.

It is is nonnengative and has nonnegative eigenvalues $R_0 = \rho(FV^{-1})$ that is, there is no other eigenvalue of K_L with modulus greater than R_0, [2] and there is a nonnegative eigenvector

φ associated with the reproduction number R_0, [2]. The eigenvector is the distribution of infected individuals which causes R_0 to be the greatest number of secondary infections per generation, [2]. Then, the reproduction number and the eigenvector φ, and R_0 can be to be the spectral radius of K_L, [2]. We will call the notation of the spectral radius as $\rho(K_L)$ which is the maximum moduli of the eigenvalues of the matrix K_L, [2].

We have two cases for K_L. The first one is when the matrix is irreducible. This means that R_0 is just an eigenvalue of K_L and has to be larger in modulus than all of the rest of the eigenvalues, [2]. In the second case, when the matrix is reducible, will have more positive real eigenvectors that correspond to R_0 for each strain of the disease, [2]. This applies mostly to the cases when we have a disease with multiple strains, [2].

Next, we need to consider some lemmas and theorems to interpret the reproduction number (R_0). This is important because $R_0 = \rho(FV^{-1})$ follows that disease-free equilibrium is asymptotically stable if $R_0 < 1$ or unstable if $R_0 > 1$, [2].

In addition, we need to know what is the spectral bound of a matrix. If we let D to be a matrix, then the spectral bound of D will be the maximum real part of all of the eigenvalues of D, [2]. Then, if a matrix W has all nonnegative entries, we write $W \geq 0$ and say it is a nonnegative matrix. If $D = sI - B$ with $B \geq 0$, we have a Z sign pattern whose off-diagonal entries are negative or zero, if $s \geq \rho(B)$ then D is an M-matrix, [2]. I stands for the identity matrix.

Lemma 2.1 [2] If D has the Z sign pattern, then $D^{-1} \geq 0$ if and only if D is a nonsingular M-matrix .

Because of the assumptions we have stated before, we know that F is nonnegative and the off-diagonal entries of the matrix V are negative or zero. Then, V has the Z sign pattern where the total column sums of V are positive or zero. This implies that V is a possibly singular M-matrix [2]. Since we assume that V is nonsingular, then $V^{-1} \geq 0$. Thus, $K_L = FV^{-1}$ is nonnegative and K_L is called the next generation matrix with large domain.

Lemma 2.2 [2] If F is a nonnegative matrix and V is a nonsingular M-matrix, then $R_0 = \rho(FV^{-1}) < 1$ if and only if all eigenvalues of $(F - V)$ have negative real parts .

Proof: We know that F is a nonnegative matrix ($F \geq 0$) and V is a nonsingular M-matrix. By lemma 2.1 $V^{-1} \geq 0$. Then, we let $(I - FV^{-1})$ have the Z sign pattern and by 2.1 this implies that $(I - FV^{-1}) \geq 0$ if and only if $\rho(FV^{-1}) < 1$. Then,

$$(V-F)^{-1} = V^{-1}(I - FV^{-1})^{-1}$$
$$V(V-F)^{-1} = (I - FV^{-1})^{-1}$$
$$= I + F(V-F)^{-1}$$

It follows that $(V-F)^{-1} \geq 0$ if and only if $(I - FV^{-1})^{-1} \geq 0$. Thus, we have that $(V-F)$ has the Z sign pattern [2] and that $(V-F)^{-1} \geq 0$ if and only if $(V-F)$ is not a singular M-matrix. Hence, the eigenvalues of all of the nonsingular M-matrix have positive real parts [2].

Theorem 2.3 [2] Consider the following disease transmission model,

$$x_i' = \mathscr{F}_i(x,y) - \mathscr{V}_i(x,y) \qquad i = 1,...,n,$$
$$y_j' = p_j(x,y) \qquad j = 1,...,m$$

Then, the disease free-equilibrium is locally asymptotically stable if $R_0 < 1$, otherwise unstable if $R_0 > 1$.

Proof: Let F be a nonnegative matrix and V be a nonsingular M-matrix. Let $J_{2,1}$ and $J_{2,2}$ be matrices of partial derivatives of p with respect to x and y evaluated at the disease free-equilibrium [2]. Then, the Jacobian matrix has the following block structure,

$$J = \begin{bmatrix} (F-V) & 0 \\ J_{2,1} & J_{2,2} \end{bmatrix}$$

When $R_0 < 1$ we say that the disease free-equilibrium is locally asymptotically stable if all of the eigenvalues of the Jacobian matrix $(F-V)$ and $J_{2,2}$ have negative real parts. By the assumption that F is nonnegative and V is a nonsigular M-matrix and by lemma 2.2 the eigenvalues of $(F-V)$ have negative real parts if and only if $\rho(FV^{-1}) < 1$ [3]. Thus, the disease free-equilibrium is stable if $R_0 = \rho(FV^{-1}) < 1$ [2].

When $R_0 > 1$ we say that the disease free-equilibrium is locally asymptotically unstable. Let $R_0 \leq 1$ for any $\varepsilon > 0$, then $((1+\varepsilon)I - FV^{-1})$ is a nonsingular M-matrix and by applying

lemma 2.1 we know that $((1+\varepsilon)I - FV^{-1})^{-1} \geq 0$. Also, all of the eigenvalues of $((1+\varepsilon)V - F)$ will have positive real parts by the proof of lemma 2.2 [2]. Because $\varepsilon > 0$ is arbitrary and the eigenvalues are continuous functions of the entries of the matrix, it follows that $(V - F)$ will have nonnegative real parts [2].

Going backward, suppose the eigenvalues of $(V - F)$ have nonnegative real parts, then for any positive ε, $(V + \varepsilon I - F)$ has to be a nonsingular M-matrix and by applying the proof of lemma 2.2 $\rho(F(V+\varepsilon I)^{-1}) < 1$ [2]. Because $\varepsilon > 0$, we have $\rho(FV^{-1}) \leq 1$. Hence, $(F - V)$ has at least one eigenvalue with positive real part if and only if $\rho(FV^{-1}) > 1$ and will be unstable whenever $R_0 > 1$ [2].

1.4.1 SEIR Basic Reproduction Number

Example 1. Consider the SEIR model that has infectivity in the exposed stage or compartment.

$$\begin{aligned} S' &= -\beta S(I + \varepsilon E) \\ E' &= \beta S(I + \varepsilon E) - \sigma E \\ I' &= \sigma E - \gamma I \\ R' &= \gamma I \end{aligned}$$

Focusing in E, we know that we have $\beta S(I + \varepsilon E)$ coming in and $-\sigma E$ coming out. The same thing for I, we have σE coming in and $-\gamma I$ coming out. Now let us consider $\mathscr{F}$ to be the inputs due to infection then, we have the following

$$\mathscr{F} = \begin{bmatrix} \beta S(I + \varepsilon E) \\ 0 \end{bmatrix}$$

Next, we consider $\mathscr{V}$ to be the outputs or movements of individuals so that, we have the following

$$\mathscr{V} = \begin{bmatrix} \sigma E & 0 \\ -\sigma E & \gamma I \end{bmatrix}$$

Now, taking their respective partial derivatives we have,

$$F = \frac{\partial \mathscr{F}}{\partial (E,I)}|_{DFE} = \begin{bmatrix} \varepsilon\beta & \beta \\ 0 & 0 \end{bmatrix}, \quad V = \frac{\partial \mathscr{V}}{\partial (E,I)}|_{DFE} = \begin{bmatrix} \sigma & 0 \\ -\sigma & \gamma \end{bmatrix}$$

By taking the inverse of V, we have the following

$$V^{-1} = \frac{1}{\sigma\gamma}\begin{bmatrix} \gamma & 0 \\ \sigma & \sigma \end{bmatrix} = \begin{bmatrix} \frac{1}{\sigma} & 0 \\ \frac{1}{\gamma} & \frac{1}{\gamma} \end{bmatrix}$$

Now, we can calculate the next generation matrix with large domain for this system of equations at the disease-free equilibrium,

$$K_L = FV^{-1} = \begin{bmatrix} \left(\frac{\varepsilon\beta}{\sigma} + \frac{\beta}{\gamma}\right) & \left(\frac{\beta}{\gamma}\right) \\ 0 & 0 \end{bmatrix}$$

The matrix FV^{-1} has rank 1 and has only one nonzero eigenvalue (ρ) and the trace of FV^{-1} is the sum of eigenvalues. Then, we can calculate R_0

$$R_0 = \frac{\varepsilon\beta}{\sigma} + \frac{\beta}{\gamma}$$

Since the new infections are in one compartment as in this case, the reproduction number R_0 is the trace of the matrix.

Example 2. To calculate basic reproduction number for thw SEIR model (1.3) we have to consider equation (1.4)[2], where $\mathscr{F}_i$ is the rate at which secondary infections increase the $i-th$ ward [2] and $\mathscr{V}_i$ is the rate at which disease decreases in the $i-th$ disease ward [2]. Then, we can construct $\mathscr{F}$ and $\mathscr{V}$ as follows

$$\mathscr{F} = \begin{bmatrix} \beta SI \\ 0 \end{bmatrix}, \quad \mathscr{V} = \begin{bmatrix} \sigma E + \mu E & 0 \\ -\sigma E & \gamma I + \mu I \end{bmatrix}$$

Now, taking their respective partial derivatives at the steady point DFE = (1,0,0) (equilibrium point) we have,

$$F = \frac{\partial \mathscr{F}}{\partial (E,I)}|_{DFE} = \begin{bmatrix} \beta \\ 0 \end{bmatrix}, \quad V = \frac{\partial \mathscr{V}}{\partial (E,I)}|_{DFE} = \begin{bmatrix} \sigma+\mu & 0 \\ -\sigma & \gamma+\mu \end{bmatrix}$$

By taking the inverse of V, we have the following

$$V^{-1} = \frac{1}{(\sigma+\mu)(\gamma+\mu)} \begin{bmatrix} \gamma+\mu & 0 \\ \sigma & \sigma+\mu \end{bmatrix} = \begin{bmatrix} \frac{1}{\sigma+\mu} & 0 \\ \frac{\sigma}{(\sigma+\mu)(\gamma+\mu)} & \frac{1}{\gamma+\mu} \end{bmatrix}$$

Now we can calculate R_0 as follows

$$K_L = FV^{-1} = \begin{bmatrix} \frac{\beta\sigma}{(\sigma+\mu)(\gamma+\mu)} & \frac{\beta}{\gamma+\mu} \\ 0 & 0 \end{bmatrix}$$

Thus, the eigenvalues are $\lambda_1 = 0$ and $\lambda_2 = \frac{\beta\sigma}{(\sigma+\mu)(\gamma+\mu)}$ and the spectral radius is the trace of FV^{-1} then, $R_0 = \rho(FV^{-1}) = \frac{\beta\sigma}{(\sigma+\mu)(\gamma+\mu)}$.

Thus, the basic reproduction in (1.3) is $R_0 = 9.94$.

CHAPTER II

NOSOCOMIAL EPIDEMIC

2.1 Nosocomial Epidemic and MERS-CoV Disease

The active research of mathematical models of outbreaks of infectious diseases have generated an important impact over the world. There have been suitable models for different types of transmission of infectious diseases. There are two distinguished transmissions, one is called zoonotic cases and the other is secondary cases. For zoonotic case, the transmission involves interactions between animals and humans. For secondary case, it involves human-to-human transmission which could happen in the community or inside a hospital. The transmission of a disease inside a hospital is called hospital acquired infection or commonly known as a nosocomial infection.

Definition 1.4.1 A **nosocomial infection**, is an infectious disease acquired in a health care facility [6].

In [4], the researchers introduce a model that considers two transmission cases: zoonotic and secondary. They also consider symptomatic and asymptomatic individuals. They had 57% were secondary symptomatic cases [4]. For the community model they estimated R_0 to be around .45. For the index case (animal-to-human transmission), R_0 was estimated to be .84 [4]. They developed a stochastic transmission model where they differentiated the two cases. They used April-October 2013 data for a hospital in Saudi Arabia. In my research, I use a SEIR compartmental transmission model for human-to-human transmission in the hospital.

The people in hospital are divided into five compartments and in a separately manner, we have mobile health care workers. For susceptible individuals we have S_i where $i = 1,2,3,4,m$. In this situation, 1 refers to reception, 2 for Intensive Care Unit (ICU) , 3 for Hemodialysis, 4 stands

for Hospital, and m refers to mobile health care workers. Accordingly, we use E_i, I_i, V_i, HS_i, HE_i, and HI_i and for quarantine Q we have HQ and Q_m.

In [9], researchers consider health care workers that move around and have the potential to transmit the disease in an intensive care unit. We use this idea to produce the MERS-CoV SEIR ward model and that every ward has its own capacity to hold patients.

In [5], authors use modeling based on the interactions in a hospital setting including the environmental load parameter and isolation patients. We use and apply this ward model technique as well as, the disease-free equilibrium in our model for this study.

We will use parameter values from previous studies to produce R_0 and to simulate by using different estimates for the behavior of MERS-CoV. In my research, we considered transition between wards, the rate of shedding the virus into the environment, cleaning rate, carrying capacity, and quarantine parameters.

Table 2.1: Cosidered Parameters of MERS-CoV.

Parameter	**Description**
ρ	Rate of shedding virus into environment
b_i	Cleaning/removal rate for $i = 1,2,3,4$
κ_i	Carrying capacity for $i = 1,2,3,4$ is for units
κ_i'	Carrying capacity (occupancy) of HCW for $i = 1,2,3,4,m$ is for units

2.1.1 MERS-CoV Disease

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a viral illness and the first outbreak was reported in Jeddah, Saudi Arabia in 2012 [4]. MERS-CoV has become one of the important nosocomial infections. It is a major health care problem in certain countries such as South Korea [10] and Saudi Arabia [4] and [10]. In this study we are going to focus on Saudi Arabia.

In the literature of MERS-CoV [4], data shows that hospitals are to be a major contributor of transmission of MERS-CoV across patients, nurses, visitors, janitors and many others occurring in different units. MERS-CoV infections occur mainly in the Intensive Care Unit (ICU) and Hemodialysis (HD) units but minimal in other wards in the hospital. Spread of MERS-CoV is

preventable via surface cleaning, hygiene (gloves, masks, etc.), machinery, ventilation, etc. Our primary concern is on the time until diagnosis and its direction, namely, the decrease or increase of the epidemic size.

2.2 Hypothesis MERS-CoV Modeling

Analyzing previous studies of MERS-CoV there is a general situation where health care workers play an important role in the spread of the disease inside a hospital and, intensive care units have the most cases. The development of control measures and active surveillance should be implemented since they are critically needed. The objective will be the study of the spread of this disease inside a hospital.

We introduce SEIR Ward model equilibrium where people such as Health Care Workers (HCW) and mobile HW, who travel between wards (units), are considered to be part of the spread. The model will be used to understand the behavior of the disease by the calculation of R_0 and to study the factors that contribute to the propagation of this disease.

2.2.1 Hospital Ward Models

We divide the hospital into a number of units or wards. In these wards the individuals interact with the environment. The first unit is the Waiting room (W) where there is an in-flow and out-flow of individuals. Patients are admitted to one of three different units: the Intensive Care Unit (ICU), the Hemodialysis unit (HD) or the Hospital (H) which is made of several wards. The units W, ICU, HD, and H have carrying capacities κ_i with $i = 1,2,3,4$, respectively, representing the maximum number of patients admissible to them. We also consider a Quarantine unit (Q) that is well isolated.

For this model, when patients (P), and health-care workers (HCW) come in contact with the disease inside the hospital they become symptomatic. We considered two types of health-care workers (HCW). The first type is the local HCW who do not have much contact with patients and the mobile HCW who have more contact with patients and move around inside the hospital.

For the waiting room we consider that individuals can get infected during the time they

stayed in the health care facilities or due to other patients around them. Also, the visitors can get infected due to visiting patients or a health care facility.

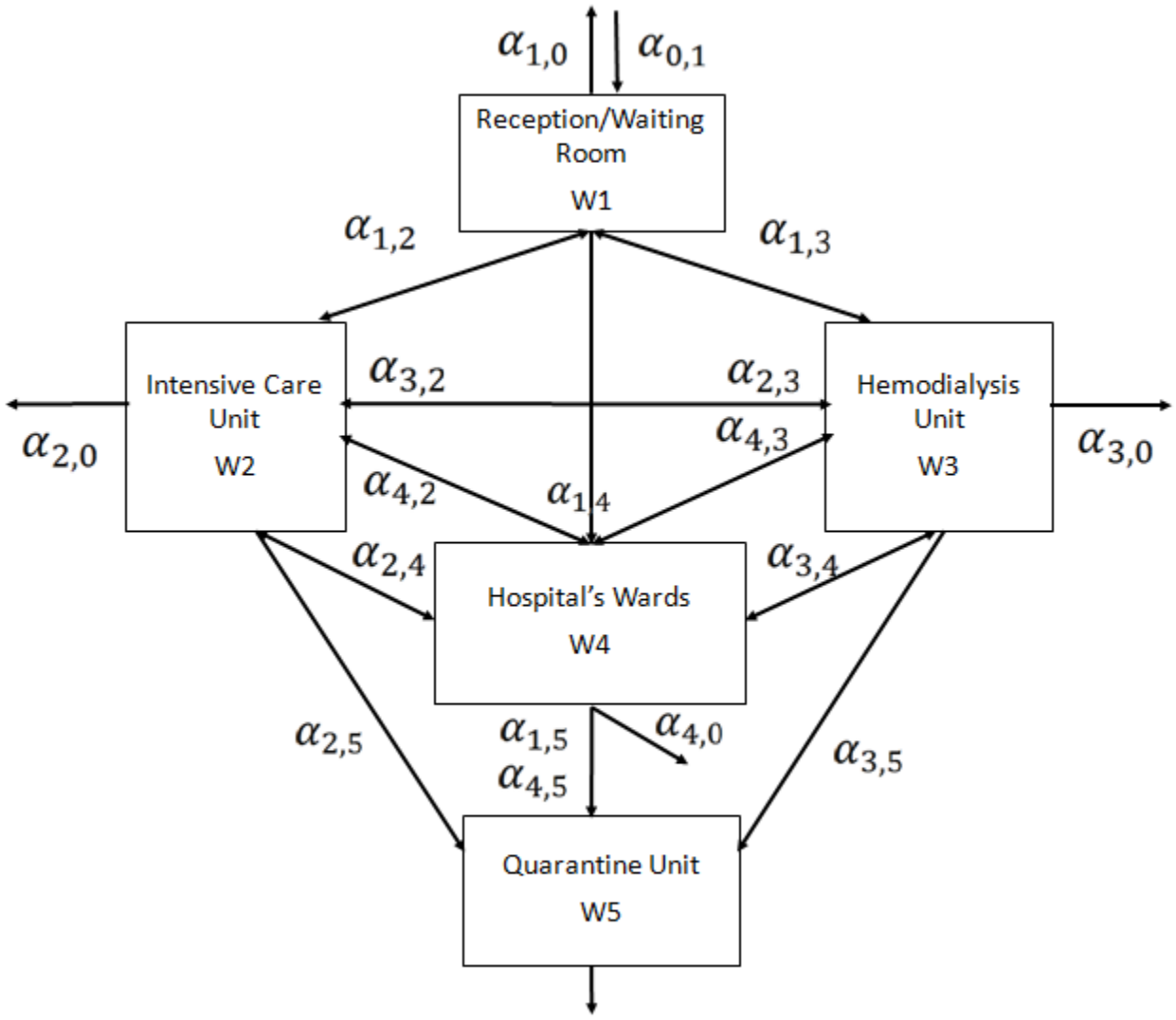


Figure 2.1: Hospital Wards Model.

Every ward has its own environment where cleaning plays an important factor in decontaminating the environment and spreading the disease. We consider human and natural overall contaminations where dust-mops and other cleaning procedures are counted as a vector. Furthermore, the following assumptions are used to create our SEIR system of equations,

1. A 100% staffing all the time (same number of HCWs).
2. A 100% occupancy (no empty beds).
3. When a Health Care Worker goes into the infected compartment and they are not active they can go into quarantine.
4. No vaccination.
5. 100 % efficacy of testing of the disease exists
6. Disease free system: An infected individual introduced into the population free of the disease [2].

2.2.2 MERS-CoV Parameters

Although data is always given to estimate parameters, we have encountered a situation where more than half of them are clueless and therefore generalized some values from [7]. The incubation period is $\frac{1}{\sigma} = 1$. The rest of the parameter values are given in Tables 2.2, 2.3, 2.4, and 2.5.

Hospital Parameters

Table 2.2: Hospital Parameters, Description and Base Values.

Parameter	Description	Base values	References
$\alpha_{0,1}$	Transition rate from the community 0 to inside unit 1	.0097	assumed
$\alpha_{1,0}$	Transition rate from unit 1 to outside community 0	.0097	assumed
$\alpha_{1,2}$	Transition rate between the unit 1 to unit 2	.0097	assumed
$\alpha_{1,3}$	Transition rate between the unit 1 to unit 3	.0097	assumed
$\alpha_{1,4}$	Transition rate between the unit 1 to unit 4	.0097	assumed
$\alpha_{1,5}$	Transition rate between the unit 1 to unit 5	.0416	assumed
$\alpha_{2,0}$	Transition rate from unit 2 to outside community 0	.0097	assumed
$\alpha_{2,3}$	Transition rate from unit 2 to unit 3	.0097	assumed
$\alpha_{2,4}$	Transition rate from unit 2 to unit 4	.0097	assumed
$\alpha_{2,5}$	Transition rate from unit 2 to unit 5	.0416	assumed
$\alpha_{3,0}$	Transition rate from unit 3 to outside community 0	.0097	assumed
$\alpha_{3,2}$	Transition rate from unit 3 to unit 2	.0097	assumed
$\alpha_{3,4}$	Transition rate from unit 3 to unit 4	.0097	assumed
$\alpha_{3,5}$	Transition rate from unit 3 to unit 5	.0416	assumed
$\alpha_{4,0}$	Transition rate from unit 4 to outside community 0	.0097	assumed
$\alpha_{4,2}$	Transition rate from unit 4 to unit 2	.0097	assumed
$\alpha_{4,3}$	Transition rate from unit 4 to unit 3	.0097	assumed
$\alpha_{4,5}$	Transition rate from unit 4 to unit 3	.0416	assumed
$\alpha_{m,5}$	Transition rate from mobile HCW to unit 5	.0833	assumed
κ_1	Carrying capacity (occupancy) for unit 1	Matlab	assumed
κ_2	Carrying capacity (occupancy) for unit 2	Matlab	assumed
κ_3	Carrying capacity (occupancy) for unit 3	Matlab	assumed
κ_4	Carrying capacity (occupancy) for unit 4	Matlab	assumed
κ_1'	Carrying capacity (occupancy) of HCW for unit 1	24	assumed
κ_2'	Carrying capacity (occupancy) of HCW for unit 2	24	assumed
κ_3'	Carrying capacity (occupancy) of HCW for unit 3	24	assumed
κ_4'	Carrying capacity (occupancy) of HCW for unit 4	24	assumed
κ_m'	Carrying capacity (occupancy) of mobile HCW	100	assumed
b_1	Cleaning/removal rate for unit 1	.1666	assumed
b_2	Cleaning/removal rate for unit 2	.1666	assumed
b_3	Cleaning/removal rate for unit 3	.1666	assumed
b_4	Cleaning/removal rate for unit 4	.1666	assumed

Disease Parameters

Table 2.3: Disease Parameters, Description and Base Values.

Parameter	Description	Base values	References
β_1	Human to human transmission rate from unit 1	.0022	assumed
β_2	Human to human transmission rate from unit 2	.0022	assumed
β_3	Human to human transmission rate from unit 3	.0022	assumed
β_4	Human to human transmission rate from unit 4	.0022	assumed
β_1'	Environment to human transmission rate from unit 1	.0024	assumed
β_2'	Environment to human transmission rate from unit 2	.0022	assumed
β_3'	Environment to human transmission rate from unit 3	.0022	assumed
β_4'	Environment to human transmission rate from unit 4	.0022	assumed
σ	Rate of becoming infectious	.0059	assumed
ρ	Rate of shedding virus into the environment	1	assumed
ε	Modulation of HCW for shedding into the environment	1	assumed
ξ	Modulation of mobile HCW for shedding into the environment	1	assumed
δ	Natural removal rate	1	assumed
c	Reduction factor for exposed	1	assumed

Community Parameters

Table 2.4: Community Parameters, Description and Dase Values.

Parameter	Description	Base values	References
P_E	Probability that admitted person is exposed	0	assumed
P_I	Probability that admitted person is infected	.001	assumed
N	Number of people in community	$1,000,000$	assumed

HCW (disease) Parameters

Table 2.5: HCW (disease) Parameters, Description and Base Values.

Parameter	Description	Base values	References
$\beta_{2,H}$	Human to Human transmission rate from unit 2 to a HCW	.0138	assumed
$\beta_{3,H}$	Human to Human transmission rate from unit 3 to a HCW	.0138	assumed
$\beta_{4,H}$	Human to Human transmission rate from unit 4 to a HCW	.0138	assumed
β_m	Human to Human transmission rate to a mobile HCW	.0416	assumed
$\beta'_{2,H}$	Environment to human transmission rate from unit 2 to a HCW	.0370	assumed
$\beta'_{3,H}$	Environment to human transmission rate from unit 3 to a HCW	.0370	assumed
$\beta'_{4,H}$	Environment to human transmission rate from unit 4 to a HCW	.0370	assumed
β'_m	Environment to human transmission rate to a mobile HCW	.0250	assumed

2.2.3 Ward SEIR Transmission Model

To understand the spread of the nosocomial disease, we consider the following SEIR-Ward Model, where S is the number of susceptible, E is the number of exposed, I is the number of infected, R is the number of recovered, and V the viral load in the environment, with all of those quantities indexed by the unit. The system of equations is at equilibrium and $S' + E' + I' = 0$ and $HS' + HE' + HI' = 0$. For health-care workers, HS is the number of susceptible, HE is the number of exposed, HI is the number of infected. We only consider mobility in ICU, HD, and hospitals wards, since for waiting room, we assumed to have no transfer rate of HCW. (See Appendix C for SEIR Ward Model Transition Diagram).

1) Reception/Waiting room

$$\frac{dS_1}{dt} = -\beta_1 S_1(cE_1 + I_1) - \beta'_1 S_1 V_1 + \alpha_{0,1}(1 - P_E - P_I)N - (\alpha_{1,0} + \alpha_{1,2} + \alpha_{1,3} + \alpha_{1,4})S_1$$

$$\frac{dE_1}{dt} = \beta_1(\kappa_1 - E_1 - I_1)(cE_1 + I_1) + \beta'_1(\kappa_1 - E_1 - I_1)V_1 + \alpha_{0,1}P_E N - (\alpha_{1,0} + \alpha_{1,2} + \alpha_{1,3} + \alpha_{1,4})E_1$$

I_1 is the number of super-spreader or community-acquired infectious individuals and is given by,

$$\frac{dI_1}{dt} = \alpha_{0,1}P_I N - (\alpha_{1,2} + \alpha_{1,3} + \alpha_{1,4})I_1$$

$$\frac{dV_1}{dt} = \rho(cE_1 + I_1) - (b_1 + \delta)V_1$$

Such that $0 \leq S_1 + E_1 + I_1 = \kappa_1$ (notice the waiting room is not always full but we assume 100% occupancy)

Where P_E is the probability that admitted individual is exposed and P_I is admitted individual is infected. Due to have one index case, we assume that, $P_E = 0$ and $P_I = \frac{1}{\alpha_{0,1}N} = \frac{1}{(\alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4})\kappa_1}$. The previous probabilities depend on the levels of the disease in the population and where $\alpha_{0,1}$ means people coming from the community goes inside the hospital. We let $\alpha_{1,5} = 0$ since there is no testing right away in waiting room .

The unit capacity stability entails that:

$$\alpha_{0,1}N = (\alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4})\kappa_1$$

where N is the target population and by solving for κ_1 we have,

$$\kappa_1 = \frac{\alpha_{0,1}N}{(\alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4})}$$

It is preferable to estimate $\alpha_{i,j}$ independently as it is independent of the disease.

Thus, $S_1 = \kappa_1 - E_1 - I_1$, which makes the equation for $\frac{dS_1}{dt}$ redundant.

2) Intensive Care Unit (ICU)

$$\frac{dS_2}{dt} = -\beta_2 S_2(c(E_2 + HE_2 + \xi HE_m) + I_2) - \beta_2' S_2 V_2 + \alpha_{1,2} S_1 + \alpha_{3,2} S_3 + \alpha_{4,2} S_4 - (\alpha_{2,0} + \alpha_{2,3} + \alpha_{2,4}) S_2$$

$$\frac{dE_2}{dt} = \beta_2(\kappa_2 - E_2 - I_2)(c(E_2 + HE_2 + \xi HE_m) + I_2) + \beta_2'(\kappa_2 - E_2 - I_2)V_2 + \alpha_{1,2} E_1 + \alpha_{3,2} E_3 + \alpha_{4,2} E_4 - (\alpha_{2,0} + \alpha_{2,3} + \alpha_{2,4}) E_2 - \sigma E_2$$

$$\frac{dI_2}{dt} = \sigma E_2 + \alpha_{1,2} I_1 + \alpha_{3,2} I_3 + \alpha_{4,2} I_4 - (\alpha_{2,3} + \alpha_{2,4} + \alpha_{2,5}) I_2$$

$$\frac{dHS_2}{dt} = \sigma HE_2 - \beta_{2,H} HS_2(c(E_2 + HE_2 + \xi HE_m) + I_2) - \beta_{2,H}' HS_2 V_2$$

$$\frac{dHE_2}{dt} = \beta_{2,H}(\kappa_2' - HE_2)(c(E_2 + HE_2 + \xi HE_m) + I_2) + \beta_{2,H}'(\kappa_2' - HE_2)V_2 - \sigma HE_2$$

$$\frac{dHI_2}{dt} = \sigma HE_2 - \alpha_{2,5} HI_2$$

$$\frac{dV_2}{dt} = \rho(c(E_2 + \varepsilon HE_2 + \xi HE_m) + I_2) - (b_2 + \delta)V_2$$

Such that $0 \leq S_2 + E_2 + I_2 = \kappa_2$ and $0 \leq HS_2 + HE_2 = \kappa_2'$

The unit capacity stability entails that:

$$\alpha_{1,2}\kappa_1 + \alpha_{3,2}\kappa_3 + \alpha_{4,2}\kappa_4 = \bar{\alpha}_2 \kappa_2 \text{ where } \bar{\alpha}_2 = \alpha_{2,0} + \alpha_{2,3} + \alpha_{2,4}$$

and by solving for κ_2 we have,

$$\kappa_2 = \frac{\kappa_1}{\alpha_{2,3}} \left(\bar{\alpha}_3 (z + ad) - \alpha_{1,3} - a\alpha_{4,3}\right)$$

$$a = \left(\alpha_{1,4} - \frac{\alpha_{2,4}\alpha_{1,3}}{\alpha_{2,3}} + fz\right) / \left(\bar{\alpha}_4 + \frac{\alpha_{2,4}\alpha_{4,3}}{\alpha_{2,3}} - fd\right)$$

$$z = (\bar{\alpha}_2 \alpha_{1,3} + \alpha_{1,2}\alpha_{2,3}) / (\bar{\alpha}_2 \bar{\alpha}_3 - \alpha_{3,2}\alpha_{2,3})$$

$$d = (\bar{\alpha}_2 \alpha_{4,3} + \alpha_{4,2}\alpha_{2,3}) / (\bar{\alpha}_2 \bar{\alpha}_3 - \alpha_{3,2}\alpha_{2,3})$$

$$f = \alpha_{3,4} + \frac{\alpha_{2,4}\bar{\alpha}_3}{\alpha_{2,3}}$$

Where, $S_2 = \kappa_2 - E_2 - I_2$

3) Hemodialysis (HD)

$$\frac{dS_3}{dt} = -\beta_3 S_3(c(E_3 + HE_3 + \xi HE_m) + I_3) - \beta_3' S_3 V_3 + \alpha_{1,3} S_1 + \alpha_{2,3} S_2 + \alpha_{4,3} S_4 - (\alpha_{3,0} + \alpha_{3,2} + \alpha_{3,4}) S_3$$

$$\frac{dE_3}{dt} = \beta_3(\kappa_3 - E_3 - I_3)(c(E_3 + HE_3 + \xi HE_m) + I_3) + \beta_3'(\kappa_3 - E_3 - I_3)V_3 + \alpha_{1,3} E_1 + \alpha_{2,3} E_2 + \alpha_{4,3} E_4 - (\alpha_{3,0} + \alpha_{3,2} + \alpha_{3,4}) E_3 - \sigma E_3$$

$$\frac{dI_3}{dt} = \sigma E_3 + \alpha_{1,3} I_1 + \alpha_{2,3} I_2 + \alpha_{4,3} I_4 - (\alpha_{3,2} + \alpha_{3,4} + \alpha_{3,5}) I_3$$

$$\frac{dHS_3}{dt} = \sigma HE_3 - \beta_{3,H} HS_3(c(E_3 + HE_3 + \xi HE_m) + I_3) - \beta_{3,H}' HS_3 V_3$$

$$\frac{dHE_3}{dt} = \beta_{3,H}(\kappa_3' - HE_3)(c(E_3 + HE_3 + \xi HE_m) + I_3) + \beta_{3,H}'(\kappa_3' - HE_3)V_3 - \sigma HE_3$$

$$\frac{dHI_3}{dt} = \sigma HE_3 - \alpha_{3,5} HI_3$$

$$\frac{dV_3}{dt} = \rho(c(E_3 + \varepsilon HE_3 + \xi HE_m) + I_3) - (b_3 + \delta)V_3$$

Such that $0 \leq S_3 + E_3 + I_3 = \kappa_3$ and $0 \leq HS_3 + HE_3 = \kappa_3'$

The unit capacity stability entails that:

$$\alpha_{1,3}\kappa_1 + \alpha_{2,3}\kappa_2 + \alpha_{4,3}\kappa_4 = \bar{\alpha}_3 \kappa_3$$

$$\bar{\alpha}_3 = \alpha_{3,0} + \alpha_{3,2} + \alpha_{3,4}$$

and by solving for κ_3 we have, $\kappa_3 = \kappa_1 (z + ad)$ where, $S_3 = \kappa_3 - E_3 - I_3$

4) Hospital (Wards)

$$\frac{dS_4}{dt} = -\beta_4 S_4(c(E_4 + HE_4 + \xi HE_m) + I_4) - \beta_4' S_4 V_4 + \alpha_{1,4} S_1 + \alpha_{2,4} S_2 + \alpha_{3,4} S_3 - (\alpha_{4,0} + \alpha_{4,2} + \alpha_{4,3}) S_4$$

$$\frac{dE_4}{dt} = \beta_4(\kappa_4 - E_4 - I_4)(c(E_4 + HE_4 + \xi HE_m) + I_4) + \beta_4'(\kappa_4 - E_4 - I_4)V_4 + \alpha_{1,4} E_1 + \alpha_{2,4} E_2 + \alpha_{3,4} E_3 - (\alpha_{4,0} + \alpha_{4,2} + \alpha_{4,3}) E_4 - \sigma E_4$$

$$\frac{dI_4}{dt} = \sigma E_4 + \alpha_{1,4} I_1 + \alpha_{2,4} I_2 + \alpha_{3,4} I_3 - (\alpha_{4,2} + \alpha_{4,3} + \alpha_{4,5}) I_4$$

$$\frac{dHS_4}{dt} = \sigma HE_4 - \beta_{4,H} HS_4(c(E_4 + HE_4 + \xi HE_m) + I_4) - \beta_{4,H}' HS_4 V_4$$

$$\frac{dHE_4}{dt} = \beta_{4,H}(\kappa_4' - HE_4)(c(E_4 + HE_4 + \xi HE_m) + I_4) + \beta_{4,H}'(\kappa_4' - HE_4)V_4 - \sigma HE_4$$

$$\frac{dHI_4}{dt} = \sigma HE_4 - \alpha_{4,5} HI_4$$

$$\frac{dV_4}{dt} = \rho(c(E_4 + \varepsilon HE_4 + \xi HE_m) + I_4) - (b_4 + \delta)V_4$$

Such that $0 \leq S_4 + E_4 + I_4 = \kappa_4$ and $0 \leq HS_4 + HE_4 = \kappa_4'$

The unit capacity stability entails that:

$$\alpha_{1,4}\kappa_1 + \alpha_{2,4}\kappa_2 + \alpha_{3,4}\kappa_3 = (\alpha_{4,0} + \alpha_{4,2} + \alpha_{4,3})\kappa_4$$

and by solving for κ_4 we have, $\kappa_4 = a\kappa_1$ where, $S_4 = \kappa_4 - E_4 - I_4$

5) Mobile HCW

$$\frac{dHS_m}{dt} = \sigma HE_m - \beta_m HS_m(c(E_2+E_3+E_4+HE_2+HE_3+HE_4+HE_m)+I_2+I_3+I_4) - \beta'_m HS_m(V_2+V_3+V_4)$$

$$\frac{dHE_m}{dt} = \beta_m(\kappa'_m - HE_m)(c(E_2+E_3+E_4+HE_2+HE_3+HE_4+HE_m)+I_2+I_3+I_4) + \beta'_m(\kappa'_m - HE_m)(V_2+V_3+V_4) - \sigma HE_m$$

$$\frac{dHI_m}{dt} = \sigma HE_m - \alpha_{m,5} HI_m$$

Such that $0 \leq HS_m + HE_m = \kappa'_m$

6) Quarantine (isolation)

$$\frac{dQ}{dt} = \alpha_{1,5} I_1 + \alpha_{2,5} I_2 + \alpha_{3,5} I_3 + \alpha_{4,5} I_4$$

$$\frac{dQ_H}{dt} = \alpha_{2,5} HI_2 + \alpha_{3,5} HI_3 + \alpha_{4,5} HI_4$$

$$\frac{dQ_m}{dt} = \alpha_{m,5} HI_m$$

2.3 NGMof MERS-CoV and Disease Free Equilibrium Point

Up to now, we can construct our matrices to do next generation matrix for MERS-CoV. Let the disease free state be $DFE \equiv (E_1^*, I_1^*, V_1^*, E_2^*, I_2^*, HE_2^*, HI_2^*, V_2^*, E_3^*, I_3^*, HE_3^*, HI_3^*, V_3^*, E_4^*, I_4^*, HE_4^*, HI_4^*, V_4^*, HE_m^*, HI_m^*) = \mathbf{0}$ which is an equilibrium point, and where $\mathbf{0}$ is a 20x1 zero vector. (See Appendix A)

$$\mathscr{F} = \begin{bmatrix} \beta_1(\kappa_1 - E_1 - I_1)(cE_1 + I_1) + \beta_1'(\kappa_1 - E_1 - I_1)V_1 \\ 0 \\ 0 \\ \beta_2(\kappa_2 - E_2 - I_2)(c(E_2 + HE_2 + \xi HE_m) + I_2) + \beta_2'(\kappa_2 - E_2 - I_2)V_2 \\ 0 \\ \beta_{2,H}(\kappa_2' - HE_2)(c(E_2 + HE_2 + \xi HE_m) + I_2) + \beta_{2,H}'(\kappa_2' - HE_2)V_2 \\ 0 \\ 0 \\ \beta_3(\kappa_3 - E_3 - I_3)(c(E_3 + HE_3 + \xi HE_m) + I_3) + \beta_3'(\kappa_3 - E_3 - I_3)V_3 \\ 0 \\ \beta_{3,H}(\kappa_3' - HE_3)(c(E_3 + HE_3 + \xi HE_m) + I_3) + \beta_{3,H}'(\kappa_3' - HE_3)V_3 \\ 0 \\ 0 \\ \beta_4(\kappa_4 - E_4 - I_4)(c(E_4 + HE_4 + \xi HE_m) + I_4) + \beta_4'(\kappa_4 - E_4 - I_4)V_4 \\ 0 \\ \beta_{4,H}(\kappa_4' - HE_4)(c(E_4 + HE_4 + \xi HE_m) + I_4) + \beta_{4,H}'(\kappa_4' - HE_4)V_4 \\ 0 \\ 0 \\ \beta_m(\kappa_m' - HE_m)(c(E_2 + E_3 + E_4 + HE_2 + HE_3 + HE_4 + HE_m) + I_2 + I_3 + I_4) + \beta_m'(\kappa_m' - HE_m)(V_2 + V_3 + V_4) \\ 0 \end{bmatrix}$$

$$\mathscr{V} = \begin{bmatrix} -\alpha_{0,1}P_E N + (\alpha_{1,0}+\alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4})E_1 \\ -\alpha_{0,1}P_I N + (\alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4})I_1 \\ -\rho(cE_1+I_1)+(b_1+\delta)V_1 \\ -(\alpha_{1,2}E_1+\alpha_{3,2}E_3+\alpha_{4,2}E_4)+(\alpha_{2,0}+\alpha_{2,3}+\alpha_{2,4})E_2+\sigma E_2 \\ -(\sigma E_2+\alpha_{1,2}I_1+\alpha_{3,2}I_3+\alpha_{4,2}I_4)+(\alpha_{2,3}+\alpha_{2,4}+\alpha_{2,5})I_2 \\ \sigma H E_2 \\ -\sigma H E_2+\alpha_{2,5}H I_2 \\ -\rho(c(E_2+\varepsilon H E_2+\xi H E_m)+I_2)+(b_2+\delta)V_2 \\ -(\alpha_{1,3}E_1+\alpha_{2,3}E_2+\alpha_{4,3}E_4)+(\alpha_{3,0}+\alpha_{3,2}+\alpha_{3,4})E_3+\sigma E_3 \\ -(\sigma E_3+\alpha_{1,3}I_1+\alpha_{2,3}I_2+\alpha_{4,3}I_4)+(\alpha_{3,2}+\alpha_{3,4}+\alpha_{3,5})I_3 \\ \sigma H E_3 \\ -\sigma H E_3+\alpha_{3,5}H I_3 \\ -\rho(c(E_3+\varepsilon H E_3+\xi H E_m)+I_3)+(b_3+\delta)V_3 \\ -(\alpha_{1,4}E_1+\alpha_{2,4}E_2+\alpha_{3,4}E_3)+(\alpha_{4,0}+\alpha_{4,2}+\alpha_{4,3})E_4+\sigma E_4 \\ -(\sigma E_4+\alpha_{1,4}I_1+\alpha_{2,4}I_2+\alpha_{3,4}I_3)+(\alpha_{4,2}+\alpha_{4,3}+\alpha_{4,5})I_4 \\ \sigma H E_4 \\ -\sigma H E_4+\alpha_{4,5}H I_4 \\ -\rho(c(E_4+\varepsilon H E_4+\xi H E_m)+I_4)+(b_4+\delta)V_4 \\ \sigma H E_m \\ -\sigma H E_m+\alpha_{m,5}H I_m \end{bmatrix}$$

CHAPTER III

MODEL ANALYSIS AND VALIDATION

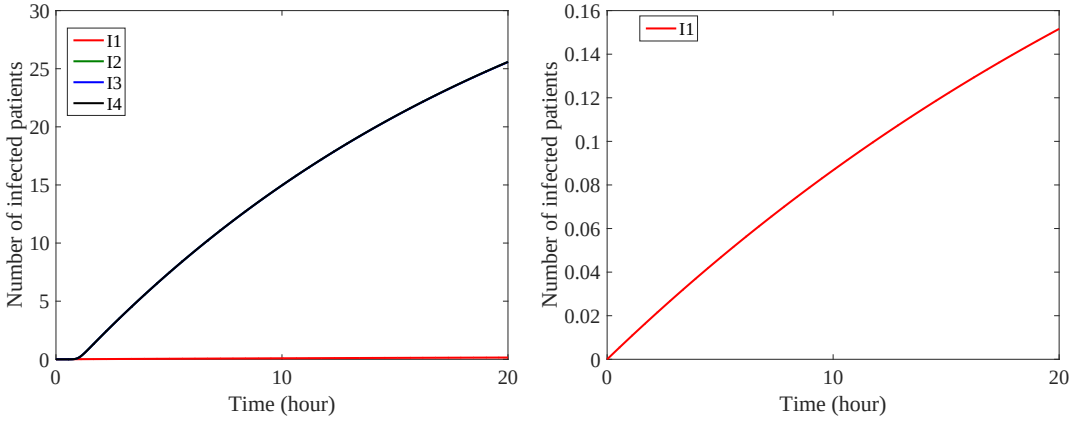
3.1 Simulations

Using the estimated parameters in Table 3.1, the equations of MERS-CoV model were solved numerically using *ode45* in *Matlab* (see code in Appendix B).

Table 3.1: Set 1 of β Values

Parameter	Description	Base Values
β_i	Human to human transmission rate where $i = 1,2,3,4$ (units)	.0022
β_i'	Environment to human transmission rate where $i = 1,2,3,4$	.0024
$\beta_{i,H}$	Human to human transmission rate from units $i = 2,3,4$ to a HCW	.0138
$\beta_{i,H}'$	Environment to human transmission rate from $i = 2,3,4$ to a HCW	.0370
β_m	Human to human transmission rate to a mobile HCW	.0416
β_m'	Environment to human transmission rate	.0250

3.1.1 Simulation of infected patients



(a) (b)

Figure 3.1: Infected Patients.

In Figure 3.1 (a), the number of infected patients (I_2 and I_3) increases and I_1 decreases at the beginning of the transmission of the disease. By letting $\beta_1 = \beta_2 = \beta_3 = \beta_4 = .0022$ the number of infected increases at the same time in wards 2, 3, and 4. This means that, in ICU, HD, and other wards, there is a prevalence of the disease. After $t = 0$, I_1 detaches from the rest of the curves, since in ward 1 (reception or waiting room) have not HCW, we may assume there is no high transmission disease. If we look closer to to I_1, Figure 3.1 (b), it is seen that it does not go stable. At the beginning, there are not many infected individuals.

3.1.2 Simulation of exposed patients

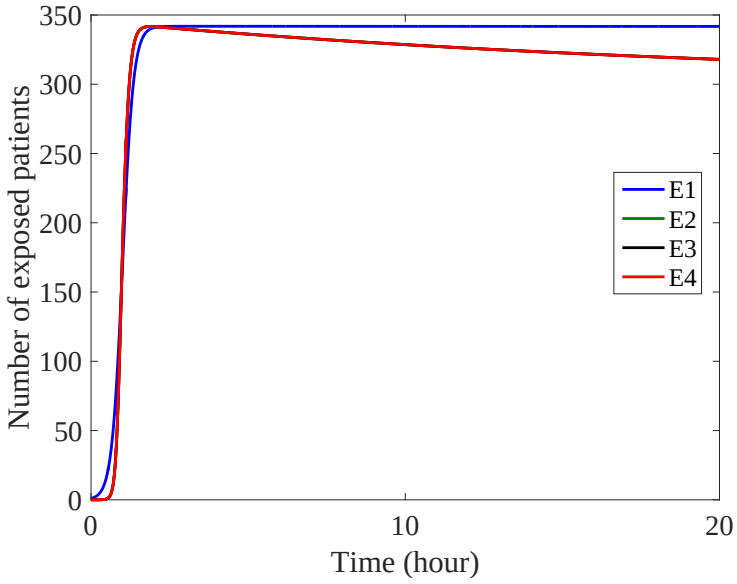


Figure 3.2: Exposed Patients.

In Figure 3.2, the number of all exposed patients increases and slightly decreases after $t = 10$. Number of exposed patients increases at the same time in wards 1, 2, and 3. Meaning that almost all of the individuals have a higher exposure to the disease. After $t = 0$, E_4 detaches from the rest of the curves, where it decreases faster than the rest. We may conclude that in ward 4 (referring to E_4) there are not many in/out flow of individuals as in other hospital wards.

3.1.3 Simulation of exposed and infected patients

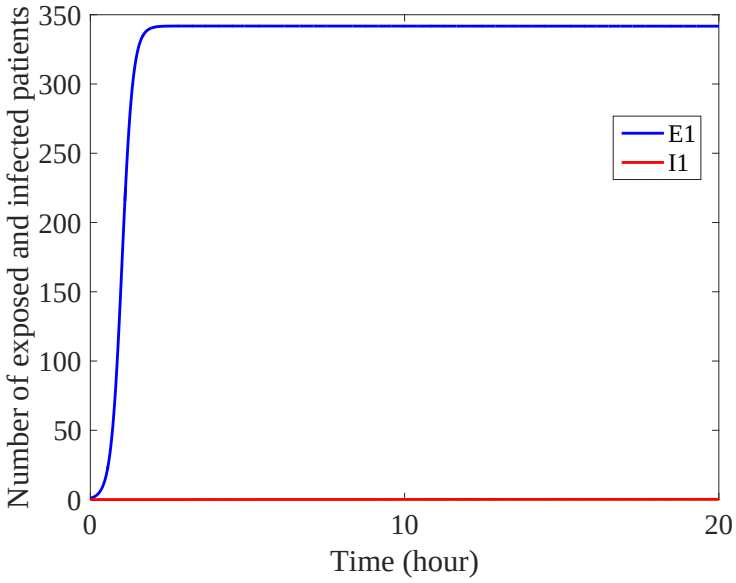
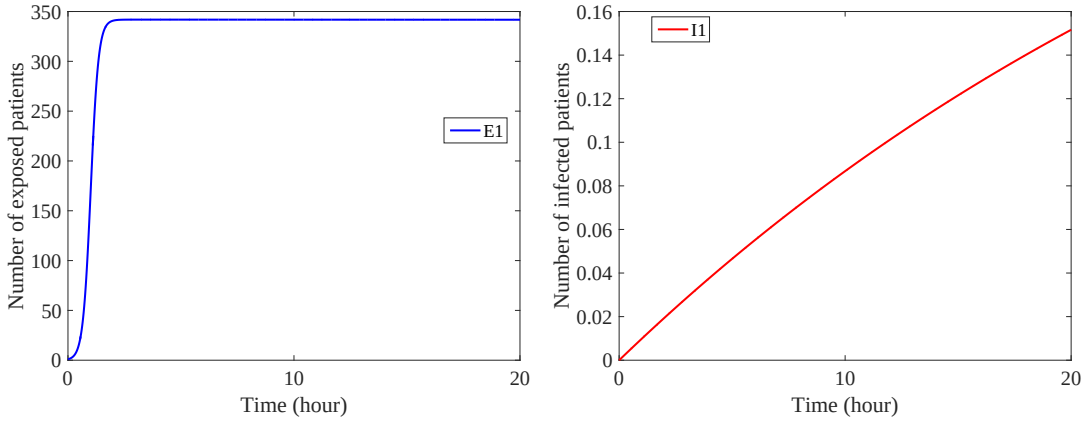


Figure 3.3: Exposed and Infected Patients in Ward 1.



(a) (b)

Figure 3.4: E and I Patients in Ward 1.

The exposed variable (E_1) in Figures 3.3 and 3.4 (a), will increase faster and after $t = 0$, it will be stable. However, in Figure 3.4 (b) the infected variable (I_1) will not be stable and it will barely increase at a low rate with a certainty that almost zero patients will not be infected.

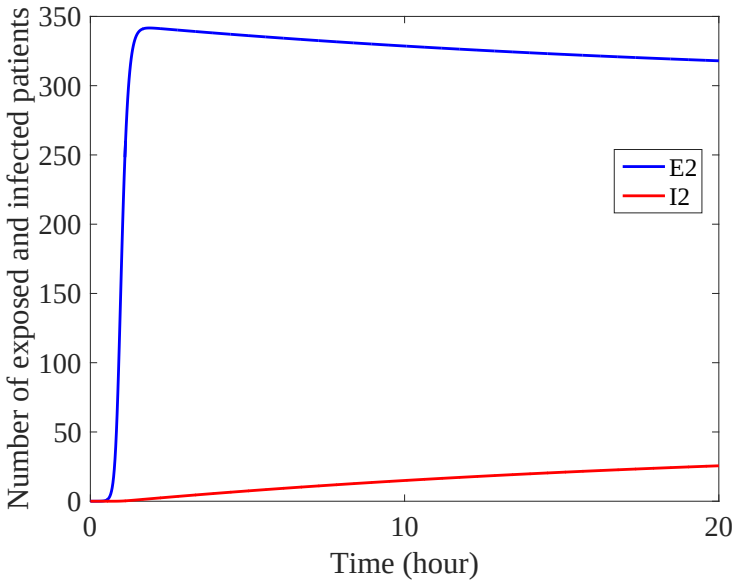


Figure 3.5: Exposed and Infected Patients in Ward 2.

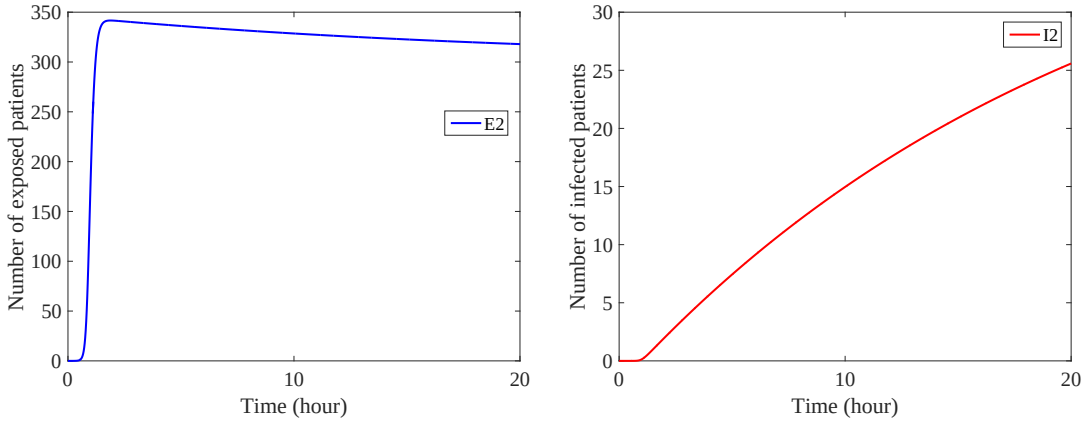
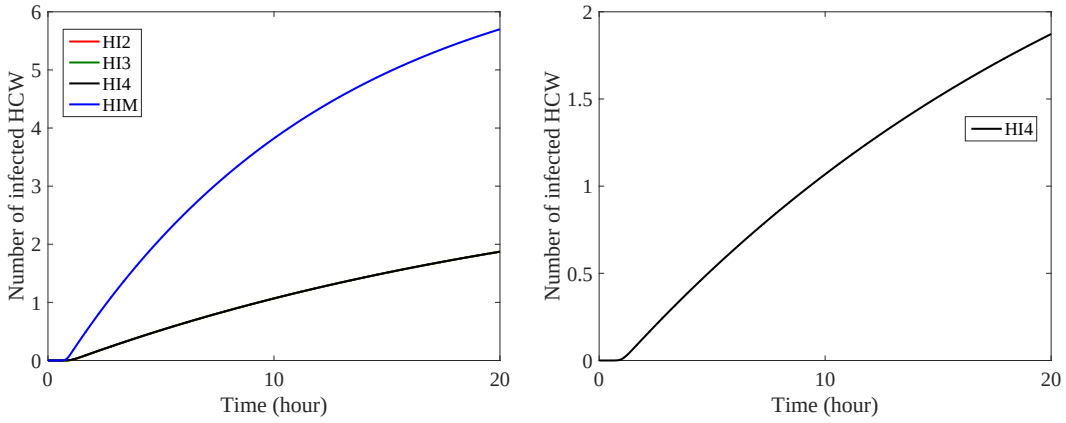


Figure 3.6: E and I Patients in Ward 2.

The exposed variable (E_2) in Figures 3.5 and 3.6 (a), will increase faster and after $t = 0$, it will decrease but will not reach stability. However, in Figure 3.6 (b) the infected variable (I_2) will not be stable and it will barely increase at a low rate after the exposed one decreases.

3.1.4 Simulation of infected HCW

Now, consider infected HCW with the same value of $\beta_1 = \beta_2 = \beta_3 = \beta_4 = .0022$.



(a) (b)

Figure 3.7: Infected HCW.

It is clear in Figure 3.7 (a) the number of infected HCW_2, HCW_3, and HCW_M increase more rapidly than HCW in ward 4 that has fewer infected individuals. We can assume that $HCW_{2,3,m}$ are the ones that contribute to the propagation of the disease. Another way to see this is that mobile HCW are moving more in those units than any other one. On the other hand, HI_4 increases at a lower pace (Figure 3.7 (b).

3.1.5 Simulation for mobile HCW

The mobile HCW for exposed and infected are shown in following Figure 3.8.

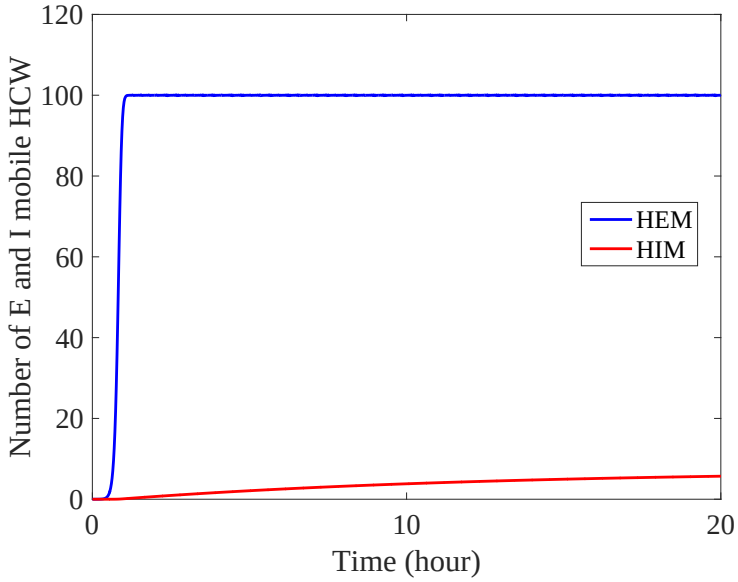


Figure 3.8: Exposed and Infected Mobile HCW.

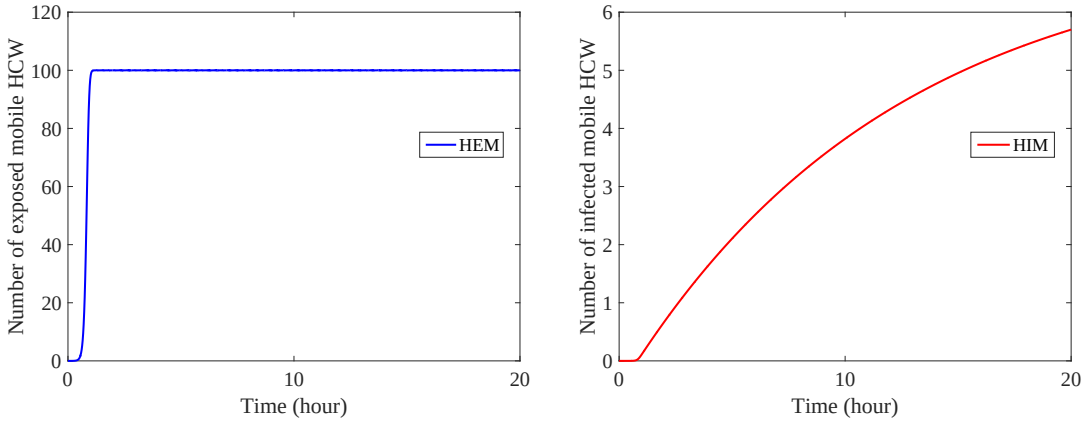


Figure 3.9: E and I Mobile HCW.

The number of exposed mobile HCW increases from the beginning of the transmission of disease at a faster rate than infected mobile HCW (Figure 3.8). And at some point in time, exposed mobile HCW will stabilize (Figure 3.9 (a)) which means that no more HCW will be exposed. Instead, infected mobile HCW (Figure 3.9 (b)) seems to be stable at the beginning but, in fact it is not so it keeps increasing at a slow pace.

3.1.6 Simulation for quarantine patients

In the hospital there is only one ward to treat patients and HCW of MERS-CoV disease. Those who get infected go immediately to quarantine and in a mathematical perspective it is treated separately from the rest of the wards and equations.

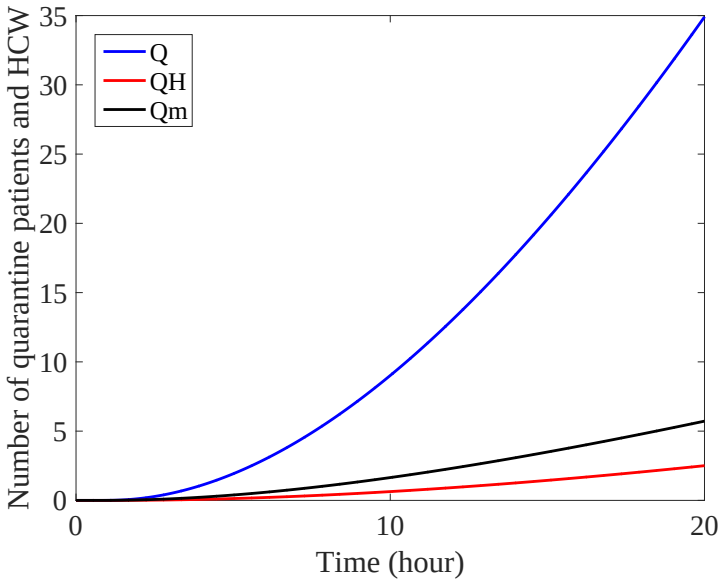


Figure 3.10: Quarantine Patients.

This figure represents that quarantine is cumulative which means there is no outflow of individuals. The appropriate reason for this graph is that the number of discovered cases goes to quarantine and stayed isolated.

Conclusion

Overall, the figures showed that exposed variables in any ward have higher number of patients than other. This indicates that people are carrying the disease and transmit it at some point in time. The graphs tell us that number of infected individuals does not increase faster than for the exposed ones. This could lead that the parameter β has a low value. The basic reproduction number for this simulation were calculated by using *ode45* in *Matlab* and came to be $R_0 = 2.9252$. This means that $R_0 > 1$ and an outbreak of the disease will be epidemic.
Similar results were given by considering another value for parameter β_i.

CHAPTER IV

CONCLUSION

This thesis emphasizes the analysis of the behavior of MERS-CoV disease in a hospital by using SEIR ward model. The next generation matrix and its properties were used to calculate the basic reproduction number by using *Matlab* codes to develop different simulations.
For future work, we would like to have real data so that we can analyze MERS-CoV disease in a deeper way and to hunt which factors contribute more to the propagation in a hospital by doing sensitivity analysis. Some questions that would be for future work are given below,

- Why is it too contagious among humans?
- Does only Hemodialysis unit have a higher transmission risk? [1]

And our future goals are the following:

1. To find the carriers that probably contribute to a large spread inside hospitals
2. To implement certain control measures such as:

   [a] Cohorting (Doctor are assigned to small and fixed number of patients)

   [b] Hygiene practices

3. To find out if there is an effective

   [a] Rapid Diagnostic Test (parameter $\alpha_{.,5}$)

   [b] Active surveillance.

   Also, to estimate quarantine variables: Q, Q_H, Q_m by using the method of non-linear least squares would be beneficial after obtaining real data.

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APPENDIX A

APPENDIX A

NEXT GENERATION MATRIX OF MERS-COV

Matrix F

Plot Matrix

$$\frac{\partial \mathscr{F}}{\partial E_1, \ldots, HI_m} = \left[\begin{array}{c|c|c|c|c} \mathscr{F}_{1,1} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \hline \mathbf{0} & \mathscr{F}_{2,2} & \mathbf{0} & \mathbf{0} & \mathscr{F}_{2,5} \\ \hline \mathbf{0} & \mathbf{0} & \mathscr{F}_{3,3} & \mathbf{0} & \mathscr{F}_{3,5} \\ \hline \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathscr{F}_{4,4} & \mathscr{F}_{4,5} \\ \hline \mathbf{0} & \mathscr{F}_{5,2} & \mathscr{F}_{5,3} & \mathscr{F}_{5,4} & \mathscr{F}_{5,5} \end{array}\right]$$

Where the block matrices are

$$\mathscr{F}_{1,1} = \begin{bmatrix} \beta_1\kappa_1 c - 2\beta_1 cE_1 - \beta_1 cI_1 - \beta_1 I_1 - \beta_1' V_1 & \beta_1\kappa_1 - \beta_1 cE_1 - \beta_1 E_1 - 2\beta_1 I_1 - \beta_1' V_1 & \beta_1'(\kappa_1 - E_1 - I_1) \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{2,2} = \begin{bmatrix} \beta_2\kappa_2 c - 2\beta_2 cE_2 - \beta_2 cI_2 - \beta_2 I_2 - \beta_2 cHE_2 - \beta_2 c\xi HE_m - \beta_2' V_2 & \beta_2\kappa_2 - \beta_2 cE_2 - \beta_2 E_2 - 2\beta_2 I_2 - \beta_2 cHE_2 - \beta_2 c\xi HE_m - \beta_2' V_2 & \beta_2\kappa_2 c - \beta_2 cE_2 - \beta_2 cI_2 & 0 & \beta_2'\kappa_2 - \beta_2' E_2 - \beta_2' I_2 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_{2,H}\kappa_2' c - \beta_{2,H} cHE_2 & \beta_{2,H}\kappa_2' - \beta_{2,H} HE_2 & \beta_{2,H}\kappa_2' c - \beta_{2,H} cE_2 - \beta_{2,H} I_2 - 2\beta_{2,H} cHE_2 - \beta_{2,H} c\xi HE_m - \beta_{2,H}' V_2 & 0 & \beta_{2,H}'\kappa_2' - \beta_{2,H}' HE_2 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{3,3} = \begin{bmatrix} \beta_3\kappa_3 c - 2\beta_3 cE_3 - \beta_3 cI_3 - \beta_3 I_3 - \beta_3 cHE_3 - \beta_3 c\xi HE_m - \beta_3' V_3 & \beta_3\kappa_3 - \beta_3 cE_3 - \beta_3 E_3 - 2\beta_3 I_3 - \beta_3 cHE_3 - \beta_3 c\xi HE_m - \beta_3' V_3 & \beta_3\kappa_3 c - \beta_3 cE_3 - \beta_3 cI_3 & 0 & \beta_3'\kappa_3 - \beta_3' E_3 - \beta_3' I_3 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_{3,H}\kappa_3' c - \beta_{3,H} cHE_3 & \beta_{3,H}\kappa_3' - \beta_{3,H} HE_3 & \beta_{3,H}\kappa_3' c - \beta_{3,H} cE_3 - \beta_{3,H} I_3 - 2\beta_{3,H} cHE_3 - \beta_{3,H} c\xi HE_m - \beta_{3,H}' V_3 & 0 & \beta_{3,H}'\kappa_3' - \beta_{3,H}' HE_3 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{4,4} = \begin{bmatrix} \beta_4\kappa_4 c - 2\beta_4 cE_4 - \beta_4 cI_4 - \beta_4 I_4 - \beta_4 cHE_4 - \beta_4 c\xi HE_m - \beta_4' V_4 & \beta_4\kappa_4 - \beta_4 cE_4 - \beta_4 E_4 - 2\beta_4 I_4 - \beta_4 cHE_4 - \beta_4 c\xi HE_m - \beta_4' V_4 & \beta_4\kappa_4 c - \beta_4 cE_4 - \beta_4 cI_4 & 0 & \beta_4'\kappa_4 - \beta_4' E_4 - \beta_4' I_4 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_{4,H}\kappa_4' c - \beta_{4,H} cHE_4 & \beta_{4,H}\kappa_4' - \beta_{4,H} HE_4 & \beta_{4,H}\kappa_4' c - \beta_{4,H} cE_4 - \beta_{4,H} I_4 - 2\beta_{4,H} cHE_4 - \beta_{4,H} c\xi HE_m - \beta_{4,H}' V_4 & 0 & \beta_{4,H}'\kappa_4' - \beta_{4,H}' HE_4 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{5,5} = \begin{bmatrix} \beta_m\kappa_m' c - \beta_m cE_2 - \beta_m cE_3 - \beta_m cE_4 - \beta_m cHE_2 - \beta_m cHE_3 - \beta_m cHE_4 - 2\beta_m cHE_m - \beta_m I_2 - \beta_m I_3 - \beta_m I_4 - \beta_m' V_2 - \beta_m' V_3 - \beta_m' V_4 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{2,5} = \begin{bmatrix} \beta_2\kappa_2 c\xi - \beta_2 E_2 c\xi - \beta_2 I_2 c\xi & 0 \\ 0 & 0 \\ \beta_{2,H}\kappa_2' c\xi - \beta_{2,H} H E_2 c\xi & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{3,5} = \begin{bmatrix} \beta_3\kappa_3 c\xi - \beta_3 E_3 c\xi - \beta_3 I_3 c\xi & 0 \\ 0 & 0 \\ \beta_{3,H}\kappa_3' c\xi - \beta_{3,H} H E_3 c\xi & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{4,5} = \begin{bmatrix} \beta_4\kappa_4 c\xi - \beta_4 E_4 c\xi - \beta_4 I_4 c\xi & 0 \\ 0 & 0 \\ \beta_{4,H}\kappa_4' c\xi - \beta_{4,H} H E_4 c\xi & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{5,2} = \begin{bmatrix} \beta_m\kappa_m' c - \beta_m c H E_m & \beta_m\kappa_m' - \beta_m H E_m & \beta_m\kappa_m' c - \beta_m c H E_m & 0 & \beta_m\kappa_m' - \beta_m H E_m \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{5,3} = \begin{bmatrix} \beta_m\kappa_m' c - \beta_m c H E_m & \beta_m\kappa_m' - \beta_m H E_m & \beta_m\kappa_m' c - \beta_m c H E_m & 0 & \beta_m\kappa_m' - \beta_m H E_m \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$\mathscr{F}_{5,4} = \begin{bmatrix} \beta_m\kappa_m' c - \beta_m c H E_m & \beta_m\kappa_m' - \beta_m H E_m & \beta_m\kappa_m' c - \beta_m c H E_m & 0 & \beta_m\kappa_m' - \beta_m H E_m \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

At the DFE $\mathscr{F}'$ is the matrix F given by

$$F = \mathscr{F}'|_{DFE} = \left[\begin{array}{c|c|c|c|c} F_{1,1} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \hline \mathbf{0} & F_{2,2} & \mathbf{0} & \mathbf{0} & F_{2,5} \\ \hline \mathbf{0} & \mathbf{0} & F_{3,3} & \mathbf{0} & F_{3,5} \\ \hline \mathbf{0} & \mathbf{0} & \mathbf{0} & F_{4,4} & F_{4,5} \\ \hline \mathbf{0} & F_{5,2} & F_{5,3} & F_{5,4} & F_{5,5} \end{array}\right]$$

Where the block matrices are

$$F_{1,1} = \begin{bmatrix} \beta_1 \kappa_1 c & \beta_1 \kappa_1 & \beta_1' \kappa_1 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$F_{2,2} = \begin{bmatrix} \beta_2 \kappa_2 c & \beta_2 \kappa_2 & \beta_2 \kappa_2 c & 0 & \beta_2' \kappa_2 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_{2,H} \kappa_2' c & \beta_{2,H} \kappa_2' & \beta_{2,H} \kappa_2' c & 0 & \beta_{2,H}' \kappa_2' \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F_{3,3} = \begin{bmatrix} \beta_3 \kappa_3 c & \beta_3 \kappa_3 & \beta_3 \kappa_3 c & 0 & \beta_3' \kappa_3 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_{3,H} \kappa_3' c & \beta_{3,H} \kappa_3' & \beta_{3,H} \kappa_3' c & 0 & \beta_{3,H}' \kappa_3' \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F_{4,4} = \begin{bmatrix} \beta_4\kappa_4 c & \beta_4\kappa_4 & \beta_4\kappa_4 c & 0 & \beta_4'\kappa_4 \\ 0 & 0 & 0 & 0 & 0 \\ \beta_{4,H}\kappa_4' c & \beta_{4,H}\kappa_4' & \beta_{4,H}\kappa_4' c & 0 & \beta_{4,H}'\kappa_4' \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F_{5,5} = \begin{bmatrix} \beta_m\kappa_m' c & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$F_{2,5} = \begin{bmatrix} \beta_2\kappa_2 c\xi & 0 \\ 0 & 0 \\ \beta_{2,H}\kappa_2' c\xi & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$F_{3,5} = \begin{bmatrix} \beta_3\kappa_3 c\xi & 0 \\ 0 & 0 \\ \beta_{3,H}\kappa_3' c\xi & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$F_{4,5} = \begin{bmatrix} \beta_4 \kappa_4 c\xi & 0 \\ 0 & 0 \\ \beta_{4,H} \kappa_4' c\xi & 0 \\ 0 & 0 \\ 0 & 0 \end{bmatrix}$$

$$F_{5,2} = \begin{bmatrix} \beta_m \kappa_m' c & \beta_m \kappa_m' & \beta_m \kappa_m' c & 0 & \beta_m \kappa_m' \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F_{5,3} = \begin{bmatrix} \beta_m \kappa_m' c & \beta_m \kappa_m' & \beta_m \kappa_m' c & 0 & \beta_m \kappa_m' \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$F_{5,4} = \begin{bmatrix} \beta_m \kappa_m' c & \beta_m \kappa_m' & \beta_m \kappa_m' c & 0 & \beta_m \kappa_m' \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

Matrix V

Plot Matrix for V which is equal to $\mathscr{V}'$ at the DFE

$$V = \mathscr{V}' = \left[\begin{array}{c|c|c|c|c} V_{1,1} & \mathbf{0} & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \hline V_{2,1} & V_{2,2} & V_{2,3} & V_{2,4} & V_{2,5} \\ \hline V_{3,1} & V_{3,2} & V_{3,3} & V_{3,4} & V_{3,5} \\ \hline V_{4,1} & V_{4,2} & V_{4,3} & V_{4,4} & V_{4,5} \\ \hline V_{5,1} & V_{5,2} & V_{5,3} & V_{5,4} & V_{5,5} \end{array}\right] \tag{1.1}$$

Where the block matrices are

$$V_{1,1} = \begin{bmatrix} \alpha_{1,0}+\alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4} & 0 & 0 \\ 0 & \alpha_{1,2}+\alpha_{1,3}+\alpha_{1,4} & 0 \\ -\rho c & -\rho & b_1+\delta \end{bmatrix}$$

$$V_{2,1} = \begin{bmatrix} -\alpha_{1,2} & 0 & 0 \\ 0 & -\alpha_{1,2} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$V_{2,2} = \begin{bmatrix} \alpha_{2,0}+\alpha_{2,3}+\alpha_{2,4}+\sigma & 0 & 0 & 0 & 0 \\ -\sigma & \alpha_{2,3}+\alpha_{2,4}+\alpha_{2,5} & 0 & 0 & 0 \\ 0 & 0 & \sigma & 0 & 0 \\ 0 & 0 & -\sigma & \alpha_{2,5} & 0 \\ -\rho c & -\rho & -\rho c\varepsilon & 0 & b_2+\delta \end{bmatrix}$$

$$V_{2,3} = \begin{bmatrix} -\alpha_{3,2} & 0 & 0 & 0 & 0 \\ 0 & -\alpha_{3,2} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{2,4} = \begin{bmatrix} -\alpha_{4,2} & 0 & 0 & 0 & 0 \\ 0 & -\alpha_{4,2} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{2,5} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ -\rho c \xi & 0 \end{bmatrix}$$

$$V_{3,1} = \begin{bmatrix} -\alpha_{1,3} & 0 & 0 \\ 0 & -\alpha_{1,3} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$V_{3,2} = \begin{bmatrix} -\alpha_{2,3} & 0 & 0 & 0 & 0 \\ 0 & -\alpha_{2,3} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{3,3} = \begin{bmatrix} \alpha_{3,0}+\alpha_{3,2}+\alpha_{3,4}+\sigma & 0 & 0 & 0 & 0 \\ -\sigma & \alpha_{3,2}+\alpha_{3,4}+\alpha_{3,5} & 0 & 0 & 0 \\ 0 & 0 & \sigma & 0 & 0 \\ 0 & 0 & -\sigma & \alpha_{3,5} & 0 \\ -\rho c & -\rho & -\rho c\varepsilon & 0 & b_3+\delta \end{bmatrix}$$

$$V_{3,4} = \begin{bmatrix} -\alpha_{4,3} & 0 & 0 & 0 & 0 \\ 0 & -\alpha_{4,3} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{3,5} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ -\rho c\xi & 0 \end{bmatrix}$$

$$V_{4,1} = \begin{bmatrix} -\alpha_{1,4} & 0 & 0 \\ 0 & -\alpha_{1,4} & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$V_{4,2} = \begin{bmatrix} -\alpha_{2,4} & 0 & 0 & 0 & 0 \\ 0 & -\alpha_{2,4} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{4,3} = \begin{bmatrix} -\alpha_{3,4} & 0 & 0 & 0 & 0 \\ 0 & -\alpha_{3,4} & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{4,4} = \begin{bmatrix} \alpha_{4,0}+\alpha_{4,2}+\alpha_{4,3}+\sigma & 0 & 0 & 0 & 0 \\ -\sigma & \alpha_{4,2}+\alpha_{4,3}+\alpha_{4,5} & 0 & 0 & 0 \\ 0 & 0 & \sigma & 0 & 0 \\ 0 & 0 & -\sigma & \alpha_{4,5} & 0 \\ -\rho c & -\rho & -\rho c\varepsilon & 0 & b_4+\delta \end{bmatrix}$$

$$V_{4,5} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ 0 & 0 \\ -\rho c \xi & 0 \end{bmatrix}$$

$$V_{5,1} = \begin{bmatrix} 0 & 0 & 0 \\ 0 & 0 & 0 \end{bmatrix}$$

$$V_{5,2} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{5,3} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{5,4} = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

$$V_{5,5} = \begin{bmatrix} \sigma & 0 & 0 & 0 \\ -\sigma & \alpha_{m,5} & 0 & 0 \end{bmatrix}$$

APPENDIX B

APPENDIX B

MATLAB CODE

```
 %% This part runs the numerical solution
%%of the ODE using Runga-Kutta 4,5 and plots I
    clear all
    clc
    y=100; tey=1000; te=tey*y;

    xspan = linspace(0,y,1+te);
    ynot = [1 0 zeros(1,21)];

    beta=.0469;betap=.0024;betah=.0338;betahp=.0370;betam=.0816;betamp=.0250;
    rho=1;
    [X,Y] =
ode45(@odeseir_TORed,xspan,ynot,[],beta,betap,betah,betahp,betam,betamp,rho);

    % List from the odeseir file
    E1=Y(:,1)';
    I1=Y(:,2)';
    E2=Y(:,4)';
    I2=Y(:,5)';
    HE2=Y(:,6)';
    HI2=Y(:,7)';
    E3=Y(:,9)';
```

```
    I3=Y(:,10)';
    HE3=Y(:,11)';
    HI3=Y(:,12)';
    E4=Y(:,14)';
    I4=Y(:,15)';
    HE4=Y(:,16)';
    HI4=Y(:,17)';
    HEM=Y(:,19)';
    HIM=Y(:,20)';
    Q=Y(:,21)';
    QH=Y(:,22)';
    Qm=Y(:,23)';


%This is the ODE SEIR function

function xprime = odeseir_TORed(t,x,beta,betap,betah,betahp,betam,betamp,rho)
%% List of variables
% 1) Reception/Waiting room
% x(1) = E1
% x(2) = I1 % super spreader
% x(3) = V1

% 2) ICU
% x(4) = E2
% x(5) = I2
% x(6) = HE2
% x(7) = HI2
% x(8) = V2

% 3) Hemodialysis
% x(9) = E3
```

```
% x(10) = I3
% x(11) = HE3
% x(12) = HI3
% x(13) = V3

% 4) Hospital (Wards)
% x(14) = E4
% x(15) = I4
% x(16) = HE4
% x(17) = HI4
% x(18) = V4

% 5) Mobile for HCW
% x(19) = HEM
% x(20) = HIM

% 6) Quarantine (isolation)
% x(21) = Q
% x(22) = QH
% x(23) = Qm

% 7) Recovery and Death
% x(24) = R
% x(25) = D

%Parameters

%Alphas
alpha12= .0097;
alpha13= .0097;
alpha14= .0097;
alpha20= .0097;
```

```
alpha23= .0097;
alpha24= .0097;
alpha30= .0097;
alpha32= .0097;
alpha34= .0097;
alpha40= .0097;
alpha42= .0097;
alpha43= .0097;
alphabar2= (alpha20+alpha23+alpha24);
alphabar3= (alpha30+alpha32+alpha34);
alphabar4= (alpha40+alpha42+alpha43);

% 1) Reception/Waiting
beta1=beta;
beta1p=betap;

alpha01in=.00001;
alpha10out=.001;
alpha15= .04166;
PE=0;
PI=.001;
b1=.1666;


% 2) ICU
beta2=beta;
beta2p=betap;
alpha25= .0416;

beta2h= betah;
beta2hp= betahp;
b2=.1666;
```

```
% 3) Hemodialysis
beta3= beta;
beta3p= betap;
alpha35= .04166;

beta3h= betah;
beta3hp= betahp;
b3=.1666;

% 4) Hospital Wards
beta4= beta;
beta4p= betap;
alpha45= .0416;

beta4h= betah;
beta4hp= betahp;
b4= .1666;

%%%%%%% General
N=1000000;
sigma= .005952381;

c= 1;
epsilon= 1;
xi= 1;
delta= 1;
alpham5=.0833;

kappa2p=24;

kappa3p=24;
```

```
kappa4p=24;

kappamp=100;


%% Auxiliary variables

f = alpha34 + (alpha24*alphabar3)/(alpha23);

z = ((alphabar2*alpha13)+(alpha12*alpha23))/
((alphabar2*alphabar3)-(alpha32*alpha23));

d = ((alphabar2*alpha43)+(alpha42*alpha23))/
((alphabar2*alphabar3)-(alpha32*alpha23));

a = (alpha14 - (alpha24*alpha13)/
(alpha23) + f*z)/(alphabar4 + (alpha24*alpha43)/(alpha23) - f*d);


%% Unit capacity stability
kappa1=(alpha01in*N)/(alpha12+alpha13+alpha14);

kappa2=(kappa1/alpha23)*(alphabar3*(z+d*a)-alpha13-alpha43*a);

kappa3=kappa1*(z+d*a);

kappa4=kappa1*a;


%% Reception/Waiting Room
xprime(1) = beta1*(kappa1-x(1)-x(2))*(c*x(1)+x(2))+
```

```
beta1p*(kappa1-x(1)-x(2))*x(3)+alpha01in*PE*N-
(alpha10out+alpha12+alpha13+alpha14)*x(1);
xprime(2) = alpha01in*PI*N-(alpha12+alpha13+alpha14)*x(2);

% Environvemnt
xprime(3) = rho*(c*x(1)+x(2))-(b1+delta)*x(3);

%% ICU
xprime(4) = beta2*(kappa2-x(4)-x(5))*(c*(x(4)+ x(6)+ xi*x(19))+ x(5))+
beta2p*(kappa2-x(4)-x(5))*x(8)+alpha12*x(1)+alpha32*x(9)+alpha42*x(14)-
(alpha20+alpha23+alpha24)*x(4)-sigma*x(4);
xprime(5) = sigma*x(4)+alpha12*x(2)+alpha32*x(10)+alpha42*x(15)-
(alpha23+alpha24+alpha25)*x(5); %-mu*x(5);
%ICU HCW
xprime(6) = beta2h*(kappa2p-x(6))*(c*(x(4)+ x(6)+ xi*x(19))+x(5))+
beta2hp*(kappa2p-x(6))*x(8)-sigma*x(6);
xprime(7) = sigma*x(6)-alpha25*x(7);
% Environvemnt
xprime(8) = rho*(c*(x(4)+ epsilon*x(6)+ xi*x(19))+x(5))-(b2+delta)*x(8);


%% Hemodialysis
xprime(9) = beta3*(kappa3-x(9)-x(10))*(c*(x(9)+ x(11)+ xi*x(19))+ x(10))+
beta3p*(kappa3-x(9)-x(10))*x(13)+alpha13*x(1)+alpha23*x(4)+alpha43*x(14)-
(alpha30+alpha32+alpha34)*x(9)-sigma*x(9);
xprime(10) = sigma*x(9)+alpha13*x(2)+alpha23*x(5)+alpha43*x(15)-
(alpha32+alpha34+alpha35)*x(10); %-mu*x(10);
%Hemodialysis HCW
xprime(11) = beta3h*(kappa3p-x(11))*(c*(x(9)+ x(11)+ xi*x(19))+x(10))+
beta3hp*(kappa3p-x(11))*x(13)-sigma*x(11);
xprime(12) = sigma*x(11)-alpha35*x(12);
```

```
% Environvemnt
xprime(13) = rho*(c*(x(9)+ epsilon*x(11)+ xi*x(19))
+x(10))-(b3+delta)*x(13);
%% Hospital Wards
xprime(14) = beta4*(kappa4-x(14)-x(15))*(c*(x(14)+ x(16)
+ xi*x(19))+ x(15))+ beta4p*(kappa4-x(14)-x(15))*x(18)+alpha14*x(1)
+alpha24*x(4)+alpha34*x(9)-
(alpha40+alpha42+alpha43)*x(14)-sigma*x(14);
xprime(15) = sigma*x(14)+alpha14*x(2)+alpha24*x(5)+alpha34*x(10)-
(alpha42+alpha43+alpha45)*x(15);
%Hemodialysis HCW
xprime(16) = beta4h*(kappa4p-x(16))*(c*(x(14)+ x(16)+ xi*x(19))+x(15))+
beta4hp*(kappa4p-x(16))*x(18)-sigma*x(16);
xprime(17) = sigma*x(16)-alpha45*x(17);
% Environvemnt
xprime(18) = rho*(c*(x(14)+ epsilon*x(16)
+ xi*x(19))+x(15))-(b4+delta)*x(18);
%% Mobile HCW
xprime(19) = betam*(kappamp-x(19))*(c*(x(4)+ x(9)+ x(14)+x(6)+x(11)
+x(16)+x(19))+x(5)+x(10)+x(15))
+betamp*(kappamp-x(19))*(x(8)+x(13)+x(18))-sigma*x(19);
xprime(20) = sigma*x(19)-alpham5*x(20);
%% Quarantine
xprime(21) =  alpha15*x(2)+alpha25*x(5)+alpha35*x(10)+alpha45*x(15);
xprime(22) =  alpha25*x(7)+alpha35*x(12)+alpha45*x(17);

% This ensures that the vector returned is a column vector
xprime = real(xprime(:));


function r0=R0(alpha12,alpha13,alpha14,alpha20,
alpha23,alpha24,alpha30,alpha32,alpha34,alpha40,...
```

```
alpha42,alpha43,alphabar2,alphabar3,
alphabar4,beta1,beta1p,alpha01in,alpha10out,alpha15,...
b1,beta2,beta2p,alpha25,beta2h,beta2hp,b2,
beta3,beta3p,alpha35,beta3h,beta3hp,...
b3,beta4,beta4p,alpha45,beta4h,beta4hp,b4,
betam,N,sigma,c,epsilon,xi,...
rho,delta,alpham5,kappa2p,kappa3p,kappa4p,kappamp)
%% Auxiliary variables

f = alpha34 + (alpha24*alphabar3)/(alpha23);

z = ((alphabar2*alpha13)+(alpha12*alpha23))/
((alphabar2*alphabar3)-(alpha32*alpha23));

d = ((alphabar2*alpha43)+(alpha42*alpha23))/
((alphabar2*alphabar3)-(alpha32*alpha23));

a = (alpha14 - (alpha24*alpha13)/
(alpha23) + f*z)/(alphabar4 + (alpha24*alpha43)/(alpha23) - f*d);



%% Unit capacity stability
kappa1=(alpha01in*N)/(alpha12+alpha13+alpha14);

kappa2=(kappa1/alpha23)*(alphabar3*(z+d*a)-alpha13-alpha43*a);

kappa3=kappa1*(z+d*a);

kappa4=kappa1*a;
```

```
%% Plots Matrices for F
F11 = [beta1*kappa1*c, beta1*kappa1, beta1p*kappa1; 0,0,0; 0,0,0];

F12 = zeros(3,5);

F13 = F12;

F14 = F12;

F15 = zeros(3,2);

%%
F21 = F12';

F22 = [beta2*kappa2*c, beta2*kappa2, beta2*kappa2*c,
0, beta2p*kappa2; 0,0,0,0,0;
beta2h*kappa2p*c, beta2h*kappa2p, beta2h*kappa2p*c,
0, beta2hp*kappa2p;0,0,0,0,0;
0,0,0,0,0];

F23 = zeros(5,5);

F24 = F23;

F25 = zeros(5,2);

F25(1,1) = beta2*kappa2*c*xi;

F25(3,1) = beta2h*kappa2p*c*xi;

%%
F31 = F12';
```

```
F32 = F23;

F33 = [beta3*kappa3*c, beta3*kappa3, beta3*kappa3*c,
0, beta3p*kappa3; 0,0,0,0,0;
beta3h*kappa3p*c, beta3h*kappa3p, beta3h*kappa3p*c,
0, beta3hp*kappa3p; 0,0,0,0,0;
0,0,0,0,0];

F34 = F23;

F35 = zeros(5,2);

F35(1,1) = beta3*kappa3*c*xi;

F35(3,1) = beta3h*kappa3p*c*xi;

%%
F41 = F12';

F42 = F23;

F43 = F23;

F44 = [beta4*kappa4*c, beta4*kappa4, beta4*kappa4*c,
0, beta4p*kappa4; 0,0,0,0,0;
beta4h*kappa4p*c, beta4h*kappa4p, beta4h*kappa4p*c,
0, beta4hp*kappa4p; 0,0,0,0,0;
0,0,0,0,0];

F45 = zeros(5,2);
```

```
F45(1,1) = beta4*kappa4*c*xi;

F45(3,1) = beta4h*kappa4p*c*xi;

%%
F51 = zeros(2,3);

F52 = [betam*kappamp*c, betam*kappamp, betam*kappamp*c, 0,
betam*kappamp;zeros(1,5)];

F53 = F52;

F54 = F52;

F55 = zeros(2,2);

F55(1,1)= betam*kappamp*c;

%% Plot Matrices for V
V11 = [(alpha10out+alpha12+alpha13+alpha14), 0, 0; 0,
(alpha12+alpha13+alpha14), 0; -1*rho*c, -1*rho, (b1+delta)];

V12 = zeros(3,5);

V13 = V12;

V14 = V12;

V15 = zeros(3,2);

%%
V21 = zeros(5,3);
```

```
V21(1,1) = -1*alpha12;

V21(2,2) = V21(1,1);

V22 = [(alpha20+alpha23+alpha24+sigma),0,0,0,0; -1*sigma,
(alpha23+alpha24+alpha25),0,0,0; 0,0,sigma,0,0; 0,0,-1*sigma,alpha25,0;
-1*rho*c,-1*rho,-1*rho*c*epsilon,0,(b2+delta)];

V23 = zeros(5,5);

V23(1,1) = -1*alpha32;

V23(2,2) = V23(1,1);

V24 = zeros(5,5);

V24(1,1) = -1*alpha42;

V24(2,2) = V24(1,1);

V25 = zeros(5,2);

V25(5,1) = -1*rho*c*xi;

%%
V31 = zeros(5,3);

V31(1,1) = -1*alpha13;

V31(2,2) = V31(1,1);
```

```
V32 = zeros(5,5);

V32(1,1) = -1*alpha23;

V32(2,2) = V32(1,1);

V33 = [(alpha30+alpha32+alpha34+sigma),0,0,0,0; -1*sigma,
(alpha32+alpha34+alpha35),0,0,0; 0,0,sigma,0,0; 0,0,-1*sigma,alpha35,0;
-1*rho*c,-1*rho,-1*rho*c*epsilon,0,(b3+delta)];

V34 = zeros(5,5);

V34(1,1) = -1*alpha43;

V34(2,2) = V34(1,1);

V35 = zeros(5,2);

V35(5,1) = -1*rho*c*xi;

%%
V41 = zeros(5,3);

V41(1,1) = -1*alpha14;

V41(2,2) = V41(1,1);

V42 = zeros(5,5);

V42(1,1) = -1*alpha24;

V42(2,2) = V42(1,1);
```

```
V43 = zeros(5,5);

V43(1,1) = -1*alpha34;

V43(2,2) = V43(1,1);

V44 = [(alpha40+alpha42+alpha43+sigma),0,0,0,0; -1*sigma,
(alpha42+alpha43+alpha45),0,0,0; 0,0,sigma,0,0; 0,0,-1*sigma,alpha45,0;
-1*rho*c,-1*rho,-1*rho*c*epsilon,0,(b4+delta)];

V45 = zeros(5,2);

V45(5,1) = -1*rho*c*xi;

%%
V51 = zeros(2,3);

V52 = zeros(2,5);

V53 = zeros(2,5);
V54 = zeros(2,5);
V55 = [sigma,0; -1*sigma,alpham5];

%%Matrix F
F = [F11,F12,F13,F14,F15; F21,F22,F23,F24,F25; F31,F32,F33,F34,F35;
F41,F42,F43,F44,F45; F51,F52,F53,F54,F55];

%%Matrix V

V = [V11,V12,V13,V14,V15; V21,V22,V23,V24,V25; V31,V32,V33,V34,V35;
V41,V42,V43,V44,V45; V51,V52,V53,V54,V55];
```

```
r0=max(abs(eig(F*inv(V))));
```

APPENDIX C

APPENDIX C

SEIR WARD MODEL TRANSFER DIAGRAM

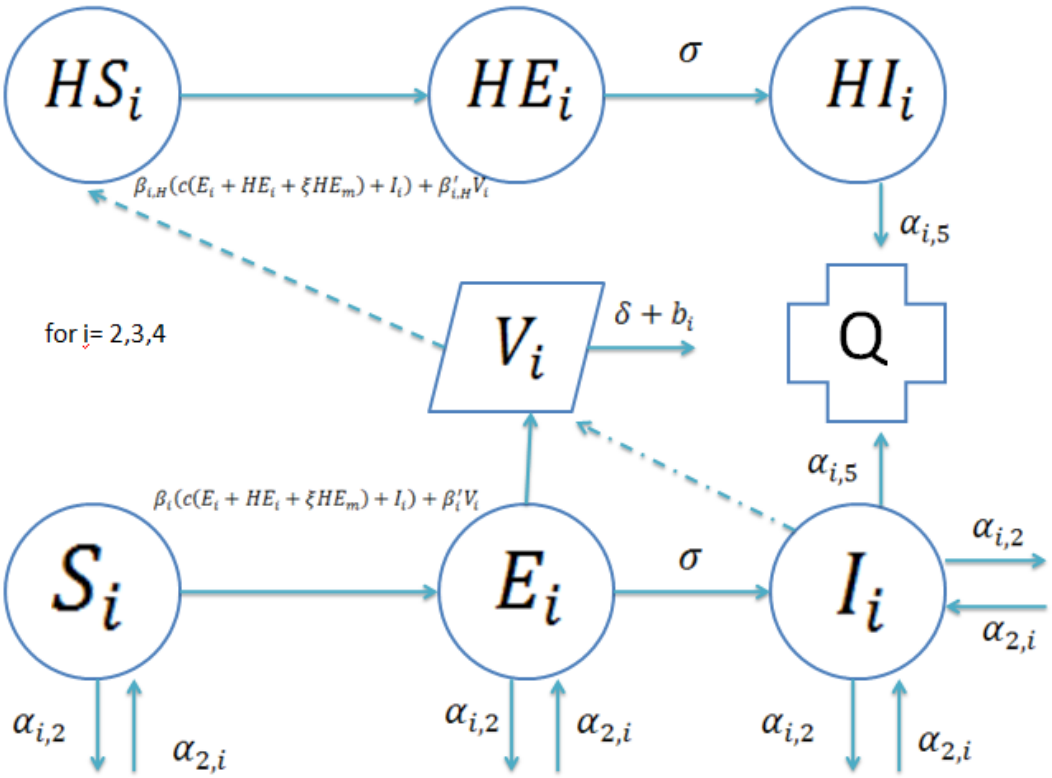

Figure 3.1: SEIR Ward Model Transfer Diagram.

BIOGRAPHICAL SKETCH

Adriana Quiroz was born in McAllen, Texas and lived 15 years in Reynosa, Tamaulipas, Mexico. She studied in Reynosa and moved to McAllen Memorial high school to continue with her studies. Afterwards, she went to South Texas College to obtained an associate degree in mathematics and pursued a master degree in The University of Texas Rio Grande Valley. She work with Dr. Yasar Tasnif and Dr. Tamer Oraby in a Faculty Research Council Grant 2015-2016 and where the title of the project was “Modeling within hospital and animal-human-human transmission of middle eastern respiratory syndrome MERS-CoV”. She received a MS in Mathematics in May 2017. You can contact her via email at: adrianaquirozg@hotmail.com