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Identifying Critical Parameters in SIR Model for Spread of Disease

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Abstract

Calculating analytical approximate solutions for non-linear infectious disease models is a difficult task. Such models often require computational tools to analyse analytical approximate methods which appear in some theoretical and practical applications in systems biology. They represent key critical elements and give some approximate solutions for such systems. The SIR epidemic disease model is given as the non-linear system of ODE's. Then, we use a proper scaling to reduce the number of parameters. We suggest Elzaki transform method to find analytical approximate solutions for the simplified model. The technique plays an important role in calculating the analytical approximate solutions. The local and global dynamics of the model are also studied. An investigation of the behaviour at infinity was conducted via finding the lines and singular points at infinity. Model dynamic results are computed in numerical simulations using Pplane8 and SimBiology Toolbox for Mathlab. Results provide a good step forward for describing the model dynamics. More interestingly, the simplified model could be accurate, robust, and used by biologists for different purposes such as identifying critical model elements.

Keywords

Mathematical Modelling, Epidemic SIR Disease Model, Stability Analysis, Analytical Approximate Solutions, Sensitivity Analysis

1. Introduction

A system of kinetic equations can be applied to describe the behaviours of biochemical kinetics. The system is obtained from the reaction mechanisms by the law of mass action. The rate constant of any given elementary reaction, known as the proportionality constant, depends on the reaction condition (temperature, solvent, PH, etc.). The reaction conditions are generally held by biochemists to avoid dealing with higher-order

complexities [1] [2] [3].

An arbitrary number n of elementary reactions can be expressed as follows:

$$\sum_{j=1}^{m}\alpha_{ij}S_j \xrightarrow{k_i} \sum_{j=1}^{m}\beta_{ij}S_j, i=1,2,\cdots,n \tag{1}$$

where S_j is the j^{th} species and k_i is the rate constant of step i. The non-negative integers α_{ij} and β_{ij} are the stoichiometric coefficients for species j occurring as a reactant and product, respectively, in the i^{th} reaction step. The rate of product of species j can be given by:

$$\frac{\mathrm{d}\left[S_j\right]}{\mathrm{d}t}=\sum_{i=1}^{n}F_{ij}=F_j, j=1,2,\cdots,m \tag{2}$$

where $\left[S_j\right]$ is the concentration of j^{th} species and F_{ij} is the rate of change of j^{th} species in reaction i. A reaction rate F_{ij} is given by the law of mass action as follows:

$$F_{ij}=\left(\beta_{ij}-\alpha_{ij}\right)k_i\sum_{l=1}^{m}\left[S_l\right]^{\alpha_{il}}, i=1,2,\cdots,n,\ \ j=1,2,\cdots,m \tag{3}$$

The readers can see further details about the chemical kinetics in [4]-[12].

The idea of sensitivity analysis has been used in dynamical analysis of biochemical kinetics and systems biology models. The concept of sensitivity analysis theory in application to chemical kinetic problems was given by Rabitz in [13]. The local and global methods of sensitivity analysis in chemical kinetics were further studied in [14]. There are also some applications of sensitivity analysis of systems biology models in [15]-[21]. More recently, the methods of local sensitivity analysis have been used to identify the critical model elements for a kinetic model of nuclear receptor signalling, the reader can see further details about the method in [10] [11]. This method is applied to determine which variable or parameter is sensitive to a particular condition which is defined by a variable or parameter. The system of ODEs discussed here is:

$$\frac{\mathrm{d}x_i}{\mathrm{d}t}=w_i\left(\boldsymbol{\mathcal{X}}(t),\boldsymbol{\mathcal{K}}\right),\ \ i=1,2,\cdots,m. \tag{4}$$

The model input $\boldsymbol{\mathcal{K}}$ is a vector of parameters, and the model output $\boldsymbol{\mathcal{X}}$ is a vector of state variables. Local sensitivity is the changes in state variables $x_i,\ i=1,2,\cdots,m$ with respect to parameters $k_p,\ p=1,2,\cdots,n$.

The general form of the local sensitivity is given as a Jacobian matrix as follows

$$\dot{\boldsymbol{\mathcal{S}}}=\boldsymbol{\mathcal{W}}_{k_p}+\boldsymbol{\mathcal{J}}.\boldsymbol{\mathcal{S}},\ \ p=1,2,\cdots,n, \tag{5}$$

where the matrices $\dot{\boldsymbol{\mathcal{S}}},\boldsymbol{\mathcal{W}}_{k_p}$ and $\boldsymbol{\mathcal{J}}$ are defined by

$$\boldsymbol{\mathcal{S}}=\begin{pmatrix}\frac{\partial x_1}{\partial k_p}\\ \frac{\partial x_2}{\partial k_p}\\ \vdots\\ \frac{\partial x_m}{\partial k_p}\end{pmatrix},\boldsymbol{\mathcal{W}}_{k_p}=\begin{pmatrix}\frac{\partial w_1}{\partial k_p}\\ \frac{\partial w_2}{\partial k_p}\\ \vdots\\ \frac{\partial w_m}{\partial k_p}\end{pmatrix},\boldsymbol{\mathcal{J}}=\begin{pmatrix}\frac{\partial w_1}{\partial x_1} & \frac{\partial w_1}{\partial x_2} & \cdots & \frac{\partial w_1}{\partial x_m}\\ \frac{\partial w_2}{\partial x_1} & \frac{\partial w_2}{\partial x_2} & \cdots & \frac{\partial w_2}{\partial x_m}\\ \vdots & \vdots & \ddots & \vdots\\ \frac{\partial w_m}{\partial x_1} & \frac{\partial w_m}{\partial x_2} & \cdots & \frac{\partial w_m}{\partial x_m}\end{pmatrix}.$$

The initial conditions of the Equation (5) are determined by the input parameter k_p

and the initial condition of the output variables x_i.

The idea of ELzaki transform was introduced by Tarig Elzaki for solving linear ordinary differential equations with constant coefficients. Then, this became more popular and works as a powerful tool in mathematics for solving some complicated equations, for example, solving high order ordinary differential equations with variable coefficients [22], applying ELzaki transform for solving the integro-differential equations [23], showing some relationships between Laplace transform and the ELzaki transform [24], solving linear systems of integro-differential equations with constant coefficients [25], a solution for nonlinear systems of differential equations using a mixture of Elzaki transform [26].

The SIR model, first published by Kermack and McKendrick in 1927 [27], is surly the most well known mathematical model for the spread of an infectious disease. Then, the model was further developed mathematically in [28] [29]. Here, people are divided into three classes: susceptible $\boldsymbol{S}$, infective $\boldsymbol{I}$ and removed $\boldsymbol{R}$. Removed individuals are no longer susceptible nor infective for whatever reason. For instance, they have recovered from the disease or they have been vaccinated. They may have been isolated from the rest of the people [30] [31] [32]. After that further explanation of the model was proposed by the authors of these papers [33] [34] [35] [36] [37].

The main problem in this study is identifying the critical model parameters. Therefore, the aim in this work is to apply some mathematical tools to simplify and analyse the model and then identifying the model elements (variables and parameters). We proposes a number of steps of model analysis, which plays in reducing the number of elements and in calculating analytical approximate solutions of the SIR model. The proposed steps and their advantages are simply given. The first step is that a proper scaling is used in order to minimize the number of elements. This becomes a good step forward for simplifying the original model. Another step is calculating some analytical approximate solutions using Elzaki transformation. Furthermore, using local sensitivity method is another important step in this study. This helps us to identify critical model parameters of the reduced model. Finally, studying the behaviour at infinity of the reduced model provide us an understanding of global dynamics and drawing the global phase portrait of the system.

2. The SIR Epidemic Disease Model

The SIR model may be diagrammed as in **Figure 1**. The chemical reactions of the model are given

$$\begin{aligned} S + I &\xrightarrow{\alpha} 2I \\ I &\xrightarrow{\beta} R \end{aligned} \tag{6}$$

where α is the rate at which susceptible people become infectious and β is the rate at which infectious people recover/develop immunity, both parameters are positive constant reactions. By using mass action law, we have the corresponding coupled differential equations

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\alpha SI, \quad \frac{\mathrm{d}I}{\mathrm{d}t} = \alpha SI - \beta I, \quad \frac{\mathrm{d}R}{\mathrm{d}t} = \beta I, \tag{7}$$

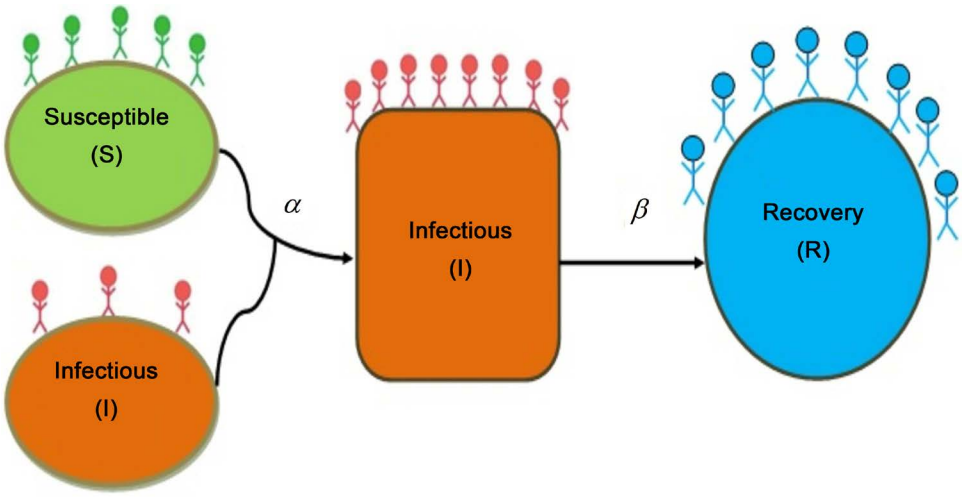


Figure 1. Scheme of the SIR infectious diseases model. Geometric shapes here represent compartments, and arrows indicate flux between the compartments.

with initial conditions

$$S(0)=S_0, I(0)=I_0, R(0)=0. \tag{8}$$

Equation (7) has a conservation law

$$S+I+R=N. \tag{9}$$

where N is a constant population. We assume in this study the population is closed with no death or births, or immigration or emigration.

The dimensionless SIR equations are then given by

$$\frac{\mathrm{d}S^*}{\mathrm{d}\tau}=-\delta S^* I^*,\quad \frac{\mathrm{d}I^*}{\mathrm{d}\tau}=\delta S^* I^*-I^*,\quad \frac{\mathrm{d}R^*}{\mathrm{d}\tau}=I^*, \tag{10}$$

where $S^*=S/N, I^*=I/N, R^*=R/N, \tau=\beta t$ and $\delta=\alpha N/\beta$.

Therefore, the conservation law (9) takes the form

$$S^*+I^*+R^*=1. \tag{11}$$

In addition, the Equation (10) is then reduced to

$$\frac{\mathrm{d}S^*}{\mathrm{d}\tau}=-\delta S^* I^*,\quad \frac{\mathrm{d}I^*}{\mathrm{d}\tau}=\delta S^* I^*-I^*, \tag{12}$$

with initial conditions $S^*(0)=S_0^*$ and $I^*(0)=I_0^*$. It can be concluded that the simplified Equation (12) is minimal in terms of the number of its elements (variables and parameters).

Many nonlinear systems of differential equations have not exact solutions. Calculating analytical approximate solutions for such systems is a difficult task. The SIR epidemic disease model is given as the non-linear system of ODE's. Equation (12) can not be solved analytically. Therefore, calculating some analytical approximate solutions for the system provides more information about the behaviours of the model dynamics. Applying the idea of Elzaki transform, we can obtain some analytical approximate solutions of the Equation (12). Take Elzaki transform of Equation (12) to get:

$$\frac{S^{**}(u)}{u}-uS^*(0)=E\left[-\delta S^* I^*\right], \frac{I^{**}(u)}{u}-uI^*(0)=E\left[\delta S^* I^*-I^*\right]. \tag{13}$$

Take the inverse Elzaki transform of Equation (13), the recursive relations are then given by

$$\begin{aligned} S^*(n+1) &= S_0^* - \delta E^{-1}\left\{uE\left[P_n\right]\right\}, \\ I^*(n+1) &= I_0^* + E^{-1}\left\{uE\left[\delta P_n - I^*(n)\right]\right\}, \end{aligned} \tag{14}$$

where

$$P_n = \sum_{r=0}^{n} I^*(r) S^*(n-r), \text{ for } n = 0,1,2,\cdots \tag{15}$$

For $n=0$, and from Equation (15) and Equation (14), we have

$$\begin{aligned} P_0 &= I_0^* S_0^*, \\ S^*(1) &= S_0^* - \delta I_0^* S_0^* t, \\ I^*(1) &= I_0^* + \left(\delta I_0^* S_0^* - I_0^*\right) t. \end{aligned} \tag{16}$$

For $n=1$, and from Equation (15) and Equation (14), we have

$$\begin{aligned} P_1 &= 2I_0^* S_0^* + \left(S_0^*\left(\delta I_0^* S_0^* - I_0^*\right) - I_0^*\left(\delta I_0^* S_0^*\right)\right) t, \\ S^*(2) &= S_0^* - \alpha_1 t - \alpha_2 t^2, \\ I^*(2) &= I_0^* + \beta_1 t + \beta_2 \frac{t^2}{2}, \end{aligned} \tag{17}$$

where,

$$\alpha_1 = 2\delta I_0^* S_0^*, \quad \alpha_2 = \frac{\delta I_0^* S_0^*}{2}\left(I_0^* S_0^* - 1 - \delta I_0^*\right)$$

$$\beta_1 = 2I_0^* S_0^* - I_0^*, \quad \beta_2 = I_0^* S_0^*\left(\delta S_0^* - \delta I_0^* - 2\right) + I_0^*.$$

For $n=2$, and again from Equations ((15) and (14)), we obtain

$$\begin{aligned} P_2 &= \sum_{r=0}^{2} I^*(r) S^*(2-r) = \beta_5 + \beta_6 t + \beta_7 t^2, \\ S^*(3) &= S_0^* - \delta\beta_5 t - \frac{\delta\beta_6}{2} t^2 - \frac{\delta\beta_7}{3} t^3, \\ I^*(3) &= I_0^* + \left(\beta_5 - I_0^*\right) t + \left(\frac{\beta_6 - \beta_1}{2}\right) t^2 + \left(\frac{2\beta_7 - \beta_2}{6}\right) t^3, \end{aligned} \tag{18}$$

where

$$\begin{aligned} \beta_3 &= I_0^* S_0^*\left(\delta S_0^* - 1 - \delta I_0^*\right), \\ \beta_4 &= \delta I_0^* S_0^*\left(\delta I_0^* S_0^* - I_0^*\right), \\ \beta_5 &= S_0^*\left(2I_0^* + S_0^*\right), \\ \beta_6 &= -I_0^*\alpha_1 + \beta_3 - \alpha_1 S_0^*, \\ \beta_7 &= -I_0^*\alpha_2 - \beta_4 - \alpha_2 S_0^*. \end{aligned}$$

In general, a series form of the model solution can be given

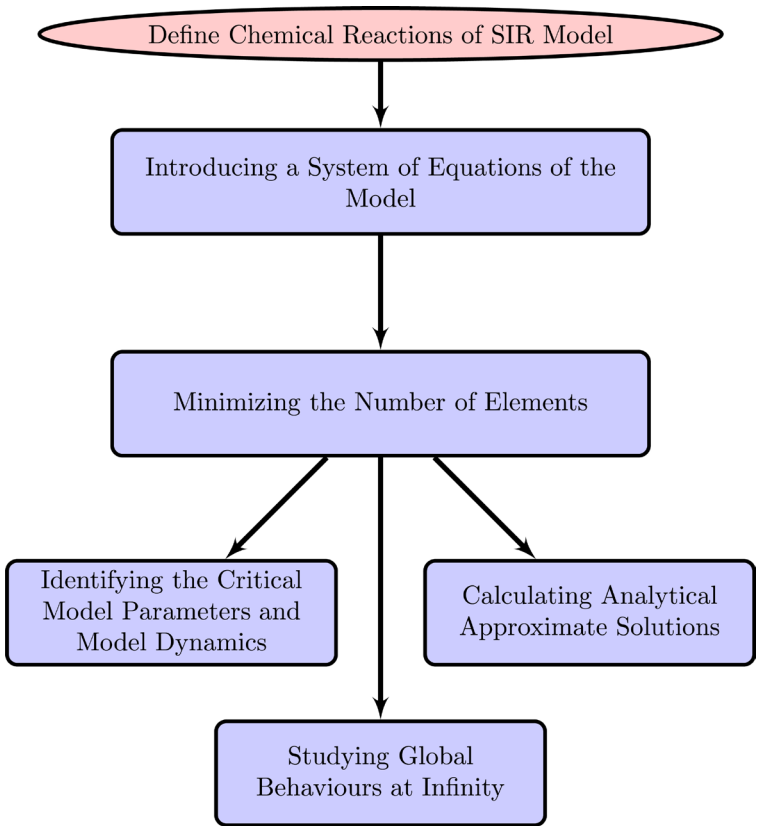
$$\begin{aligned} S^*(t) &= \sum_{k=0}^{\infty} S^*(k) \approx S^*(0) + S^*(1) + S^*(2) + S^*(3) + \cdots \\ I^*(t) &= \sum_{k=0}^{\infty} I^*(k) \approx I^*(0) + I^*(1) + I^*(2) + I^*(3) + \cdots \end{aligned} \tag{19}$$

3. Proposed Steps of Model Analysis and Simplification

In this work, we propose some steps of model analysis and simplification for the SIR epidemic disease model. The suggested steps are used for minimizing the number of elements (variables and parameters), calculating analytical approximate solutions and identifying critical model parameters. The proposed steps in this study are presented below:

1) Define chemical mechanisms of SIR Model.
2) Define a kinetic model of biochemical reactions as a system of ODEs using the mass action law.
3) Eliminate some variables based on the stoichiometric conservation laws, and use proper scaling for the kinetic equations and determine the minimal number of parameters.
4) Apply Elzaki transform method to calculate analytical approximate solutions of the reduced model.
5) Simulate the reduced model dynamics for different parameter values using Pplane8 for Mathlab. Analyse the reduced models to identify the critical model parameters by the local sensitivity analysis in numerical simulations using the SimBiology Toolbox for Mathlab.
6) Study the global behaviours of the reduced model at infinity.

The above steps can be simply presented in the following flowchart:



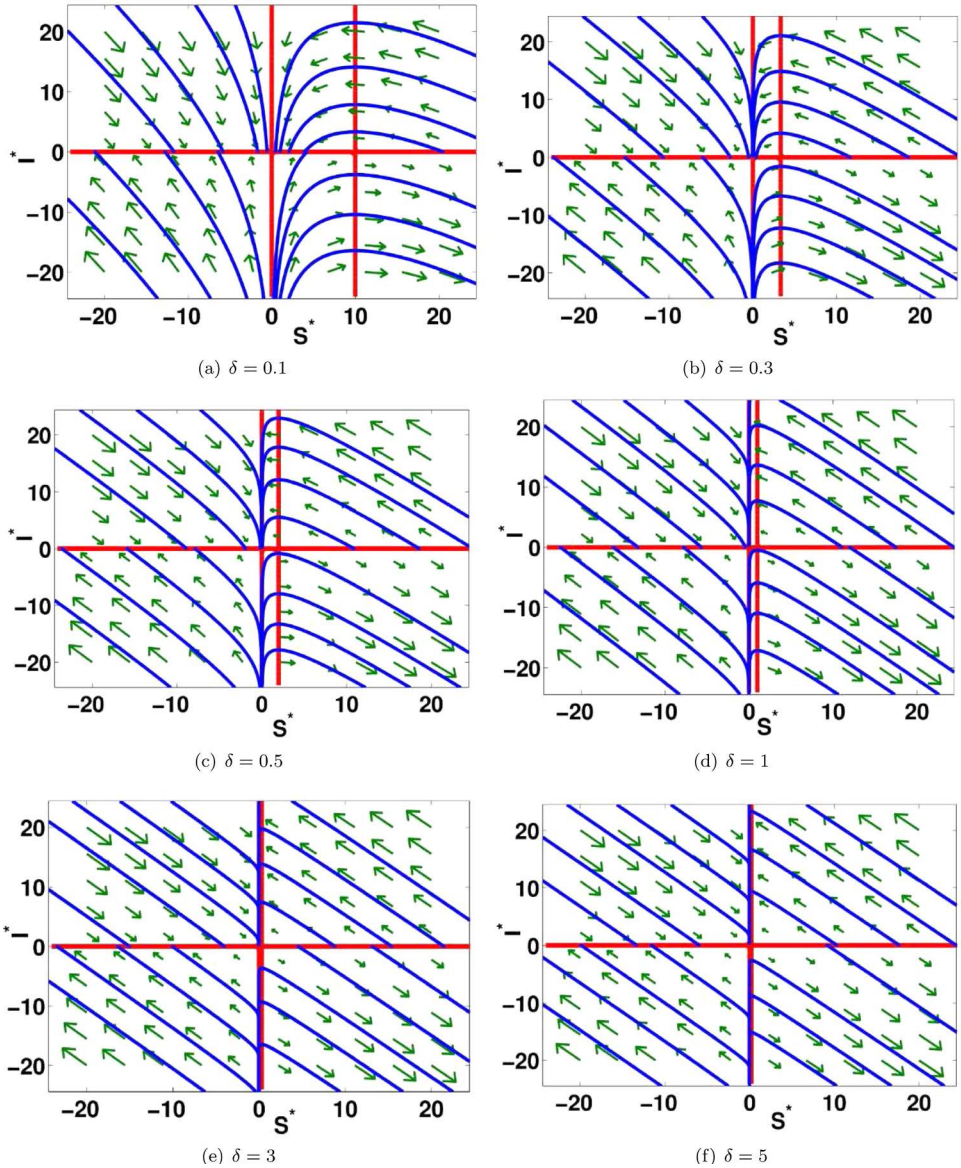
The flowchart of proposed steps of model analysis and simplification, the steps are presented in the order of their application.

4. Local Behaviours of the Simplified Model

We use Pplane8 for Mathlab to study the stability analysis of the Equation (12) and to compute numerical simulations in S^*I^*-plane, we also identify model nullclines; see Figure 2. It can be concluded that the model has the same stability properties at different values for the parameter used.

Furthermore, we identify the model interacting and numerical simulations in two and three dimensional planes, for different values of δ; see Figure 3 and Figure 4. We notice that the dynamics of susceptible and infective people go to stable state very quickly as δ becomes larger. Results are given here by using Pplane8 for Mathlab.

In addition, we calculate the local sensitivity of state variables S^* and I^* with respect to the given parameter δ to identify critical mode parameters. We identify that infective people are more sensitive to the constant rate δ when $\delta \in (0, 0.4)$ while

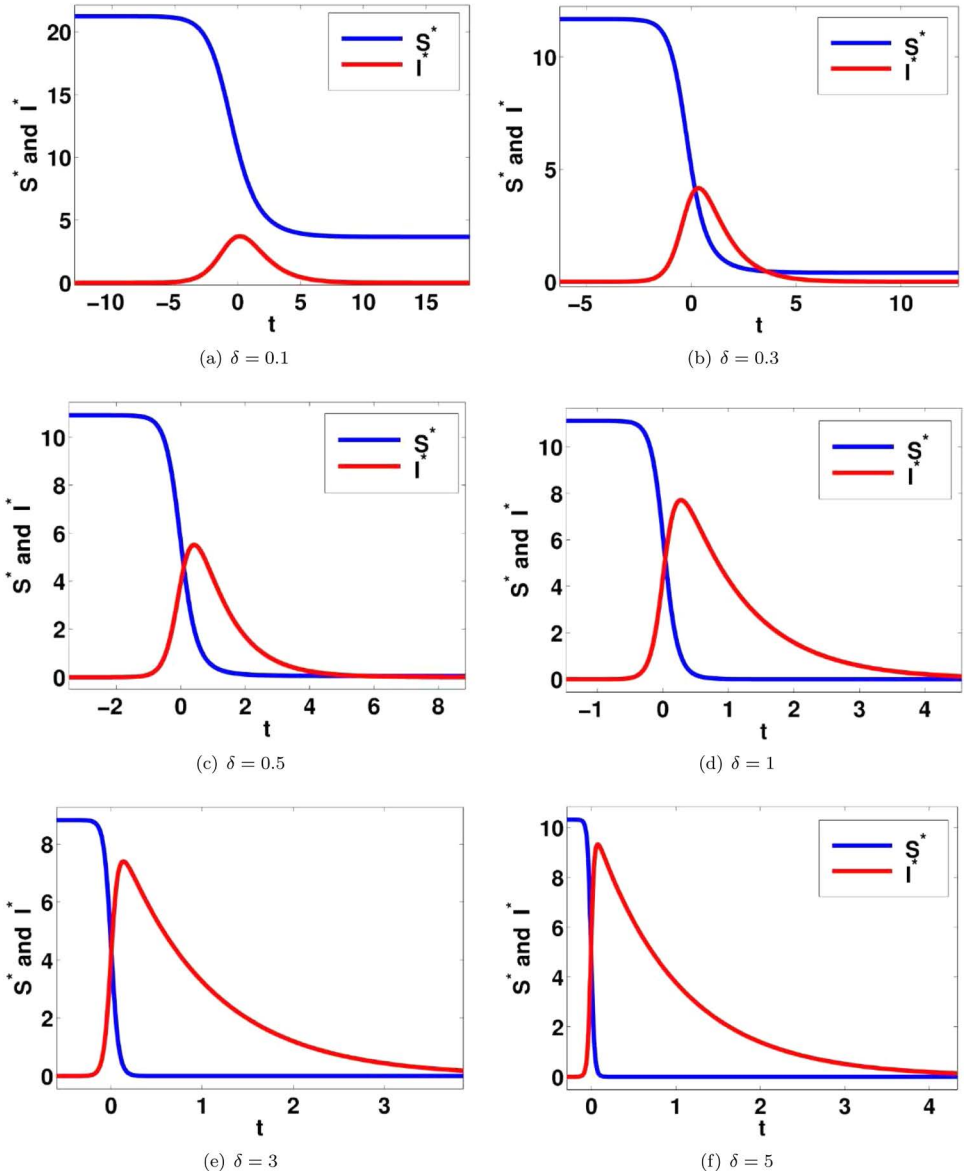


(a) $\delta = 0.1$ (b) $\delta = 0.3$

(c) $\delta = 0.5$ (d) $\delta = 1$

(e) $\delta = 3$ (f) $\delta = 5$

Figure 2. Dynamics of the Equation (12) and numerical simulations using Pplane8 for Mathlab in S^*I^*-plane for different values of parameter δ, red lines stand for model nullclines.



(a) $\delta = 0.1$ (b) $\delta = 0.3$

(c) $\delta = 0.5$ (d) $\delta = 1$

(e) $\delta = 3$ (f) $\delta = 5$

Figure 3. Dynamics of the simplified model and numerical simulations using Pplane8 for Mathlab in two dimensional plane, for different values of parameter δ.

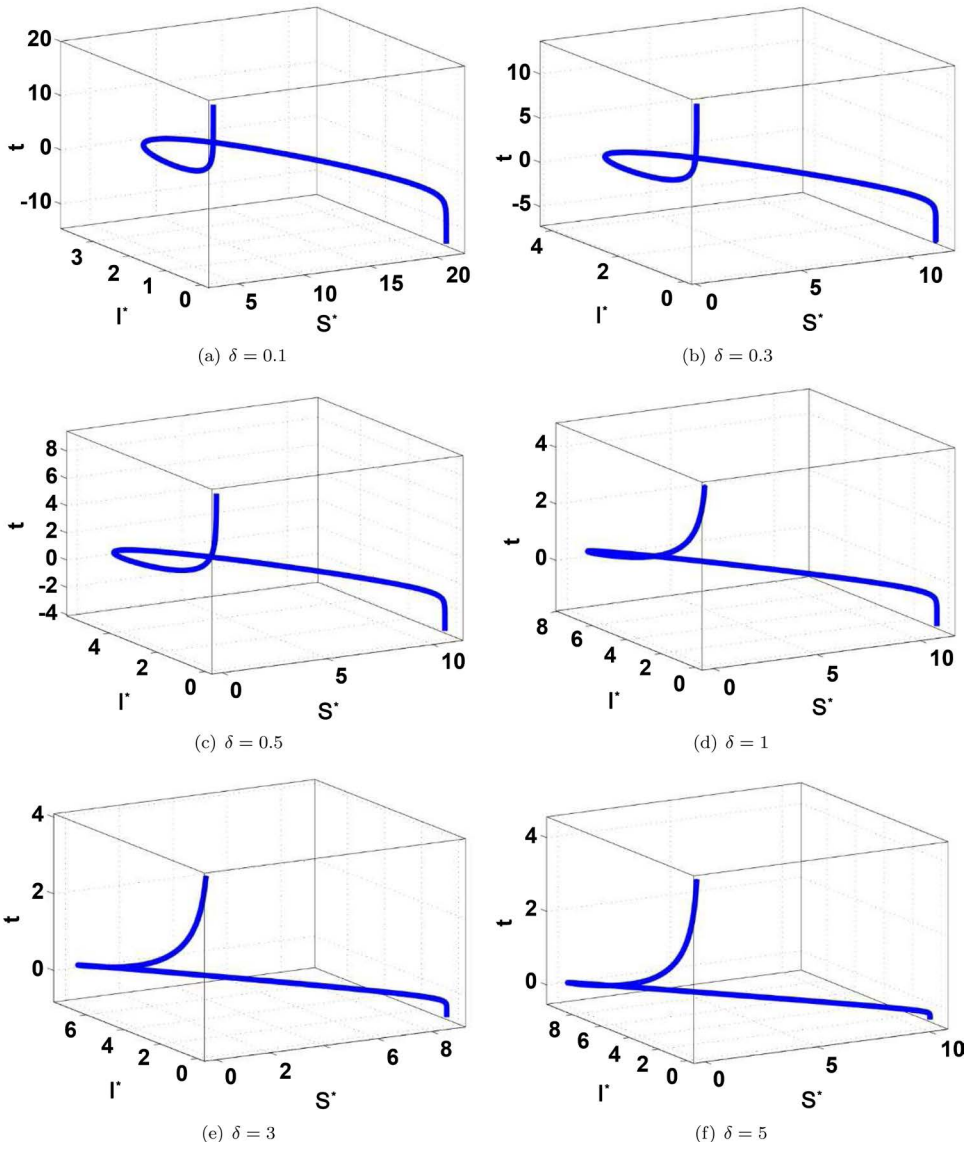
they are less sensitive to the given parameter δ as $\delta > 0.4$. More interestingly, both susceptible and infective people have same sensitivity to δ when $\delta = 0.4$; see **Figure 5**. Results here are computed in numerical simulations using the SimBiology Toolbox for Mathlab in the time interval $[0,10]$ unites of time. Identifying critical model parameters in this study is a good step forward for describing and understanding the model dynamics in systems biology.

5. The Global Behaviours of the Simplified Model

This section is devoted to examine the global phase portrait for Equation (12) by studying the isoclines and the behaviours at infinity. The isoclines are the lines with equal slope. These lines are an important role in sketching the phase portrait. It is easy to know where the trajectories have vertical and horizontal tangent lines by finding the

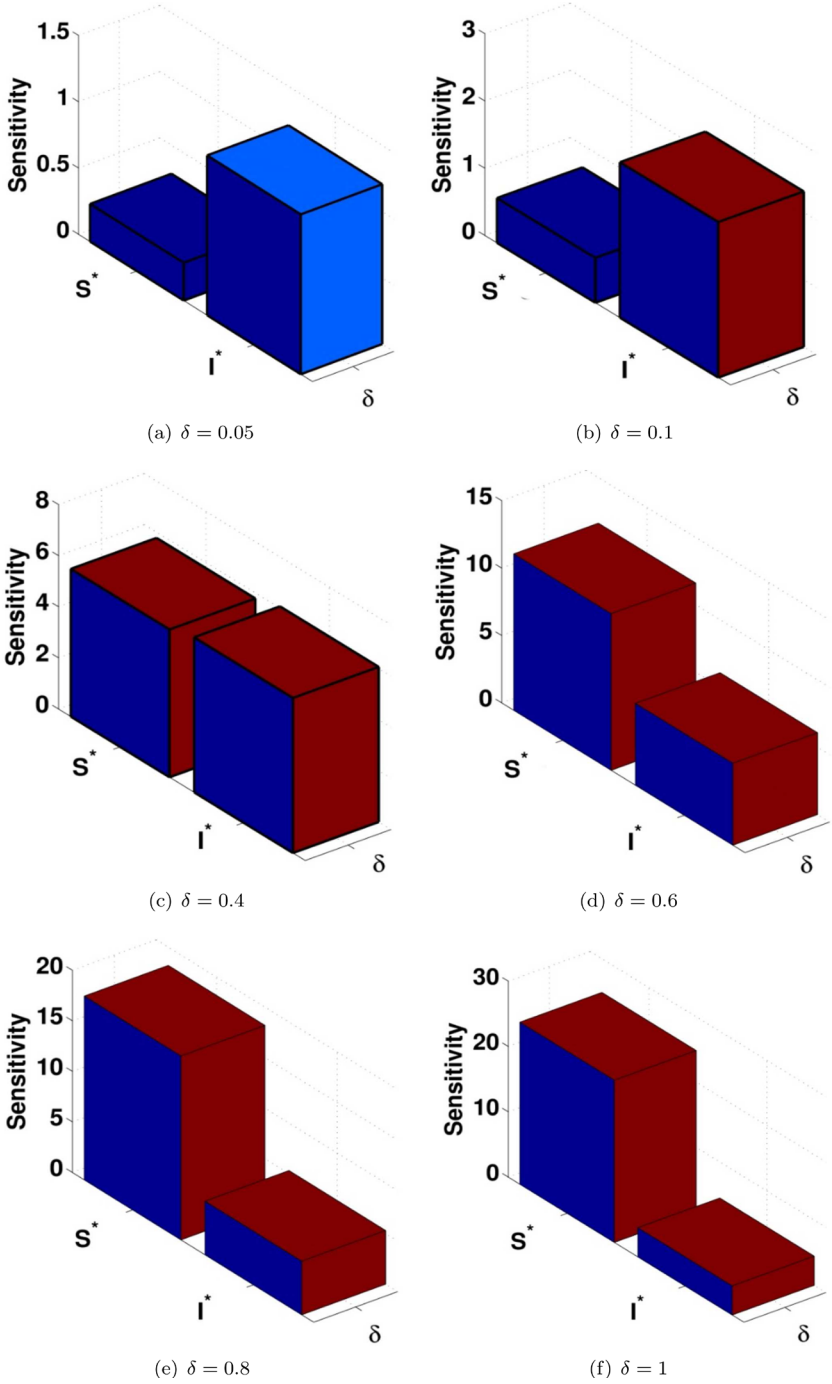
isoclines for $\frac{\mathrm{d}S^*}{\mathrm{d}\tau}$ and $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}$. There are no motion horizontally and vertically when $\frac{\mathrm{d}S^*}{\mathrm{d}\tau}=0$ and $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}=0$ respectively. The vertical trajectories are given by $\frac{\mathrm{d}S^*}{\mathrm{d}\tau}=0$ which are $S^*=0$ and $I^*=0$. The horizontal trajectories are given by $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}=0$ which are $\delta S^*-1=0$. From above, we note that $S^*=0$ is an invariant line and $I^*=0$ is a line of singularities. Since the Jacobian matrix at each points on the line of singularities, $I^*=0$, are 0 and δS^*-1, therefore the singular points that are belonging to the left side of the vertical line, $S^*=\frac{1}{\delta}$, are stable and on the other side are unstable.

Here, we study the direction of trajectories in the quadrants. In the first quadrant,



(a) $\delta=0.1$ (b) $\delta=0.3$ (c) $\delta=0.5$ (d) $\delta=1$ (e) $\delta=3$ (f) $\delta=5$

Figure 4. Dynamics of the simplified model and numerical simulations using Pplane8 for Mathlab in three dimensional plane, for different values of parameter δ.



(a) $\delta = 0.05$ (b) $\delta = 0.1$

(c) $\delta = 0.4$ (d) $\delta = 0.6$

(e) $\delta = 0.8$ (f) $\delta = 1$

Figure 5. The local sensitivity of state variables S^* and I^* with respect to the given parameter δ for different values, using the SimBiology Toolbox for Mathlab in the time interval $[0,10]$ unites of time.

since S^* and I^* are positive, then $\frac{\mathrm{d}S^*}{\mathrm{d}\tau}$ is always negative, $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}$ is negative where $S^* < \frac{1}{\delta}$ and $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}$ is positive where $S^* > \frac{1}{\delta}$. In the second and third quadrants, $\frac{\mathrm{d}S^*}{\mathrm{d}\tau} > 0$, $\frac{\mathrm{d}I^*}{\mathrm{d}\tau} < 0$ and $\frac{\mathrm{d}S^*}{\mathrm{d}\tau} < 0$, $\frac{\mathrm{d}I^*}{\mathrm{d}\tau} > 0$ respectively. In the fourth quadrant, $\frac{\mathrm{d}S^*}{\mathrm{d}\tau}$

is always positive, but $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}$ is positive where $S^* < \frac{1}{\delta}$ and $\frac{\mathrm{d}I^*}{\mathrm{d}\tau}$ is negative where $S^* > \frac{1}{\delta}$.

The second required one is the line at infinity. It is a projective line that is added to the affine plane. Finding them including singular points and studying the behaviours at infinity of the reduced Equation (12) is very important to an understanding its global dynamics. For this purpose, the two below nonlinear change of variables are used individually.

$$X = \frac{1}{S^*}, \text{ and } Y = \frac{I^*}{S^*}; S^* \neq 0. \tag{20}$$

$$X = \frac{S^*}{I^*}, \text{ and } Y = \frac{1}{I^*}; I^* \neq 0. \tag{21}$$

Salih in [38] have used above transformation in three dimensional case. The points $(0, Y_0)$ and $(X_0, 0)$ where $\dot{X}$, and $\dot{Y}$ vanish are obtained from the nonlinear change of coordinates (20) and (21) respectively. These are the singular points of the new system that are corresponding to the singular points at infinity for simplified Equation (12).

Applying the nonlinear change of variables (20) on the reduced Equation (12) and after rescaling of the variables, the new system is obtained

$$\begin{aligned} \dot{X} &= \delta XY, \\ \dot{Y} &= -Y(-\delta + X - \delta Y). \end{aligned} \tag{22}$$

The above system has two singular points $S_\infty(0,0)$ and $L_{1\infty}(0,-1)$. The first one is the intersection point of the line at infinity $L_\infty = \{X = 0\}$ and S^* − axis, the system at that point has Jacobian matrix

$$J = \begin{bmatrix} 0 & 0 \\ 0 & \delta \end{bmatrix}, \tag{23}$$

with a positive δ and one zero eigenvalues, therefore the singular point is unstable. The Jacobian at the second singular point $L_\infty(0,-1)$ is given by

$$J = \begin{bmatrix} -\delta & 0 \\ 1 & -\delta \end{bmatrix}, \tag{24}$$

with two negative eigenvalues $-\delta$ and $-\delta$, the singular point is stable.

The system below is obtained by applying the nonlinear change of variables Equation (21) on Equation (12) after rescaling of variables

$$\begin{aligned} \dot{X} &= -X(\delta + \delta X - Y), \\ \dot{Y} &= -Y(\delta X - Y). \end{aligned} \tag{25}$$

System (25) has only two singular points $I_\infty(0,0)$ and $L_{2\infty}(-1,0)$. At the first singular point $I_\infty(0,0)$, Equation (12) has Jacobian matrix

$$J = \begin{bmatrix} -\delta & 0 \\ 1 & 0 \end{bmatrix}, \tag{26}$$

which it has one negative eigenvalue $-\delta$ and a zero eigenvalue. At the second singu-

lar point $L_{2\infty}(-1,0)$, Equation (12) has Jacobian matrix

$$J = \begin{bmatrix} \delta & -1 \\ 0 & \delta \end{bmatrix}, \tag{27}$$

which it has two positive eigenvalues δ and δ. **Figure 6** shows the dynamics behaviours at an affine plane and also at infinity, which exams a good understanding of the global behaviours of the Equation (12). We note that, the sum of the ratio of eigenvalues of either line is unity according to an index formula Lins Neto [39].

6. Conclusion

Mathematical presentations and numerical simulations of infectious disease models are crucial topics in systems biology. Describing the dynamics of such systems often requires some techniques of model analysis. We studied an epidemic disease model called SIR model with three species and two parameters. We proposed a number of steps of

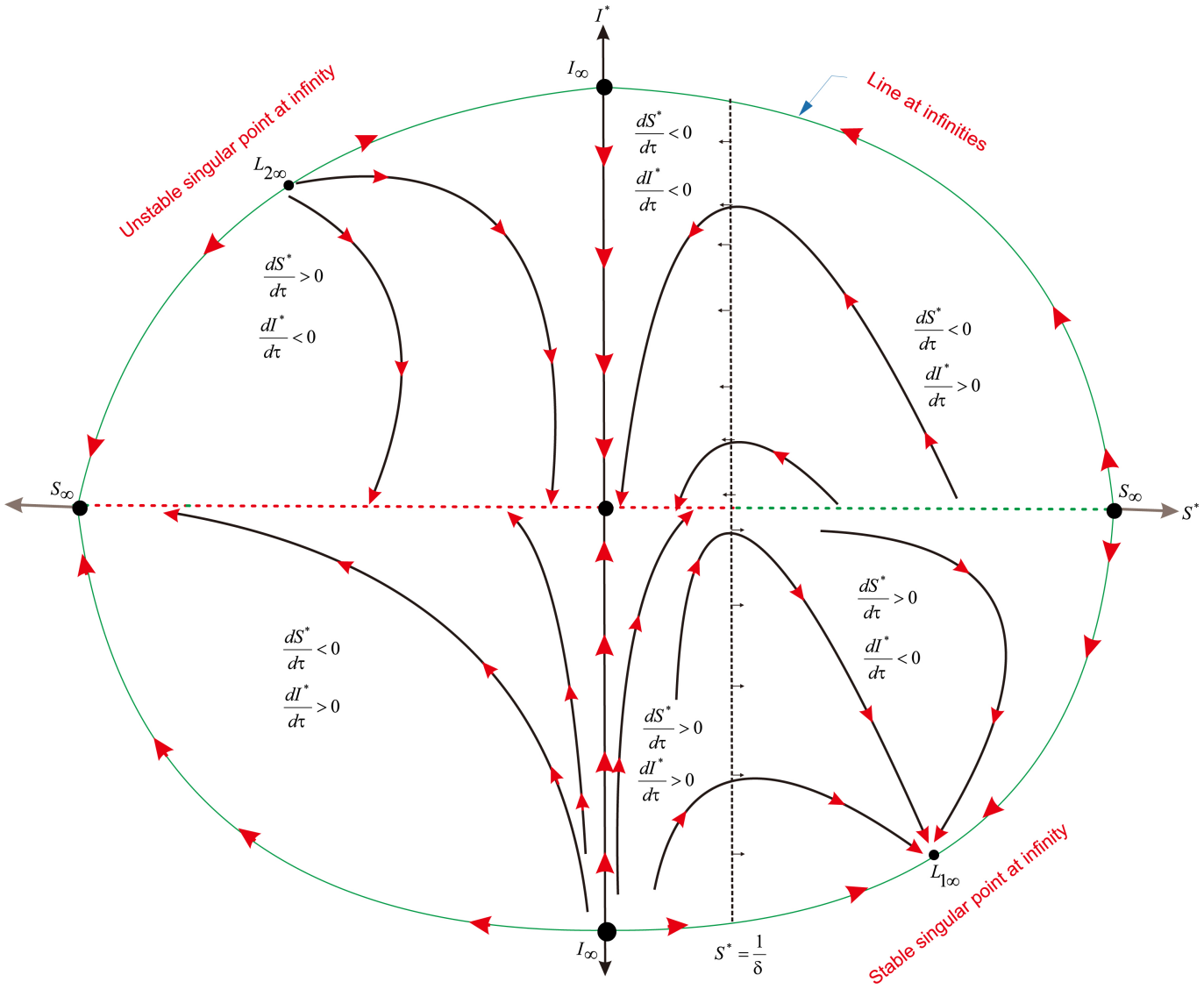


Figure 6. Global phase portraits of the simplified Equation (12); the green solid curves depict the line at infinities, the green dotted lines depict unstable singular points and the red dotted line depict stable singular point.

model analysis. The suggested steps of model analysis here importantly play in reducing the number of elements and in calculating analytical approximate solutions of the SIR model. The simplified model helps to study the full model of SIR in different ways. Firstly, identifying the critical model parameters of the reduced model becomes much easier compared to the full model. Secondly, the mathematical representation of the reduced model can help to integrate experimental knowledge into a coherent picture. Furthermore, studying the behaviour at infinity of the reduced model helped us to understand its global dynamics and to draw the global phase portrait of the system. Finally, the reduced model could be accurate, robust, and applied by biologists for various purposes. The proposed techniques here of model analysis will be applied to a wide range of complex infectious disease models in systems biology.

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