

DISEASE TRANSMISSION MSEIR MODEL WITH INDIVIDUALS TRAVELING BETWEEN PATCHES i AND $i + 1$

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ABSTRACT. In this article we want to formulate a disease transmission model, MSEIR model, for a population with individuals travelling between patches i and $i + 1$ and we derive an explicit formula for the basic reproductive number, R_0 , employing the spectral radius of the next generation operator. Also, in this article we show that a system of ordinary differential equations for this model has a unique disease-free equilibrium and it is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

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1. Introduction

Mathematical modelling is an important device to analyze and control the speed of infectious diseases increase in a society. In these models there are parameters and other variables of the problem. Mathematical models have important tools in analyzing the spread and control of infectious diseases. The model formulation process clarifies assumptions, variables, and parameters; moreover, models provide conceptual results such as thresholds, basic reproduction numbers, contact numbers, and replacement numbers.

Mathematical models and computer simulations are useful experimental tools for building and testing theories, assessing quantitative conjectures, answering specific questions, determining sensitivities to changes in parameter values, and estimating key parameters from data. Understanding the transmission characteristics of infectious diseases in communities, regions, and countries can lead to better approaches to decrease the transmission of these diseases.

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Mathematical models are used in comparing, planning, implementing, evaluating, and optimizing various detection, prevention, therapy, and control programs. Epidemiology modelling can contribute to the design and analysis of epidemiological surveys, suggest crucial data that should be collected, identify trends, make general forecasts, and estimate the uncertainty in forecasts [3, 4]. Compartments with labels such as M, S, E, I, and R are often used for the epidemiological classes as shown in figure 1. The class M contains these infants with passive immunity. After the maternal antibodies disappear from the passive immunity body, the infant moves to the susceptible class S [6].

In figure 1 we see a MSEIR epidemiological model. In this model A is new born's with passive immunity that enter M class, B is new born's without passive immunity that enter S class, αM is the transfer out of the passively immune class, ϵE is the transfer out of the exposed class, γI is the recovery rate from the infectious class, d is the natural death rate and a is the rate of death due to the disease, r is the average number of contacts per unit of time per individual, β is the probability of transmitting the infection per contact. Therefore, $1/\epsilon$ is the mean latent period and $1/\gamma$ is the mean infectious period [6].

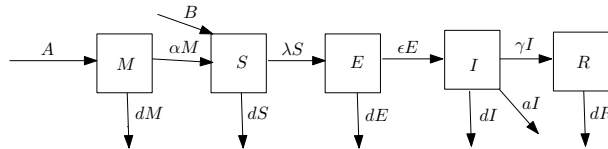


FIGURE 1.

The population dynamics for this model is given by the following system of ordinary differential equations,

$$\begin{aligned} \frac{dM}{dt} &= A - (\alpha + d)M, \\ \frac{dS}{dt} &= B + \alpha M - (d + \lambda)S, \\ \frac{dE}{dt} &= \lambda S - (\epsilon + d)E, \\ \frac{dI}{dt} &= \epsilon E - (d + a + \gamma)I, \\ \frac{dR}{dt} &= \gamma I - dR, \end{aligned}$$

with $\lambda(t) = r\beta \frac{I(t)}{N(t)}$. Where $N(t) = M(t) + S(t) + E(t) + I(t) + R(t)$ is the total population number at time t . The basic reproductive for the MSEIR model is [6],

$$R_0 = \frac{r\beta\epsilon}{(d + a + \gamma)(\epsilon + d)} \quad (1)$$

2. MSEIR Model with n Patches

In figure 2 we consider an MSEIR epidemic model for transmission of a communicable disease with population travel between n patches. The number of immunity, susceptible, exposed, infectious and recovered individuals in patch i at time t , is denoted by $M_i(t)$, $S_i(t)$, $E_i(t)$, $I_i(t)$ and $R_i(t)$, respectively. We assume there is population travel between patches i and $i + 1$ with different travel rates for each compartment.

The population dynamics for this *MSEIR* model is given by the following system of $5n$ ordinary differential equations with $i = 1, 2, \dots, n$.

$$\frac{dM_1}{dt} = A_1 + m_{2,1}M_2 - (m_{1,2} + \alpha_1 + d_1)M_1, \tag{2}$$

$$\begin{aligned} \frac{dM_i}{dt} = & A_i + m_{i+1,i}M_{i+1} + m_{i-1,i}M_{i-1} - (m_{i,i+1} + \\ & m_{i,i-1} + \alpha_i + d_i)M_i; 2 \leq i \leq n - 1, \end{aligned} \tag{3}$$

$$\frac{dM_n}{dt} = A_n + m_{n-1,n}M_{n-1} - (m_{n,n-1} + \alpha_n + d_n)M_n, \tag{4}$$

$$\frac{dS_1}{dt} = B_1 + \alpha_1M_1 + p_{2,1}S_2 - (p_{1,2} + d_1 + \lambda_1)S_1, \tag{5}$$

$$\begin{aligned} \frac{dS_i}{dt} = & B_i + \alpha_iM_i + p_{i-1,i}S_{i-1} + p_{i+1,i}S_{i+1} - (p_{i,i+1} + \\ & p_{i,i-1} + d_i + \lambda_i)S_i; 2 \leq i \leq n - 1, \end{aligned} \tag{6}$$

$$\frac{dS_n}{dt} = B_n + \alpha_nM_n + p_{n-1,n}S_{n-1} - (p_{n,n-1} + d_n + \lambda_n)S_n, \tag{7}$$

$$\frac{dE_1}{dt} = \lambda_1S_1 + e_{2,1}E_2 - (e_{1,2} + \epsilon_1 + d_1)E_1, \tag{8}$$

$$\begin{aligned} \frac{dE_i}{dt} = & \lambda_iS_i + e_{i+1,i}E_{i+1} + e_{i-1,i}E_{i-1} - (e_{i,i-1} + \\ & e_{i,i+1} + \epsilon_i + d_i)E_i; 2 \leq i \leq n - 1, \end{aligned} \tag{9}$$

$$\frac{dE_n}{dt} = \lambda_nS_n + e_{n-1,n}E_{n-1} - (e_{n,n-1} + \epsilon_n + d_n)E_n, \tag{10}$$

$$\frac{dI_1}{dt} = \epsilon_1E_1 + q_{2,1}I_2 - (q_{1,2} + a_1 + d_1 + \gamma_1)I_1, \tag{11}$$

$$\begin{aligned} \frac{dI_i}{dt} = & \epsilon_iE_i + q_{i+1,i}I_{i+1} + q_{i-1,i}I_{i-1} - (q_{i,i-1} + q_{i,i+1} \\ & a_i + d_i + \gamma_i)I_i; 2 \leq i \leq n - 1, \end{aligned} \tag{12}$$

$$\frac{dI_n}{dt} = \epsilon_nE_n + q_{n-1,n}I_{n-1} - (q_{n,n-1} + a_n + d_n + \gamma_n)I_n, \tag{13}$$

$$\frac{dR_1}{dt} = \gamma_1I_1 + r_{2,1}R_2 - (r_{1,2} + d_1)R_1, \tag{14}$$

$$\frac{dR_i}{dt} = \gamma_i I_i + r_{i+1,i} R_{i+1} + r_{i-1,i} R_{i-1} - (r_{i,i+1} + r_{i,i-1} + d_i) R_i; \quad 2 \leq i \leq n-1, \tag{15}$$

$$\frac{dR_n}{dt} = \gamma_n I_n + r_{n-1,n} R_{n-1} - (r_{n,n-1} + d_n) R_n, \tag{16}$$

with

$$\lambda_i(t) = r\beta_i \frac{I_i(t)}{N_i(t)}.$$

Here

$$N_i(t) = M_i(t) + S_i(t) + E_i(t) + I_i(t) + R_i(t)$$

is the total population number in patch i at time t , A_i is the number of individuals born with passive immunity per unit time, B_i is the number of individuals born without passive immunity per unit time, d_i is the natural death rate, a_i is the rate of death due to the disease in patch i , α_i is the rate of loss of passive immunity, ϵ_i is the rate that exposed individuals become infectious and γ_i is the recovery rate. Thus $1/d_i$ is the average lifetime and $1/\epsilon_i$ is the average exposed period. The rate at immunity, susceptible, exposed, infectious and recovered individuals travel from patch i to patch $i+1$ is denoted by $m_{i,i+1}$, $p_{i,i+1}$, $e_{i,i+1}$, $q_{i,i+1}$ and $r_{i,i+1}$, respectively and from patch $i+1$ to i is denoted by $m_{i+1,i}$, $p_{i+1,i}$, $e_{i+1,i}$, $q_{i+1,i}$ and $r_{i+1,i}$, respectively. It is assumed that all parameters are positive constants except that a_i can be zero. The total population size in all patches is $N(t) = \sum_{i=1}^n N_i(t)$.

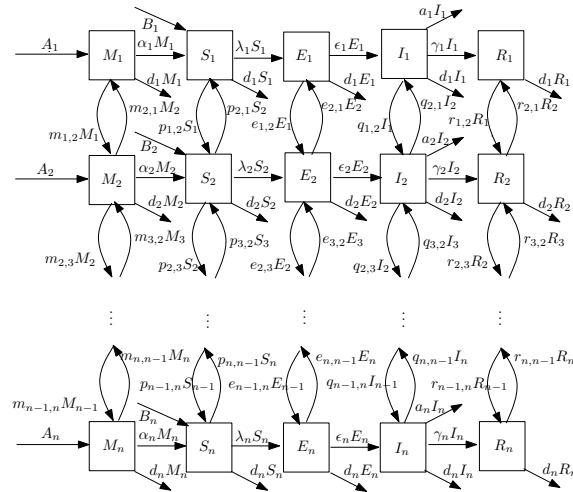


FIGURE 2.

Theorem 1. *System (2)-(16) has a unique disease-free equilibrium.*

Proof. In disease-free equilibrium of system (2)-(16) all infected variables set zero, namely $E_i = I_i = 0$ for $i = 1, 2, \dots, n$. Setting $E_i = I_i = 0$ for $i = 1, 2, \dots, n$ at $\frac{dR_i}{dt} = 0$, for $i = 1, 2, \dots, n$ gives,

$$-KR = 0,$$

with

$$K = \begin{bmatrix} r_{1,2} + d_1 & -r_{2,1} & 0 & 0 & \dots & 0 \\ -r_{1,2} & f_2 & -r_{3,2} & 0 & \dots & 0 \\ 0 & -r_{2,3} & f_3 & -r_{4,3} & \dots & 0 \\ 0 & \ddots & \ddots & \ddots & \dots & 0 \\ \vdots & \vdots & -r_{n-2,n-1} & f_{n-1} & -r_{n,n-1} & 0 \\ 0 & 0 & 0 & \dots & -r_{n-1,n} & r_{n,n-1} + d_n \end{bmatrix}$$

and

$$R = [R_1, R_2, \dots, R_n]^T$$

where $f_i = r_{i,i+1} + r_{i,i-1} + d_i$; $2 \leq i \leq n - 1$. Since matrix K is irreducible [1] and so, K has a positive inverse [1], thus it can be seen that $R_i = 0$ for $i = 1, 2, \dots, n$. A disease-free equilibrium for model (2)-(16) is thus given by,

$$M_i = M_i^0, S_i = S_i^0, E_i = I_i = R_i = 0 \text{ for } i = 1, 2, \dots, n.$$

At equilibrium $\frac{dM_i}{dt} = 0, \frac{dS_i}{dt} = 0$ and from (2)-(4), (5)-(7),

$$M^0 = [M_1^0, M_2^0, \dots, M_n^0]^T \text{ and } S^0 = [S_1^0, S_2^0, \dots, S_n^0]^T,$$

satisfies the linear systems $C_1 M^0 = A$ with $A = [A_1, A_2, \dots, A_n]^T$ and $C_2 S^0 = B$ with $B = [B_1 + \alpha_1 M_1, B_2 + \alpha_2 M_2, \dots, B_n + \alpha_n M_n]^T$ and

$$C_1 = \begin{bmatrix} m_{1,2} + \alpha_1 + d_1 & -m_{2,1} & 0 & 0 & \dots & 0 \\ -m_{1,2} & b_2 & -m_{3,2} & 0 & \dots & 0 \\ 0 & -m_{2,3} & b_3 & -m_{4,3} & \dots & 0 \\ 0 & \ddots & \ddots & \ddots & \dots & 0 \\ \vdots & \vdots & -m_{n-2,n-1} & b_{n-1} & -m_{n,n-1} & 0 \\ 0 & 0 & 0 & \dots & -m_{n-1,n} & m_{n,n-1} + d_n \end{bmatrix}$$

and

$$C_2 = \begin{bmatrix} p_{1,2} + d_1 & -m_{2,1} & 0 & 0 & \dots & 0 \\ -p_{1,2} & \theta_2 & -p_{3,2} & 0 & \dots & 0 \\ 0 & -p_{2,3} & \theta_3 & -p_{4,3} & \dots & 0 \\ 0 & \ddots & \ddots & \ddots & \dots & 0 \\ \vdots & \vdots & -p_{n-2,n-1} & \theta_{n-1} & -p_{n,n-1} & 0 \\ 0 & 0 & 0 & \dots & -p_{n-1,n} & p_{n,n-1} + d_n \end{bmatrix}$$

with $b_i = m_{i,i+1} + m_{i,i-1} + d_i$; $2 \leq i \leq n - 1$ and $\theta_i = p_{i,i+1} + p_{i,i-1} + d_i$; $2 \leq i \leq n - 1$. Since matrix C_1 and C_2 are irreducible [1] and so, C_1 and C_2 have positive inverses [1]. Thus there are unique solutions, given by $M^0 = C_1^{-1}A$ and $S^0 = C_2^{-1}B$. This gives the unique disease-free equilibrium.

Theorem 2. Let R_0 be the basic reproductive number for system (2)-(16), then the disease-free equilibrium of system (2)-(16) is locally asymptotically stable if $R_0 < 1$ and unstable if $R_0 > 1$.

Proof. We order variables as,

$$E_1, \dots, E_n, I_1, \dots, I_n, M_1, \dots, M_n, S_1, \dots, S_n, R_1, \dots, R_n,$$

and we take the vector of infected variables as, $v = (E_1, \dots, E_n, I_1, \dots, I_n)$. The disease-free equilibrium, E_0 , is locally asymptotically stable if all eigenvalues of the Jacobian matrix of system (2)-(16) at E_0 , namely,

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

have negative real parts, and unstable if J has at least one eigenvalue with positive real part. The eigenvalue of J are the eigenvalues of $F - V$ and those of $J_{2,2}$. To determine F and V we consider W and U , where,

$$W = [r\beta_1 \frac{S_1 I_1}{N_1}, r\beta_2 \frac{S_2 I_2}{N_2}, \dots, r\beta_n \frac{S_n I_n}{N_n}, 0, \dots, 0]^T$$

and

$$U = \begin{bmatrix} -e_{2,1}E_2 + (e_{1,2} + \epsilon_1 + d_1)E_1 \\ -e_{3,2}E_3 + K_2E_2 - e_{1,2}E_1 \\ \vdots \\ -e_{n,n-1}E_n + K_{n-1}E_{n-1} - e_{n-2,n-1}E_{n-2} \\ (e_{n,n-1} + \epsilon_n + d_n)E_n - e_{n-1,n}E_{n-1} \\ -\epsilon_1E_1 - q_{2,1}I_2 + (q_{1,2} + a_1 + d_1 + \gamma_1)I_1 \\ -\epsilon_2E_2 - q_{3,2}I_3 + Q_2I_2 - q_{1,2}I_1 \\ \vdots \\ -\epsilon_{n-1}E_{n-1} - q_{n,n-1}I_n + Q_{n-1}I_{n-1} - q_{n-2,n-1}I_{n-2} \\ -\epsilon_nE_n - q_{n-1,n}I_{n-1} + (q_{n,n-1} + a_n + d_n + \gamma_n)I_n \end{bmatrix} \tag{17}$$

where $K_i = e_{i,i-1} + e_{i,i+1} + \epsilon_i + d_i$ ($2 \leq i \leq n - 1$), and $Q_i = q_{i,i-1} + q_{i,i+1} + a_i + d_i + \gamma_i$ ($2 \leq i \leq n - 1$). In the disease-free equilibrium linearizing $W - U$, gives the $F - V$ where $F = [\frac{\partial W_i}{\partial v_i}]$ and $V = [\frac{\partial U_i}{\partial v_i}]$. Therefore, matrices F and V are

as follows,

$$F = \begin{bmatrix} 0 & F_{1,2} \\ 0 & 0 \end{bmatrix} \text{ and } V = \begin{bmatrix} V_{1,1} & 0 \\ V_{2,1} & V_{2,2} \end{bmatrix}$$

where $F_{1,2} = \text{diag}(r\beta_1, r\beta_2, \dots, r\beta_n)$,

$$V_{1,1} = \begin{bmatrix} k_1 & -e_{2,1} & 0 & 0 & \dots & 0 \\ -e_{1,2} & k_2 & -e_{3,2} & 0 & \dots & 0 \\ 0 & -e_{2,3} & k_3 & -e_{4,3} & \dots & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & 0 & 0 & -e_{n-2,n-1} & k_{n-1} & -e_{n,n-1} \\ 0 & 0 & 0 & 0 & -e_{n-1,n} & k_n \end{bmatrix}, \tag{18}$$

$$V_{2,2} = \begin{bmatrix} l_1 & -q_{2,1} & 0 & 0 & \dots & 0 \\ -q_{1,2} & l_2 & -q_{3,2} & 0 & \dots & 0 \\ 0 & -q_{2,3} & l_3 & -q_{4,3} & \dots & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & 0 & 0 & -q_{n-2,n-1} & l_{n-1} & -q_{n,n-1} \\ 0 & 0 & 0 & 0 & -q_{n-1,n} & l_n \end{bmatrix} \tag{19}$$

and

$$V_{2,1} = \text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n)$$

with

$$\begin{aligned} k_1 &= e_{1,2} + \epsilon_1 + d_1, \\ k_i &= e_{i,i+1} + e_{i,i-1} + \epsilon_i + d_i \quad ; \quad 2 \leq i \leq n-1, \\ k_n &= e_{n,n-1} + \epsilon_n + d_n, \\ l_1 &= q_{1,2} + a_1 + d_1 + \gamma_1, \\ l_i &= q_{i,i+1} + q_{i,i-1} + a_i + d_i + \gamma_i \quad ; \quad 2 \leq i \leq n-1, \\ l_n &= q_{n,n-1} + a_n + d_n + \gamma_n. \end{aligned}$$

Matrices $V_{1,1}$ and $V_{2,2}$ are non-singular M-matrices [1], therefore, have positive inverses. In matrix

$$J_{2,2} = \begin{bmatrix} -C_1 & L \\ 0 & -C_2 \end{bmatrix} \tag{20}$$

matrices C_1 and C_2 are non-singular M-matrices [1]. Thus $J_{2,2}$ has all eigenvalues with negative real parts. Consequently the local stability of the disease-free equilibrium depends only on eigenvalues of $F - V$. All eigenvalues of $F - V$ have negative real parts if only if $s(F - V) < 0$ if only if $\rho(FV^{-1}) < 1$ [11]. Since V has a positive inverse, then FV^{-1} is a non-negative matrix. Now, we have,

$$FV^{-1} = \begin{bmatrix} 0 & F_{1,2} \\ 0 & 0 \end{bmatrix} \begin{bmatrix} V_{1,1}^{-1} & 0 \\ Y & V_{2,2}^{-1} \end{bmatrix} = \begin{bmatrix} F_{1,2}Y & F_{1,2}V_{2,2}^{-1} \\ 0 & 0 \end{bmatrix} \tag{21}$$

where $Y = V_{2,2}^{-1} \text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n) V_{1,1}^{-1}$. For find the basic reproductive number we use the formula in [11], it follows that,

$$R_0 = \rho(FV^{-1}) = \rho(\text{diag}(r\beta_1, r\beta_2, \dots, r\beta_n) V_{2,2}^{-1} \text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n) V_{1,1}^{-1}). \tag{22}$$

If $R_0 < 1$ then $s(F - V) < 0$, therefore all the eigenvalues lie in the left half plane, so system (2)-(16) is locally asymptotically stable. Similarly if $R_0 > 1$ then $s(F - V) > 0$, thus at least one eigenvalue lies in the right half plane, so system (2)-(16) is unstable.

Theorem 3. *If we do not have any travel between patches, then the basic reproductive number in patch i given by,*

$$R_0^{(i)} = \frac{r\beta_i\epsilon_i}{(\epsilon_i + d_i)(a_i + d_i + \gamma_i)}. \quad (23)$$

Proof. If we dont have travel between patches, then we have,

$$\frac{dM_i}{dt} = A_i + (\alpha_i + d_i)M_i, \quad (24)$$

$$\frac{dS_i}{dt} = B_i + \alpha_i M_i - d_i S_i + \lambda_i S_i, \quad (25)$$

$$\frac{dE_i}{dt} = \lambda_i S_i - (\epsilon_i + d_i)E_i; 1 \leq i \leq n \quad (26)$$

$$\frac{dI_i}{dt} = \epsilon_i E_i - (a_i + d_i + \gamma_i)I_i, \quad (27)$$

$$\frac{dR_i}{dt} = \gamma_i I_i - d_i R_i. \quad (28)$$

Linearizing system (24)-(28) around disease-free equilibrium gives the Jacobian matrix J^0 as,

$$J^0 = \begin{bmatrix} J_{1,1}^0 & J_{1,2}^0 \\ 0 & F_i - V_i \end{bmatrix} \quad (29)$$

where

$$J_{1,1}^0 = \begin{bmatrix} \alpha_i + d_i & 0 \\ \alpha_i & -d_i \end{bmatrix}, J_{1,2}^0 = \begin{bmatrix} 0 & 0 \\ 0 & -r\beta_i \end{bmatrix}, \quad (30)$$

$$F_i = \begin{bmatrix} 0 & r\beta_i \\ \epsilon_i & 0 \end{bmatrix}, V_i = \begin{bmatrix} \epsilon_i + d_i & 0 \\ 0 & a_i + d_i + \gamma_i \end{bmatrix}. \quad (31)$$

The stability of the Jacobian matrix J^0 at the disease-free equilibrium is completely by the stability of $F_i - V_i$. Since, F_i is a non-negative matrix and V_i is a non-singular M-matrix [1], therefore the reproductive number, $R_0^{(i)}$, is equal to the spectral radius of the next generation operator $F_i V_i^{-1}$ [11],

$$R_0^{(i)} = \rho(F_i V_i^{-1}) = \frac{r\beta_i\epsilon_i}{(\epsilon_i + d_i)(a_i + d_i + \gamma_i)}; 1 \leq i \leq n. \quad (32)$$

Theorem 4. *Suppose in Theorem 3 we have $\Lambda = \Lambda_i = a_i + d_i + \gamma_i$, $\epsilon_i = \epsilon$ and $d_i = d$ for each $i = 1, 2, \dots, n$, also. Then*

$$\min_{i=1, \dots, n} R_0^{(i)} \leq R_0 \leq \max_{i=1, \dots, n} R_0^{(i)}. \tag{33}$$

Proof. Without loss of generality take $\beta_1 \leq \beta_2 \leq \dots \leq \beta_n$, thus we have,

$$\min_{i=1, \dots, n} R_0^{(i)} = R_0^{(1)} = \frac{r\beta_1\epsilon}{(\epsilon + d)\Lambda} \leq \dots \leq \frac{r\beta_n\epsilon}{(\epsilon + d)\Lambda} = R_0^{(n)} = \max_{i=1, \dots, n} R_0^{(i)}. \tag{34}$$

Let $V_{1,1}^{-1} = X = [x_{ij}]$ and $V_{2,2}^{-1} = D = [d_{ij}]$. From (22) we have,

$$R_0 = \rho(\text{diag}(r\beta_1, r\beta_2, \dots, r\beta_n)D\text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n)X). \tag{35}$$

If we take $L = \text{diag}(r\beta_1, r\beta_2, \dots, r\beta_n)D\text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n)X$, then we have,

$$L = \begin{bmatrix} r\beta_1\epsilon(d_{11}x_{11} + \dots + d_{1n}x_{1n}) & \dots & r\beta_1\epsilon(d_{11}x_{1n} + \dots + d_{1n}x_{nn}) \\ \vdots & \vdots & \vdots \\ r\beta_n\epsilon(d_{n1}x_{11} + \dots + d_{nn}x_{n1}) & \dots & r\beta_n\epsilon(d_{n1}x_{1n} + \dots + d_{nn}x_{nn}) \end{bmatrix}. \tag{36}$$

Let the sum of the entries in the first column of L denoted by $[\Delta L]_1$ with $\Delta = (1, 1, \dots, 1)^T$. Then we have,

$$[\Delta L]_1 = r\beta_1\epsilon(d_{11}x_{11} + \dots + d_{1n}x_{1n}) + \tag{37}$$

$$\vdots \tag{38}$$

$$r\beta_n\epsilon(d_{n1}x_{11} + \dots + d_{nn}x_{n1}) \tag{39}$$

$$\leq r\beta_n\epsilon \sum_{i=1}^n x_{i1}(d_{1i} + \dots + d_{ni}) = \frac{r\beta_n\epsilon}{\Lambda} \sum_{i=1}^n x_{i1}. \tag{40}$$

The last equality follows from the fact that $\Delta V_{2,2} = \Lambda\Delta$, thus $\Delta D = (\frac{1}{\Lambda})\Delta$. The column sum of $V_{1,1}$ is $\epsilon + d$, thus $\Delta X = (\frac{1}{\epsilon+d})\Delta$. Therefore we have,

$$[\Delta L]_1 \leq \frac{r\beta_n\epsilon}{\Lambda(\epsilon + d)} = R_0^{(n)} = \max_{i=1, \dots, n} R_0^{(i)}. \tag{41}$$

Similarly we have,

$$\min_{i=1, \dots, n} R_0^{(i)} = R_0^{(1)} = \frac{r\beta_1\epsilon}{\Lambda(\epsilon + d)} \leq [\Delta L]_1. \tag{42}$$

For every column of L these inequalities are true. The spectral radius of a nonnegative matrix lies between its minimum and maximum column sums [1], thus we have,

$$\min_{i=1, \dots, n} R_0^{(i)} \leq R_0 = \rho(\text{diag}(r\beta_1, r\beta_2, \dots, r\beta_n)D\text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n)X) \leq R_0^{(n)} = \max_{i=1, \dots, n} R_0^{(i)}. \tag{43}$$

Corollary 1. *If in Theorem 4 we take $\beta_i = \beta$, then we have,*

$$R_0 = R_0^{(i)}; 1 \leq i \leq n. \tag{44}$$

Theorem 5. Suppose $e_{i,i-1} = q_{i,i-1} = 0$ for each $i = 2, \dots, n$. Then the basic reproductive number, R_0 , for system (2)-(16) given by

$$R_0 = \max_{i=1, \dots, n} \left\{ \frac{r\beta_n \epsilon_n}{(\epsilon_n + d_n)(a_n + d_n + \gamma_n)}, \frac{r\beta_i \epsilon_i}{(e_{i,i+1} + \epsilon_i + d_i)(q_{i,i+1} + a_i + d_i + \gamma_i)} \right\}. \tag{45}$$

Proof. First we need to find $V_{1,1}^{-1}$ and $V_{2,2}^{-1}$,

$$V_{1,1}^{-1} = \begin{bmatrix} \frac{1}{k_1} & 0 & 0 & 0 & \dots & 0 \\ y_{2,1} & \frac{1}{k_2} & 0 & 0 & \dots & 0 \\ y_{3,1} & y_{3,2} & \frac{1}{k_3} & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & 0 \\ y_{n-1,1} & y_{n-1,2} & y_{n-1,3} & y_{n-1,4} & \frac{1}{k_{n-1}} & 0 \\ y_{n,1} & y_{n,2} & y_{n,3} & \dots & y_{n,n-1} & \frac{1}{k_n} \end{bmatrix} \tag{46}$$

and

$$V_{2,2}^{-1} = \begin{bmatrix} \frac{1}{l_1} & 0 & 0 & 0 & \dots & 0 \\ z_{2,1} & \frac{1}{l_2} & 0 & 0 & \dots & 0 \\ z_{3,1} & z_{3,2} & \frac{1}{l_3} & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & 0 \\ z_{n-1,1} & z_{n-1,2} & z_{n-1,3} & z_{n-1,4} & \frac{1}{l_{n-1}} & 0 \\ z_{n,1} & z_{n,2} & z_{n,3} & \dots & z_{n,n-1} & \frac{1}{l_n} \end{bmatrix} \tag{47}$$

with

$$y_{i,j} = -\frac{\prod_{k=j}^{i-1} e_{k,k+1}}{\prod_{k=j}^i k_k} \text{ and } z_{i,j} = -\frac{\prod_{k=j}^{i-1} \epsilon_{k,k+1}}{\prod_{k=j}^i l_k} \text{ for } 2 \leq i \leq n \text{ and } 1 \leq j \leq i-1.$$

Now, for find reproductive number we can use formula (22),

$$R_0 = \rho(FV^{-1}) = \rho(\text{diag}(r\beta_1, r\beta_2, \dots, r\beta_n)V_{2,2}^{-1}\text{diag}(\epsilon_1, \epsilon_2, \dots, \epsilon_n)V_{1,1}^{-1}) = \rho(H) \tag{48}$$

with

$$H = \begin{bmatrix} \frac{r\beta_1 \epsilon_1}{l_1 k_1} & 0 & 0 & 0 & \dots & 0 \\ \cdot & \frac{r\beta_2 \epsilon_2}{l_2 k_2} & 0 & 0 & \dots & 0 \\ \cdot & \cdot & \frac{r\beta_3 \epsilon_3}{l_3 k_3} & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \ddots & \ddots & 0 \\ \cdot & \cdot & \dots & \cdot & \frac{r\beta_{n-1} \epsilon_{n-1}}{l_{n-1} k_{n-1}} & 0 \\ \cdot & \cdot & \cdot & \dots & \cdot & \frac{r\beta_n \epsilon_n}{l_n k_n} \end{bmatrix}. \tag{49}$$

Therefore, we have,

$$R_0 = \max_{i=1, \dots, n} \left\{ \frac{r\beta_n \epsilon_n}{(\epsilon_n + d_n)(a_n + d_n + \gamma_n)}, \frac{r\beta_i \epsilon_i}{(e_{i,i+1} + \epsilon_i + d_i)(q_{i,i+1} + a_i + d_i + \gamma_i)} \right\}. \tag{50}$$

Corollary 2. *If we Suppose $e_{i,i-1} = q_{i,i-1} = 0$ for each $i = 2, \dots, n$. Then the modified reproductive number, $\tilde{R}_0^{(i)}$, for system (2)-(16) in patch i given by,*

$$\tilde{R}_0^{(i)} = \frac{r\beta_i\epsilon_i}{(e_{i,i+1} + \epsilon_i + d_i)(q_{i,i+1} + a_i + d_i + \gamma_i)} \quad (i = 1, 2, \dots, n - 1), \quad (51)$$

$$\tilde{R}_0^{(n)} = R_0^{(n)} = \frac{r\beta_n\epsilon_n}{(\epsilon_n + d_n)(a_n + d_n + \gamma_n)}. \quad (52)$$

Corollary 3. *Let in system (2)-(16), $e_{i,i+1} = e_{i+,i} = q_{i,i+1} = q_{i+,i} = 0$ for $i = 1, 2, \dots, n$ then $V_{1,1} = \text{diag}(\epsilon_1 + d_1, \dots, \epsilon_n + d_n)$ and $V_{2,2} = \text{diag}(k_1, \dots, k_n)$. In this case, the matrix*

$$F_{1,2}V_{2,2}^{-1}\text{diag}(\epsilon_1, \dots, \epsilon_n)V_{1,1}^{-1}$$

is diagonal, therefore we have,

$$R_0 = \max_{i=1, \dots, n} R_0^{(i)} = \max_{i=1, \dots, n} \frac{r\beta_i\epsilon_i}{k_i(\epsilon_i + d_i)}. \quad (53)$$

Example 1. In Figure 3 to explain formula (22), we use the following model parameters,

$A_1 = 300, A_2 = 250, A_3 = 150, A_4 = 200, B_1 = 500, B_2 = 400, B_3 = 200, B_4 = 300, M_1(0) = 800, M_2(0) = 700, M_3(0) = 600, M_4(0) = 500, S_1(0) = 2400, S_2(0) = 1200, S_3(0) = 1500, S_4(0) = 2000, I_1(0) = 50, I_2(0) = 40, I_3(0) = 30, I_4(0) = 20, E_1(0) = E_2(0) = E_3(0) = E_4(0) = R_1(0) = R_2(0) = R_3(0) = R_4(0) = 0, r = 100, d_1 = 0.005, d_2 = 0.004, d_3 = 0.003, d_4 = 0.002, \alpha_1 = 0.04, \alpha_2 = 0.05, \alpha_3 = 0.02, \alpha_4 = 0.01, \epsilon_1 = 0.08, \epsilon_2 = 0.06, \epsilon_3 = 0.04, \epsilon_4 = 0.02, \gamma_1 = 0.08, \gamma_2 = 0.01, \gamma_3 = 0.06, \gamma_4 = 0.05, a_1 = 0.6, a_2 = 0.8, a_3 = 0.7, a_4 = 0.5, m_{1,2} = 0.03, m_{2,1} = 0.008, m_{2,3} = 0.02, m_{3,2} = 0.006, m_{3,4} = 0.01, m_{4,3} = 0.03, p_{1,2} = 0.02, p_{2,1} = 0.005, p_{2,3} = 0.01, p_{3,2} = 0.01, p_{3,4} = 0.03, p_{4,3} = 0.005, e_{1,2} = 0.01, e_{2,1} = 0.001, e_{2,3} = 0.02, e_{3,2} = 0.01, e_{3,4} = 0.03, e_{4,3} = 0.005, q_{1,2} = 0.04, q_{2,1} = 0.03, q_{2,3} = 0.02, q_{3,2} = 0.02, q_{3,4} = 0.04, q_{4,3} = 0.01, r_{1,2} = 0.04, r_{2,1} = 0.02, r_{2,3} = 0.02, r_{3,2} = 0.01, r_{3,4} = 0.03, r_{4,3} = 0.07.$

and

$\beta_1 = 0.016, \beta_2 = 0.02, \beta_3 = 0.012, \beta_4 = 0.02$, for $R_0 > 1$ and $\beta_1 = 0.007, \beta_2 = 0.008, \beta_3 = 0.009, \beta_4 = 0.005$, for $R_0 < 1$.

Example 2. If in Example 1 we take,

$$e_{2,3} = e_{3,2} = e_{3,4} = e_{4,3} = q_{2,3} = q_{3,2} = q_{3,4} = q_{4,3} = 0,$$

then,

$$V_{1,1} = \begin{bmatrix} V_{1,1}^{1,1} & 0 \\ 0 & V_{1,1}^{2,2} \end{bmatrix} \text{ and } V_{2,2} = \begin{bmatrix} V_{2,2}^{1,1} & 0 \\ 0 & V_{2,2}^{1,1} \end{bmatrix} \quad (54)$$

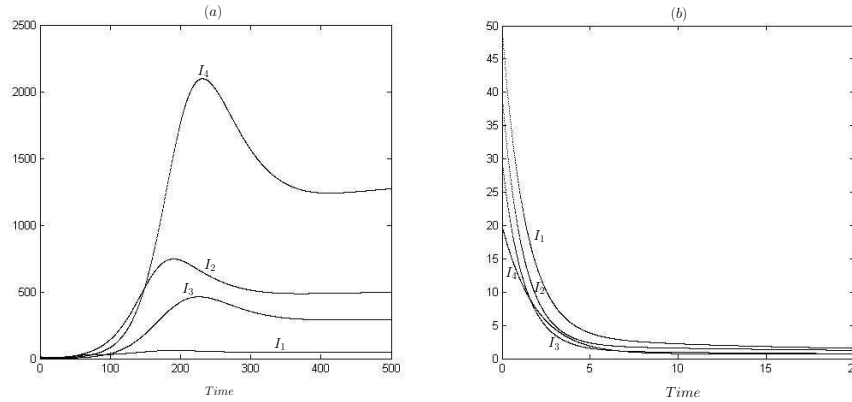


FIGURE 3. (a): $R_0 = \max 2.9594, 1.9604, 1.6291, 0.6609 = 2.9594 > 1$ and (b): $R_0 = \max 0.9154, 0.8196, 0.6419, 0.4256 = 0.9154 < 1$.

with

$$V_{1,1}^{1,1} = \begin{bmatrix} k_1 & -e_{2,1} \\ -e_{1,2} & k_2 \end{bmatrix}, V_{1,1}^{2,2} = \begin{bmatrix} k_3 & 0 \\ 0 & k_4 \end{bmatrix}, \tag{55}$$

$$V_{2,2}^{1,1} = \begin{bmatrix} l_1 & -q_{2,1} \\ -q_{1,2} & l_2 \end{bmatrix}, V_{2,2}^{2,2} = \begin{bmatrix} l_3 & 0 \\ 0 & l_4 \end{bmatrix}. \tag{56}$$

Therefore,

$$R_0 = \rho(\text{diag}(r\beta_1, r\beta_2, r\beta_3, r\beta_4)V_{2,2}^{-1}\text{diag}(\epsilon_1, \epsilon_2, \epsilon_3, \epsilon_4)V_{1,1}^{-1}) \tag{57}$$

$$= \rho(\text{diag}(r\beta_1, r\beta_2)(V_{2,2}^{1,1})^{-1}\text{diag}(\epsilon_1, \epsilon_2)(V_{1,1}^{1,1})^{-1}) \tag{58}$$

$$\rho(\text{diag}(r\beta_3, r\beta_4)(V_{2,2}^{2,2})^{-1}\text{diag}(\epsilon_3, \epsilon_4)(V_{1,1}^{2,2})^{-1}) \tag{59}$$

$$= \max\{\tilde{R}_0^{(1,2)}, R_0^{(3,4)}\} = \max\{\tilde{R}_0^{(1,2)}, R_0^{(3)}, R_0^{(4)}\}, \tag{60}$$

where,

$$R_0^{(3)} = \frac{r\beta_3\epsilon_3}{k_3l_3}, R_0^{(4)} = \frac{r\beta_4\epsilon_4}{k_4l_4} \text{ and } \tilde{R}_0^{(1,2)} = \rho(Q) \tag{61}$$

with

$$Q = \begin{bmatrix} \frac{(r\beta_1k_2)(\epsilon_1l_2)+(r\beta_1e_{2,1})(\epsilon_2q_{1,2})}{(k_1k_2-e_{1,2}e_{2,1})(l_1l_2-q_{1,2}q_{2,1})} & \frac{(r\beta_1k_2)(\epsilon_1q_{2,1})+(r\beta_1e_{2,1})(\epsilon_2l_1)}{(k_1k_2-e_{1,2}e_{2,1})(l_1l_2-q_{1,2}q_{2,1})} \\ \frac{(r\beta_2e_{1,2})(\epsilon_1l_2)+(r\beta_2k_1)(\epsilon_2q_{2,1})}{(k_1k_2-e_{1,2}e_{2,1})(l_1l_2-q_{1,2}q_{2,1})} & \frac{(r\beta_2e_{1,2})(\epsilon_1q_{2,1})+(r\beta_2k_1)(\epsilon_2l_1)}{(k_1k_2-e_{1,2}e_{2,1})(l_1l_2-q_{1,2}q_{2,1})} \end{bmatrix}. \tag{62}$$

Now, we use

$\beta_1 = 0.017, \beta_2 = 0.018, \beta_3 = 0.019, \beta_4 = 0.005$, for $R_0 > 1, \tilde{R}_0^{(1,2)} > 1, R_0^{(3)} > 1, R_0^{(4)} < 1$ and $\beta_1 = 0.007, \beta_2 = 0.008, \beta_3 = 0.007, \beta_4 = 0.015$, for $R_0 > 1, \tilde{R}_0^{(1,2)} < 1, R_0^{(3)} < 1, R_0^{(4)} > 1$ (Figure 4).

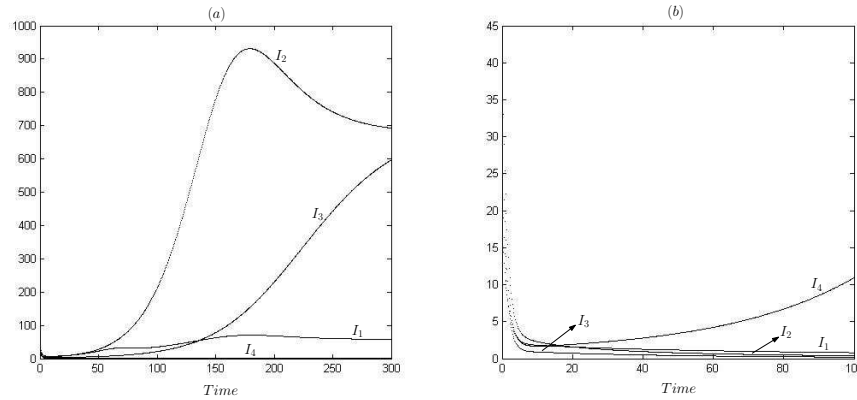


FIGURE 4. (a): $\tilde{R}_0^{(1,2)} = \max\{2.1656, 1.8015\} = 2.1656 > 1, R_0^{(3)} = 2.3164 > 1, R_0^{(4)} = 0.8235 < 1, R_0 = 2.3164 > 1$ and (b): $\tilde{R}_0^{(1,2)} = \max\{0.9324, 0.7657\} = 0.9324 < 1, R_0^{(3)} = 0.8534 < 1, R_0^{(4)} = 2.4704 > 1, R_0 = 2.4704 > 1$.

Example 3. If in Example 2 we take, $e_{2,1} = q_{2,1} = 0$, then,

$$R_0 = \max_{i=2,3,4} \{R_0^{(1)}, R_0^{(i)}\} \tag{63}$$

with

$$R_0^{(1)} = \frac{r\beta_1\epsilon_1}{(e_{1,2} + \epsilon_1 + d_1)(q_{1,2} + a_1 + d_1 + \gamma_1)}, \tag{64}$$

$$R_0^{(i)} = \frac{r\beta_i\epsilon_i}{(\epsilon_i + d_i)(a_i + d_i + \gamma_i)}; i = 2, 3, 4. \tag{65}$$

Now, we use, $\beta_1 = 0.007, \beta_2 = 0.008, \beta_3 = 0.017, \beta_4 = 0.015$, for $R_0^{(1)}, R_0^{(2)} < 1, R_0^{(3)}, R_0^{(4)} > 1, R_0 > 1$ and $\beta_1 = 0.0082, \beta_2 = 0.0082, \beta_3 = 0.0081, \beta_4 = 0.006$ for $R_0^{(1)}, R_0^{(2)}, R_0^{(3)}, R_0^{(4)}, R_0 < 1$ (Figure 5).

Example 4. If in Example 3 we take, $e_{1,2} = q_{1,2} = 0$, which mean we do not have to travel between I_i, I_{i+1} and E_i, E_{i+1} . Then we have,

$$R_0 = \max_{i=1,2,3,4} \frac{r\beta_i\epsilon_i}{(\epsilon_i + d_i)(a_i + d_i + \gamma_i)}. \tag{66}$$

Now, we use, $\beta_1 = 0.014, \beta_2 = 0.012, \beta_3 = 0.014, \beta_4 = 0.012$, for $R_0^{(i)} > 1 (i = 1, 2, 3, 4), R_0 > 1$ and $\beta_1 = 0.007, \beta_2 = 0.007, \beta_3 = 0.008, \beta_4 = 0.006$, for $R_0^{(1)}, R_0^{(4)}, R_0^{(2)}, R_0^{(3)}, R_0 < 1$ (Figure 6).

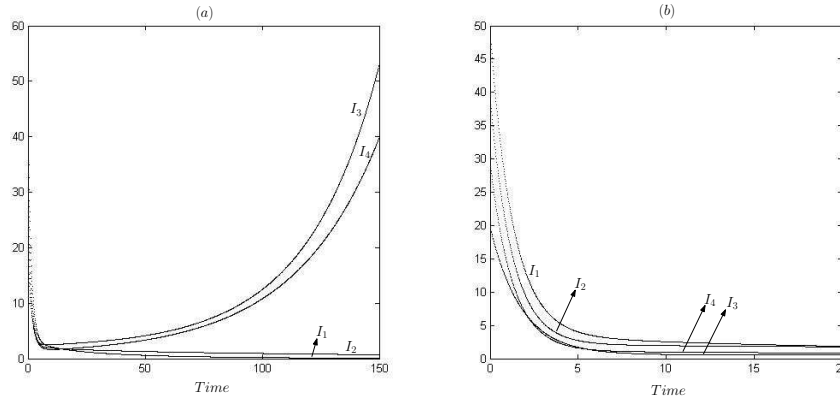


FIGURE 5. (a): $R_0 = \max\{R_0^{(1)} = 0.8131 < 1, R_0^{(2)} = 0.9214 < 1, R_0^{(3)} = 2.0726 > 1, R_0^{(4)} = 2.4704 > 1\} = 2.4704 > 1$ and (b): $R_0 = \max\{R_0^{(1)} = 0.9525 < 1, R_0^{(2)} = 0.9444 < 1, R_0^{(3)} = 0.9875 < 1, R_0^{(4)} = 0.9881 < 1\} = 0.9525 < 1$.

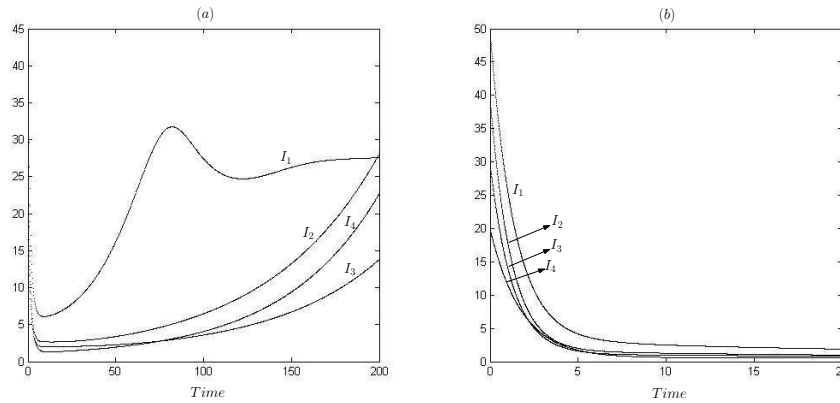


FIGURE 6. (a): $R_0^{(1)} = 1.9236 > 1, R_0^{(2)} = 1.3821 > 1, R_0^{(3)} = 1.7068 > 1, R_0^{(4)} = 1.3821 > 1, R_0 = 1.9236 > 1$ and (b): $R_0^{(1)} = 0.9618 < 1, R_0^{(2)} = 0.8062 < 1, R_0^{(3)} = 0.9753 < 1, R_0^{(4)} = 0.9881 < 1, R_0 = 0.9881 < 1$

Example 5. Suppose that we do not have to travel between patches and we used, $\beta_1 = 0.017, \beta_2 = 0.006, \beta_3 = 0.014, \beta_4 = 0.004, d_1 = 0.005, d_2 = 0.004, d_3 = 0.003, d_4 = 0.002, a_1 = 0.6, a_2 = 0.8, a_3 = 0.7, a_4 = 0.5$ for Figure 7.(a) and $\beta_1 = 0.036, \beta_2 = 0.042, \beta_3 = 0.026, \beta_4 = 0.036, d_1 = 0.5, d_2 = 0.4, d_3 = 0.3, d_4 = 0.2, a_1 = a_2 = a_3 = a_4 = 0$ for Figure 7.(b).

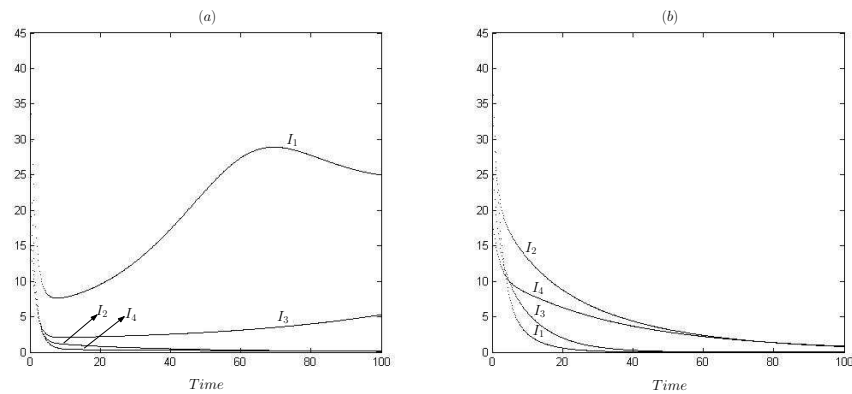


FIGURE 7. (a): $R_0^{(1)} = 2.3358 > 1$, $R_0^{(2)} = 0.6910 < 1$, $R_0^{(3)} = 1.7068 > 1$, $R_0^{(4)} = 0.6588 < 1$ and (b): $R_0^{(1)} = 0.8561 < 1$, $R_0^{(2)} = 1.3362 > 1$, $R_0^{(3)} = 0.8497 < 1$, $R_0^{(4)} = 1.3091 > 1$

3. Conclusion

One of the fundamental questions of mathematical epidemiology is to find threshold conditions that determine whether an infectious disease will spread in a susceptible population when the disease is introduced into the population. The threshold conditions are characterized by the so called reproductive number or contact number, commonly denoted by R_0 in mathematical epidemiology [9, 8, 10]. The reproductive number plays an important role in understanding transmission dynamics of epidemics and predicting spread of epidemics. In this article first we formulate a heterogeneous model, then we used the spectral radius of the next generation operator of infection [2, 5, 7], in finding a formula for the reproductive number, R_0 , thus if $R_0 < 1$ the modelled disease dies out and if $R_0 > 1$ the disease spreads in the population. As an instance in in Example 1 we see that for $R_0 < 1$ the disease dies out (Figure 3.(b)) and for $R_0 > 1$ the disease spreads in the population (Figure 3.(b)).

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