

A mathematical modeling and dynamical features in the spreading of virus infectious diseases

Research Article

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Abstract: We consider a compartmental model in epidemiology which leads to a nonlinear system of ordinary differential equations used to describe the spread of infectious diseases. Mathematical analysis is used to study the dynamical behavior of this model. A threshold parameter R_0 is identified which governs the spread of diseases, and this parameter is known as the basic reproductive number. The models have at least two equilibria, an endemic equilibrium and the disease-free equilibrium. We demonstrate that the disease will die out, if the basic reproductive number $R_0 < 1$. This is the case of a disease-free state, with no infection in the population. Otherwise the disease may become endemic if the basic reproductive number R_0 is bigger than unity. Furthermore, stability analysis for both endemic and disease-free steady states are investigated and we also give some numerical simulations.

MSC: 97M10 • 97M60 • 93D05

Keywords: Basic reproductive number • Disease-free equilibrium • Stability analysis • Numerical simulation

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1. Introduction

Infectious diseases such as measles, influenza, smallpox, tuberculosis, malaria, etc., have been having a great influence on human life. Almost every year millions of people die from different infectious diseases. The most important concerns about any infectious disease is the ability to invade a population. The goal of the study of infectious diseases via mathematical population models is to understand how infectious diseases are propagated in terms of numbers of people affected and also to find the best possible strategies to control the spread of a disease or to eradicate it. Mathematical modeling approaches therefore also provide powerful tools for epidemiological policy decision making in many countries, and among other health authorities. These models are often the only practical approach for answering questions about which prevention or control procedure is most effective.

There is on record, in relatively distant history, some interesting mathematical intervention in epidemiological situations. In 1760, Daniel Bernoulli carried out the first application of mathematical modeling to the spread of infectious disease which was described in the paper of Zhou and Liu [1]. Even though his work existed before the identification of the agent responsible for the transmission of smallpox by a century, he formulated and solved a differential equation which described the dynamics of the infection which is still of great importance even today. In 1906, Hamer [2] formulated and analyzed a discrete time model in attempting to understand the recurrence of measles epidemics. His

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model may have been the first to assume that the incidence depends on the product of the densities of the susceptibles and infectives. The models proposed by Kermack and McKendrick [3], published in 1927, had a great influence on the modeling framework. Their SIR model tracks the numbers of susceptible, infective and recovered individuals during an epidemic with the help of ordinary differential equations. Anderson and May [4] showed that the well-known standard mathematical models of the spread of infectious diseases have been useful for many different diseases in various regions all over the world. The serious development of mathematical epidemiology was delayed by lack of understanding of the mechanism of infectious spread until the beginning of 20th century.

Most traditional compartmental models descend from the classical SIR model of Kermack and McKendrick, where the population is divided into the classes of susceptible, infected, and recovered (S , I and R) individuals. For some diseases, such as influenza and tuberculosis, on sufficient contact with an infectious individual, a susceptible becomes exposed for a while, that is, infected but not yet infectious. Thus, it is reasonable to introduce a latent compartment, leading to an SEIR model. Such models have been widely discussed in the literature. One of the fundamental results in mathematical epidemiology is that most mathematical epidemic models usually exhibit "threshold" behavior stated as follows: if the average number of secondary infections caused by an average infective, called the basic reproduction number, is less than one the disease will die out, while if it exceeds one there will be an endemic (see [5, 6]). The organization of this paper is as follows: In the next section, the mathematical model is formed. In section 3, Mathematical analysis with existence and stability of disease-free and endemic equilibria are investigated. In section 4, the significance of our analytical and numerical simulations are discussed. Finally, the conclusion are summarized in section 5.

2. Mathematical model

2.1. General model

We have four different compartments in this model (S, E, I, R) and the population is assumed to be homogeneous-mixed. Thus the host population of a size N is fixed over time and divided into four epidemiological compartments:

- Susceptible compartment $S(t)$, which denotes individuals who are susceptible to catch the virus, and so might become infectious if exposed.
- Exposed compartment $E(t)$, which denotes the individuals who are infected but the symptoms of the virus are not yet visible.
- Infectious compartment $I(t)$, which denotes infectious individuals who are suffering the symptoms of the diseases and are able to spread the virus through contact with the susceptible class of individuals.
- Recovered compartment $R(t)$, which denotes individuals who have immunity to the infection and, consequently, do not affect the transmission dynamics, in any way, when in contact with other individuals.

The SEIR model is an extension of the simpler SIR model [3]. The particularity of the SEIR model is in the exposed compartment, which is characterized by infected individuals that cannot communicate yet the virus. These individuals are in the so called latent period [7]. For infectious virus, this stage makes all sense since it takes a certain time for a susceptible individual at time t , denoted by $S(t)$, to enter the Infectious compartment $I(t)$. Because the recovered individuals $R(t)$ have immunity to the infection, they do not affect the transmission dynamics in any way when in contact with other individuals. Fig. 1 shows the diagrammatic representation of virus progress in an individual.

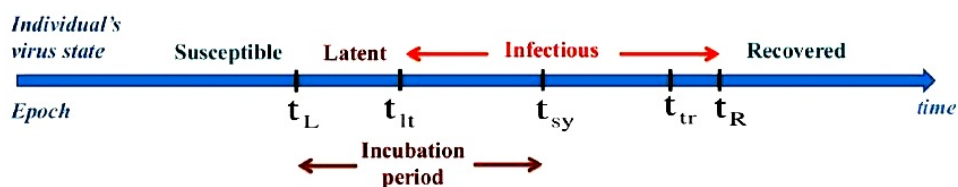


Fig. 1. Disease progression in an individual by using the SEIR model, where infectious occurs at t_L , latency to infectious transition at t_{It} , symptoms appear at t_{sy} , first transmission to another susceptible at t_{tr} , and individual is no longer infectious (recovered) at t_R .

The transmission of the virus is then described by the following system of nonlinear ordinary differential equations:

$$\begin{cases} \frac{dS(t)}{dt} = \beta S(t)I(t), \\ \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t), \\ \frac{dR(t)}{dt} = \mu I(t). \end{cases} \quad (1)$$

where $\beta \geq 0$ is the transmission rate; $\gamma \geq 0$ is the infectious rate; and $\mu \geq 0$ is the recovery rate. The initial conditions are given:

$$S(0) = S_0 \geq 0, \quad E(0) = E_0 \geq 0, \quad I(0) = I_0 \geq 0, \quad R(0) = R_0 \geq 0.$$

From (1), we see that $\frac{d}{dt}[S(t) + E(t) + I(t) + R(t)] = 0$, that is, the population N is constant along time:

$$S(t) + E(t) + I(t) + R(t) = N \quad \text{for any } t \geq 0.$$

2.2. SEIR model with demographic effects

We expand the SEIR model by including demographic effects: we assume a constant birth rate δ and a natural death rate λ , obtaining

$$\begin{cases} \frac{dS(t)}{dt} = \delta N - \beta S(t)I(t) - \lambda S(t), \\ \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t) - \lambda E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t) - \lambda I(t), \\ \frac{dR(t)}{dt} = \mu I(t) - \lambda R(t). \end{cases} \quad (2)$$

With initial conditions

$$S(0) = S_0 \geq 0, \quad E(0) = E_0 \geq 0, \quad I(0) = I_0 \geq 0, \quad R(0) = R_0 \geq 0.$$

The diagram below represent the SEIR model during horizontal transmission,

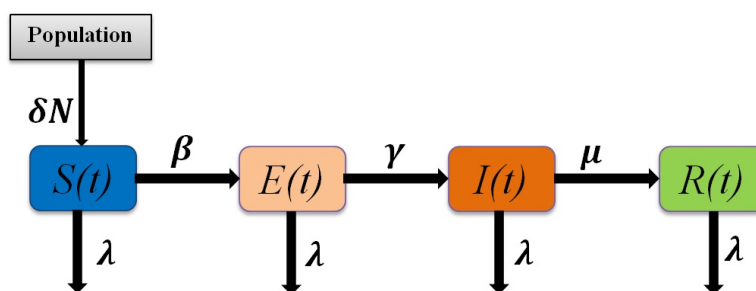


Fig. 2. A flowchart of possible states in an SEIR epidemic model.

3. Mathematical analysis

We now answer some fundamental questions about the compartmental model. In particular we will show that solutions to the given model exist for all positive time, and are unique. Later we will show that the solutions converge to one of two possible steady-states and that the solutions to the given model remain positive given positive initial conditions. This last property is important since it shows that the model is biologically relevant. We consider the first three equations of (2) for the model mathematical analysis, since $R(t)$ does not appear in the first three equations of (2), so it is enough to analyze the reduced system.

3.1. Properties of solutions

The first step in examining given model is to prove that a solution to the initial-value problem does, in fact, exist, and that this solution is unique.

Theorem 3.1.

Let $S_0, E_0, I_0 \in \mathbb{R}$ be given. There exists $t_0 > 0$ and continuously differentiable functions $\{S, E, I : [0, t_0] \rightarrow \mathbb{R}\}$ such that the ordered triple (S, E, I) satisfies (2) and $(S, E, I)(0) = (S_0, E_0, I_0)$.

Proof. To prove the result, we utilize the classical Picard-Lindelöf Theorem (cf. [8]). Since the system of ODEs is autonomous, it suffices to show that the function $f : \mathbb{R}^3 \rightarrow \mathbb{R}^3$ defined by

$$f(y) = \begin{pmatrix} \delta N - \beta y_1 y_3 - \lambda y_1 \\ \beta y_1 y_3 - (\gamma + \lambda) y_2 \\ \gamma y_2 - (\mu + \lambda) y_3 \end{pmatrix}$$

is locally Lipschitz in its y argument. In fact, it is enough to notice that the Jacobian matrix

$$\nabla f(y) = \begin{pmatrix} -\beta y_3 - \lambda & 0 & -\beta y_1 \\ \beta y_3 & -(\gamma + \lambda) & \beta y_1 \\ 0 & \gamma & -(\mu + \lambda) \end{pmatrix}$$

is linear in y and therefore locally bounded for every $y \in \mathbb{R}^3$. Hence, f has a continuous, bounded derivative on any compact subset of \mathbb{R}^3 and so f is locally Lipschitz in y . By the Picard-Lindelöf Theorem, there exists a unique solution, $y(t)$, to the ordinary differential equation $y'(t) = f(y(t))$ with initial value $y(0) = y_0$ on $[0, t_0]$ for some time $t_0 > 0$. \square

Additionally, we may show that for positive initial data, solutions remain positive as long as they exist. A fortunate byproduct of this result is that the solutions are also bounded.

Theorem 3.2.

(Boundedness and Positivity). Assume the initial conditions of (2) satisfy $S_0 > 0, E_0 > 0$, and $I_0 > 0$. If the unique solution provided by Theorem 3.1 exists on the interval $[0, t_0]$ for some $t_0 > 0$, then the functions $S(t), E(t)$ and $I(t)$ will be bounded and remain positive for all $t \in [0, t_0]$.

Proof. We assume that $S(t), E(t)$, and $I(t)$ initially have positive values. From the previous theorem, there exists a t^* such that the solution exists on $[0, t^*]$. Let us denote by T^* the largest time for which all populations remain positive, or more precisely

$$T^* = \sup\{t \in [0, t^*] : S(s), E(s), I(s) > 0, \forall s \in [0, t]\}.$$

Then on the interval $[0, T^*]$, we can estimate the population values.

Recall that all constants in the system are positive. Using this and the positivity of solutions on $[0, T^*]$, we can place lower bounds on $\frac{dE}{dt}$ and $\frac{dI}{dt}$ since

$$\begin{aligned} \frac{dE(t)}{dt} &= \beta S(t)I(t) - \gamma E(t) - \lambda E(t) \geq -(\gamma + \lambda)E \\ \text{i.e. } E(t) &\geq E(0)e^{-(\gamma + \lambda)t} > 0. \end{aligned}$$

and

$$\begin{aligned} \frac{dI(t)}{dt} &= \gamma E(t) - \mu I(t) - \lambda I(t) \geq -(\mu + \lambda)I \\ \text{i.e. } I(t) &\geq I(0)e^{-(\mu + \lambda)t} > 0. \end{aligned}$$

for $t \in [0, T^*]$. Similarly, we can place an upper bound on $\frac{dS}{dt}$ so that

$$\begin{aligned} \frac{dS(t)}{dt} &= \delta N - \beta S(t)I(t) - \lambda S(t) \leq \delta N \\ \text{i.e. } S(t) &\leq S(0) + \delta N t \leq C_1(1 + t). \end{aligned}$$

where the constant C_1 depends on the upper bound of δN and $S(0)$. We can sum the equations for $\frac{dE}{dt}$ and $\frac{dI}{dt}$ and place bounds on this sum that is

$$\begin{aligned}\frac{d}{dt}(E+I) &= \beta SI - \lambda E - (\mu + \lambda)I \leq \beta SI + \lambda E \\ &\leq \beta C_1(1+t)I + \lambda E \\ &\leq C_2(1+t)(E+I) \quad \text{where } C_2 \geq \max\{\beta C_1, \lambda\}\end{aligned}$$

$$\text{i.e. } (E+I)(t) \leq C_3 e^{t^2}.$$

for $t \in [0, T^*]$ where $C_3 > 0$ depends upon $C_2, E(0)$, and $I(0)$ only. Since $E(t)$ and $I(t)$ is positive, we can place an upper bound on both E and I by

$$C_3 e^{t^2} \geq (E+I)(t) \geq E(t),$$

and

$$C_3 e^{t^2} \geq (E+I)(t) \geq I(t).$$

With these bounds in place, we can now examine $S(t)$ and bound it from below using

$$\begin{aligned}\frac{dS}{dt} &= \delta N - \beta SI - \lambda S(t) \geq -\beta SI - \lambda S \geq -\lambda S - \beta C_3 e^{t^2} S \\ &\geq -C_4(1+e^{t^2})S \quad \text{where } C_4 \geq \max\{\beta C_3, \lambda\} \\ \Rightarrow \frac{dS}{dt} + C_4(1+e^{t^2})S &\geq 0 \\ \text{i.e. } S(t) &\geq S(0)e^{-C_4 \int_0^t (1+e^{\tau^2}) d\tau} > 0.\end{aligned}$$

Thus, the values of $S(t), E(t)$, and $I(t)$ stay strictly positive for all of $[0, T^*]$, including at time T^* . By continuity, there must exist a $t > T^*$ such that $S(t), E(t)$, and $I(t)$ are still positive. This contradicts the definition of T^* , and shows that $S(t), E(t)$, and $I(t)$ are strictly positive on the entire interval $[0, t^*]$. Additionally, on this same interval, all of the functions remain bounded, so the interval of existence can be extended further. In fact, the bounds on $S(t), E(t)$, and $I(t)$ derived above hold on any compact time interval. Thus, we may extend the time interval on which the solution exists to $[0, t_0]$ for any $t_0 > 0$ and from the above argument, the solutions remain both bounded and positive on $[0, t_0]$. \square

With this, we have a general idea that the model is sound, and can say with certainty that it remains biologically valid as long as it began with biologically-reasonable (i.e, positive) data.

3.2. Basic reproduction number

Theorem 3.3.

Let $S(t), E(t), I(t), R(t)$ be a solution of the SEIR model (2). Then the basic reproduction ratio is given by

$$R_0 = \frac{\beta \gamma \delta N}{\lambda(\gamma + \lambda)(\mu + \lambda)}. \quad (3)$$

Proof. For computing the basic reproduction ratio R_0 , we apply the next generation method [9, 10]. Assume that there are n infective classes in the model and define the vector $\bar{x} = x_i$, where $x_i, i = 1, 2, \dots, n$, denotes the number or the proportion of individuals in the i th infective class.

Let $F_i(\bar{x})$ be the rate of appearance of new infections in the i th class and let $V_i(\bar{x}) = V_i^-(\bar{x}) - V_i^+(\bar{x})$, where V_i^+ consists of transfer of individuals into class i and V_i^- consists of transfer of individuals out of class i . The difference $F_i(\bar{x}) - V_i(\bar{x})$ gives the rate of change of x_i . Notice that F_i consists of new infections from susceptible, whereas V_i includes the transfer of infected individuals from one infected class to another [10]. We can then form the next generation matrix from the partial derivatives of F_i and V_i :

$$F = \left[\frac{\partial F_i(x_0)}{\partial x_j} \right] \quad \text{and} \quad V = \left[\frac{\partial V_i(x_0)}{\partial x_j} \right],$$

where $i, j = 1, 2, \dots, n$ and x_0 is the initial condition of the epidemic. The basic reproduction ratio R_0 is given by the dominant eigenvalue of the matrix FV^{-1} [10]. Applying the next generation method to the SEIR model (2), and since

we are only concerned with individuals that spread the infection, we only need to model the exposed, E , and infected, I , classes. Let us define the model dynamics using the equations

$$\begin{cases} \frac{dE(t)}{dt} = \beta S(t)I(t) - \gamma E(t) - \lambda E(t), \\ \frac{dI(t)}{dt} = \gamma E(t) - \mu I(t) - \lambda I(t). \end{cases}$$

For this system,

$$F = \begin{pmatrix} 0 & \beta\delta N \\ 0 & \lambda \end{pmatrix},$$

where δ is the birth rate and λ is the death rate, and

$$V = \begin{pmatrix} \gamma + \lambda & 0 \\ -\gamma & \mu + \lambda \end{pmatrix}.$$

Then,

$$FV^{-1} = \begin{pmatrix} \frac{\gamma\beta\delta N}{\lambda(\gamma + \lambda)(\mu + \lambda)} & \frac{\beta\delta N}{\lambda(\mu + \lambda)} \\ 0 & 0 \end{pmatrix}.$$

The dominant eigenvalue R_0 of FV^{-1} is given by expression (3). \square

The basic reproduction number R_0 is the average number of secondary infections produced when one single infected individual is introduced into a host population where everyone is susceptible [10]. Note that our model R_0 above is a product of the average number susceptible per unit time (in the presence of natural death) and the rate of the disease transmission by an infective over the period of his/her infectivity. It is indeed a threshold quantity that helps to determine whether an outbreak of infectious disease dies out or spreads in a community. When $R_0 < 1$, the disease die out without any medical interventions but when $R_0 > 1$, the disease becomes endemic and this necessitates the introduction of some control measures in order to curtail the situation.

3.3. Analysis of the equilibria

Let us find the equilibria points of the system of equations (2) that describes the model. By setting the right-hand side of (2) to zero, we get

$$\delta N - \beta S(t)I(t) - \lambda S(t) = 0, \quad (4)$$

$$\beta S(t)I(t) - \gamma E(t) - \lambda E(t) = 0, \quad (5)$$

$$\gamma E(t) - \mu I(t) - \lambda I(t) = 0. \quad (6)$$

By adding (4) and (5), we obtain that $\delta N - \lambda S(t) - (\gamma + \lambda)E(t) = 0$. Then,

$$S = \frac{\delta N - (\gamma + \lambda)E}{\lambda}. \quad (7)$$

From (6) we obtain that

$$I = \frac{\gamma E}{\mu + \lambda}. \quad (8)$$

From (5), (7) and (8), we get

$$E \left(\frac{\beta\gamma(\delta N - (\gamma + \lambda)E)}{\lambda(\mu + \lambda)} - (\gamma + \lambda) \right) = 0.$$

Therefore,

$$E = 0 \quad \text{or} \quad E = \frac{\delta N}{(\gamma + \lambda)} - \frac{\lambda(\mu + \lambda)}{\beta\gamma}.$$

For $E = 0$, from (7-8) we obtain a virus free equilibrium given by $Q_0 = \left(\frac{\delta N}{\lambda}, 0, 0 \right)$ and another equilibrium point called endemic equilibrium point given by $Q^* = (S^*, E^*, I^*)$ where

$$S^* = \frac{(\gamma + \lambda)(\mu + \lambda)}{\beta\gamma}, \quad E^* = \frac{\delta N}{(\gamma + \lambda)} - \frac{\lambda(\mu + \lambda)}{\beta\gamma} \quad \text{and} \quad I^* = \frac{\gamma\delta N}{(\gamma + \lambda)(\mu + \lambda)} - \frac{\lambda}{\beta}.$$

3.4. Local stability of the equilibria

For linear ODEs, it is well-known that the stability properties depend only upon the eigenvalues of the system. However, our model (2) is nonlinear, and thus we must rely on linearization and a theorem of Hartman & Grobman [11] to unify the local behavior of the linear and nonlinear systems.

We will investigate the local stability properties of these equilibria by approximating the nonlinear system of differential equations (2) with a linear system at the points Q_0 and Q^* . Then, we locally perturb the system from equilibrium and examine the resulting long time behavior. This is done by linearizing the system about each equilibria, using the Jacobian for (2):

$$J = \begin{pmatrix} -\beta I - \lambda & 0 & -\beta S \\ \beta I & -(\gamma + \lambda) & \beta S \\ 0 & \gamma & -(\mu + \lambda) \end{pmatrix}.$$

Then, by studying the linearized system

$$\dot{z}(t) = J(Q)z(t), \quad (9)$$

we can investigate the stability of each equilibrium point $Q = Q_0$ and $Q = Q^*$. As we will see below, this property depends only on a single number, referred to as the basic reproduction number, R_0 given by (3). We now prove two theorems that demonstrate the relationship between the value of R_0 and the local asymptotic stability of equilibria.

Theorem 3.4.

The disease free equilibrium is locally asymptotically stable if $R_0 < 1$.

Proof. Evaluating matrix J at the disease free equilibrium $Q_0 = \left(\frac{\delta N}{\lambda}, 0, 0\right)$ gives

$$J(Q_0) = \begin{pmatrix} -\lambda & 0 & \frac{-\beta\delta N}{\lambda} \\ 0 & -(\gamma + \lambda) & \frac{\beta\delta N}{\lambda} \\ 0 & \gamma & -(\mu + \lambda) \end{pmatrix}.$$

The corresponding characteristic equation can be written as

$$|xI - J(Q_0)| = 0$$

or

$$(x + \lambda) \left((x + \gamma + \lambda)(x + \mu + \lambda) - \frac{\gamma\beta\delta N}{\lambda} \right) = 0$$

Thus, $x = -\lambda < 0$ is one negative eigenvalue of the system, The remaining quadratic equation is

$$x^2 + a_1x + a_2 = 0$$

where $a_1 = \gamma + 2\lambda + \mu$ and $a_2 = (\gamma + \lambda)(\mu + \lambda) - \frac{\gamma\beta\delta N}{\lambda}$. Thus, the other eigenvalues are

$$x_{\pm} = \frac{-(\gamma + 2\lambda + \mu) \pm \sqrt{(\gamma + 2\lambda + \mu)^2 - 4 \left\{ (\gamma + \lambda)(\mu + \lambda) - \frac{\gamma\beta\delta N}{\lambda} \right\}}}{2}$$

Since the first term under the square root is nonnegative, these eigenvalues have negative real part if and only if

$$\begin{aligned} 4 \left\{ (\gamma + \lambda)(\mu + \lambda) - \frac{\gamma\beta\delta N}{\lambda} \right\} &> 0, \\ \Rightarrow 4(\gamma + \lambda)(\mu + \lambda)(1 - R_0) &> 0. \end{aligned}$$

Since all parameters are positive, we see that all eigenvalues possess negative real part if and only if $R_0 < 1$. Thus, in this case the origin is a locally asymptotically stable equilibrium for the system (9). Finally, by the Hartman-Grobman Theorem, the asymptotic behavior of (2) is equivalent to that of this linear system for local perturbations, and the result follows. \square

Remark 3.1.

The case $R_0 = 1$ is a critical threshold point where the disease free equilibrium Q_0 loses its asymptotic stability and simply becomes (neutrally) stable. Moreover, it becomes unstable immediately $R_0 > 1$ and this will lead to the existence of a stable endemic equilibrium Q^* . Note that $R_0 = 1$ can literally be viewed as a transcritical bifurcation point where stability is exchanged between Q_0 and Q^* .

Theorem 3.5.

The endemic equilibrium is locally asymptotically stable if $R_0 > 1$.

Proof. Evaluating matrix J at the endemic equilibrium $Q^* = \left(\frac{\delta N}{\lambda R_0}, \frac{\lambda(\mu + \lambda)}{\beta\gamma}(R_0 - 1), \frac{\lambda}{\beta}(R_0 - 1) \right)$ gives

$$J(Q^*) = \begin{pmatrix} -\lambda R_0 & 0 & \frac{-\beta\delta N}{\lambda R_0} \\ \lambda(R_0 - 1) & -(\gamma + \lambda) & \frac{\beta\delta N}{\lambda R_0} \\ 0 & \gamma & -(\mu + \lambda) \end{pmatrix}.$$

The characteristic polynomial of $J(Q^*)$ is given by

$$x^3 + a_1x^2 + a_2x + a_3 = 0, \tag{10}$$

where

$$\begin{aligned} a_1 &= \gamma + 2\lambda + \mu + \lambda R_0, \\ a_2 &= \gamma\lambda + \gamma\mu + \lambda^2 + \lambda\mu + \frac{\beta\gamma\delta N}{\lambda R_0} + \gamma\lambda R_0 + 2\lambda^2 R_0 + \lambda\mu R_0, \\ a_3 &= 2\beta\gamma\delta N - \frac{\beta\gamma\delta N}{R_0} + \gamma\lambda^2 R_0 + \gamma\lambda\mu R_0 + \lambda^3 R_0 + \lambda^2\mu R_0. \end{aligned}$$

According to the Routh-Hurwitz criteria, all roots of this cubic equation like (10) possess negative real part if and only if $a_1, a_2, a_3 > 0$ and $a_1 a_2 > a_3$. Hence, it is sufficient to show that $R_0 > 1$ if and only if the Routh-Hurwitz criteria are satisfied. Clearly, $a_1, a_2, a_3 > 0$ if $R_0 > 1$. Now

$$\begin{aligned} a_1 a_2 - a_3 &= \gamma^2\lambda + \gamma^2\mu + 3\gamma\lambda^2 + 4\gamma\lambda\mu + \gamma\mu^2 + 2\lambda^3 + 3\lambda^2\mu + \lambda\mu^2 - \beta\gamma\delta N + \frac{\beta\gamma^2\delta N}{\lambda R_0} + \frac{\beta\gamma\delta\mu N}{\lambda R_0} + \frac{3\beta\gamma\delta N}{R_0} \\ &\quad + \gamma^2\lambda R_0 + \gamma\lambda^2 R_0^2 + 4\gamma\lambda^2 R_0 + 2\gamma\lambda\mu R_0 + 2\lambda^3 R_0^2 + 4\lambda^3 R_0 + \lambda^2\mu R_0^2 + 4\lambda^2\mu R_0 + \lambda\mu^2 R_0 > 0. \end{aligned}$$

Therefore, by Routh-Herwitz criteria, we conclude that the eigenvalues of $J(Q^*)$ are all negative when $R_0 > 1$ and the proof is complete. □

3.5. Global stability of the equilibria

Theorem 3.6.

If $R_0 \leq 1$, the disease-free equilibrium Q_0 is globally asymptotically stable and the disease dies out. But if $R_0 > 1$, then Q_0 is unstable.

Proof. To investigate the global stability of Q_0 , consider the following Lyapunov function

$$V(S, E, I) = \gamma E + (\gamma + \lambda)I.$$

Now

$$\begin{aligned} \frac{dV}{dt} &= \gamma \frac{dE}{dt} + (\gamma + \lambda) \frac{dI}{dt} \\ &= (\gamma\beta S - (\gamma + \lambda)(\mu + \lambda)) I \\ &\leq \left(\gamma\beta \frac{\delta N}{\lambda} - (\gamma + \lambda)(\mu + \lambda) \right) I \\ &= (\gamma + \lambda)(\mu + \lambda) (R_0 - 1) I \leq 0. \end{aligned}$$

It is important to note that, $\frac{dV}{dt} = 0$ only when $I = 0$. Therefore, the maximum invariant set in $\{(S, E, I) \in \Omega : \frac{dV}{dt} \leq 0\}$ is the singleton set $\{Q_0\}$. Hence, the global stability of Q_0 when $R_0 \leq 1$ follows from LaSalle’s invariance principle [12]. □

Theorem 3.7.

If $R_0 > 1$, then there exist an endemic equilibrium Q^* (in addition to the disease-free equilibrium) and it is globally stable.

Proof. Given that $R_0 > 1$, then the existence of the endemic equilibrium is guaranteed. Considering a Lyapunov function candidate

$$\begin{aligned} V(S, E, I) &= \left(S - S^* - S^* \ln \frac{S}{S^*} \right) + \left(E - E^* - E^* \ln \frac{E}{E^*} \right) + \frac{(\gamma + \lambda)}{\gamma} \left(I - I^* - I^* \ln \frac{I}{I^*} \right) \\ \Rightarrow \frac{dV}{dt} &= \left(1 - \frac{S^*}{S} \right) \frac{dS}{dt} + \left(1 - \frac{E^*}{E} \right) \frac{dE}{dt} + \frac{(\gamma + \lambda)}{\gamma} \left(1 - \frac{I^*}{I} \right) \frac{dI}{dt}. \end{aligned}$$

Substituting the expressions of the derivatives from system (2) and using the relation

$$\delta N = \beta S^* I^* + \lambda S^*.$$

We get

$$\begin{aligned} \frac{dV}{dt} &= \left(1 - \frac{S^*}{S} \right) [-\lambda(S - S^*) + \beta S^* I^* - \beta S I] + \left(1 - \frac{E^*}{E} \right) [\beta S I - (\gamma + \lambda) E] \\ &\quad + \frac{(\gamma + \lambda)}{\gamma} \left(1 - \frac{I^*}{I} \right) [\gamma E - (\mu + \lambda) I] \\ &= -\lambda \frac{(S - S^*)^2}{S} + \beta S^* I^* - \beta S^* I^* \frac{S^*}{S} + \beta S^* I - \beta S I \frac{E^*}{E} + (\gamma + \lambda) E^* - (\gamma + \lambda) E \frac{I^*}{I} - \frac{(\gamma + \lambda)}{\gamma} (\mu + \lambda) I \\ &\quad + \frac{(\gamma + \lambda)}{\gamma} (\mu + \lambda) I^*. \end{aligned}$$

Since $\gamma E^* = (\mu + \lambda) I^*$, This implies that

$$\beta S^* I - \frac{(\gamma + \lambda)}{\gamma} (\mu + \lambda) I = \beta S^* I - (\gamma + \lambda) E^* \frac{I}{I^*} = [\beta S^* I^* - (\gamma + \lambda) E^*] \frac{I}{I^*} = 0.$$

So

$$\begin{aligned} \frac{dV}{dt} &= -\lambda \frac{(S - S^*)^2}{S} + 3(\gamma + \lambda) E^* - \beta S^* I^* \frac{S^*}{S} - \beta S I \frac{E^*}{E} - (\gamma + \lambda) E \frac{I^*}{I} \\ &= -\lambda \frac{(S - S^*)^2}{S} + (\gamma + \lambda) E^* \left(3 - \frac{S^*}{S} - \frac{S E^* I}{S^* E I^*} - \frac{E I^*}{E^* I} \right) \leq 0. \end{aligned}$$

Since the arithmetic mean is greater than or equal to the geometric mean of the quantities $\frac{S^*}{S}$, $\frac{S E^* I}{S^* E I^*}$, $\frac{E I^*}{E^* I}$ that is

$$\frac{S^*}{S} + \frac{S E^* I}{S^* E I^*} + \frac{E I^*}{E^* I} - 3 \geq 0.$$

So the maximum invariant set in $\{(S, E, I) \in \Omega : \frac{dV}{dt} \leq 0\}$ is the singleton set $\{Q^*\}$. By LaSalle's invariant principle [12], the endemic equilibrium Q^* is globally asymptotically stable if $R_0 > 1$. \square

4. Numerical results of the SEIR model

In this section, we give the numerical simulation which demonstrate the theoretical results for the SEIR model. We simulate the SEIR model using Runge-Kutta methods to illustrate the dynamics of the system. The numerical simulation was carried out using Matlab. The Table 1 shows the parameters used in the simulations and the parameters are chosen arbitrarily.

We firstly consider the numerical simulation of the SEIR model when $R_0 < 1$. Therefore we obtain $R_0 = 0.35$, when $\delta = 0.08$, $\beta = 0.09$, $\gamma = 0.76$, $\mu = 0.048$, and $\lambda = 0.08$. In our simulation, we also assume that population size is constant with natural mortality rate of individuals λ is equal to the birth rate δ with $N = 1$. Now in Fig. 3, we observe that the number of susceptible individuals and recovery individuals increases during the first 10 days. This graph also shows that the number of infected individuals and exposed individuals sharply decreases to zero. After 50 days the disease seems to disappears form the host population. Our numerical simulations indicate that the disease-free equilibrium in these model is globally stable.

Furthermore, we simulate the SEIR model using different parameters, we get $R_0 = 1.94$. where, $\delta = 0.08$, $\beta = 0.3$, $\gamma = 0.90$, $\mu = 0.062$, and $\lambda = 0.08$. Fig. 4 shows that the number of susceptible individuals and recovered individuals also increase from the first 10 days of the model, while exposed individuals and infected individuals decreasing. As time progresses, the exposed and infected individuals still exist in the host population, this shows that there is an endemic disease within the population. therefore the disease-free equilibrium seems to be in an unstable state as the time increases.

Table 1. The parameter definitions and values for SEIR model

Parameters	Description	Value
δ	Birth rate	0.08
β	Transmission coefficient/ Effective contact rate	[0.09, 0.3]
λ	Natural mortality rate	0.08
γ	Disease outcome rate	[0.76, 0.90]
μ	Recovery rate	[0.048, 0.062]
S_0	Percentage of Initial Susceptible individuals	0.073
E_0	Percentage of Initial Exposed individuals	0.25
I_0	Percentage of Initial Infected individuals	0.53
R_0	Percentage of Initial recovered individuals	0.15

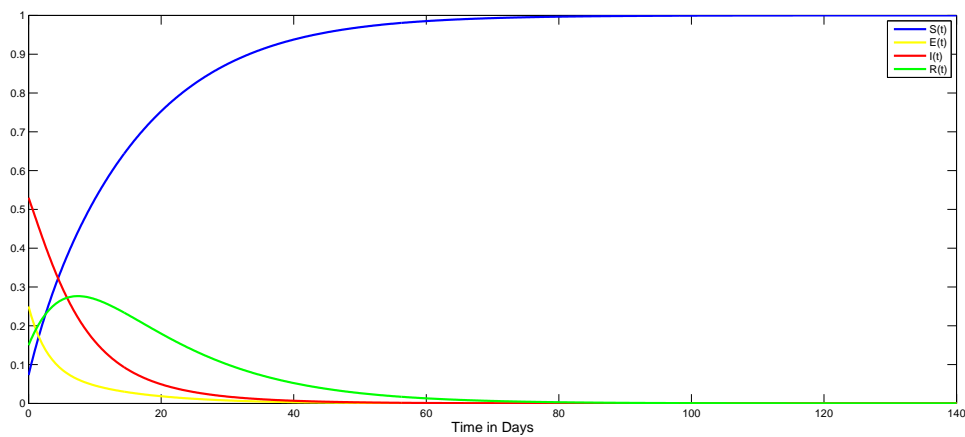


Fig. 3. The plot shows the global stability of the SEIR epidemic model, when $R_0 = 0.35$.

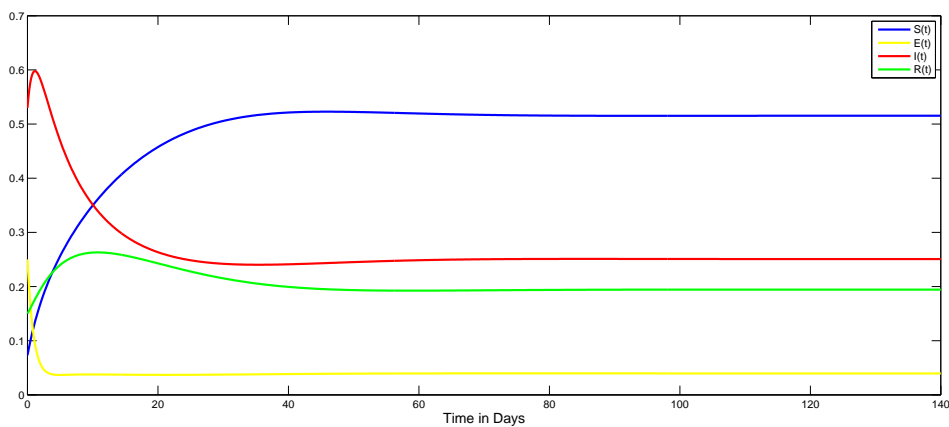


Fig. 4. The plot shows unstable SEIR epidemic model, when $R_0 = 1.94$.

5. Conclusion

Numerous epidemiological models have a disease-free equilibrium at which the population remains free of the disease. These models usually have the threshold parameter known as the basic reproductive number R_0 , which governs the spread of diseases, and is also related to the long term behaviours and the level of intervention necessary for eradication. We define R_0 as the average number of secondary infectious cases produced by an infectious individual in a totally susceptible population during the entire infectious period. If $R_0 < 1$, then the disease eventually dies out from the population because on average, each infected cannot guarantee transmission of the infectious agent to one susceptible. Therefore the disease-free equilibrium is asymptotically stable and the population cannot be invaded by

the disease. On the other hand if $R_0 > 1$, then each infected individual produces, on average, more than one new infection, and the disease can spread in the population. Therefore the disease-free equilibrium is unstable and invasion is always possible.

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