Journal of Nonlinear Modeling and Analysis
Volume 6, Number 4, December 2024, 1046–1063
http://jnma-online.com
DOI:10.12150/jnma.2024.1046

Global Stability of an SIR Model Characterized by Vaccination and Treatment

G. Shailaja[1,†] and M. A. Srinivas[2]

Abstract The global dynamics of a SIR model characterized by both vaccination and treatment are considered in the present paper. Global stability ensures convergence to an equilibrium solution irrespective of the initial state of infection. Various independent sets of sufficient conditions on parameters and functional relations are obtained through Lyapunov functionals for stability. It is also established how a disease-free environment can be provided by a proper combination of treatment and vaccination, which is a unique feature as far as SIR models are concerned, as many of the studies have ignored the influence of treatment. Results are illustrated with numerical examples and simulations are provided to visualize the illustrations.

Keywords Infectious disease model, vaccination and treatment, Lyapunov function, equilibrium, global stability

MSC(2010) 37L45, 37D35, 34D23.

1. Introduction

Infectious diseases are mainly caused due to disharmonious ecological interaction amongst microbial infectious agents (bacteria, fungi, parasites, or viruses) and a host. The disease dynamics are influenced by biological, social, behavioral, cultural and environmental changes. Intrinsic to the continuous process of globalization and urbanization, which can build up or ease the hosts exposure to the sources of disease and consequently its transmission in the population, there is a constant transformation in the interaction dynamics ([9]). A critical understanding of transmission dynamics and the connection between various influencing factors is important for the coherent development of an effective plan of action for prevention, control and health assistance. For a field scientist engaged in this activity, it is a difficult question in general, to appraise the rate of the spread of disease and the control of parameters. Also, the affordability of clinical trials and modification costs are another challenge. This situation demands methods/ strategies that have the potential to deal with the disease outbreak when it is in an active phase.

In this frame of reference, mathematical modelling is able to provide useful insights regarding transmission patterns and the detection of parameters to mitigate

[†]the corresponding author.
Email address: 249shailaja@gmail.com (G. Shailaja),
massrinivas@gmail.com (M. A. Srinivas)
[1]Department of Humanities and Sciences, Malla Reddy College of Engineering and Technology, Secunderabad, 500100, India.
[2]Department of Mathematics, JNTUH College of Engineering, Hyderabad, 500085, India.

disease in the population. Mathematical models have the ability to translate biological, clinical, environmental, epidemiological and social data into mathematical equations and vice versa. This adaptive nature helps in developing models using collected information from experimental trials, which can be utilized to study the epidemiological behavior of the infectious disease and analyze the effectiveness of interventions taking into consideration several factors that could influence the dynamics of the disease transmission. The rational development of effective, low-cost strategies for prevention and control, health assistance and development of health policies are essential for guiding public health decision-making [18, 42]. One of the very popular models used to study infectious diseases is the susceptible, infected and recovered populations (SIR, for short) model. In this context, mathematical models have been developed to study about the dynamics of the disease such as Influenza A [6], Zika [29], Ebola [41], SARS [3, 25], MERS [1, 23], malaria [4, 7], yellow fever [28], cholera [38], chikungunya [11, 26], dengue [13, 27, 43] and COVID-19 [8, 10, 16, 21, 24, 30, 34, 40]. One may refer to [2, 5, 12, 14, 15, 17, 19, 20, 33, 37, 39] for some more models available in literature.

In this paper, we are going to make a detailed analysis of the global dynamics of an SIR model in which the roles of vaccination and treatment in controlling the spread of disease are the main focus. The model ([35]) is described by the following system of equations:

$$\begin{aligned} u^{'} &= a - bf(u,v) - du - cV(u) + \alpha w, \\ v^{'} &= b_1 f(u,v) - rP(v) - d_1 v, \\ w^{'} &= rP(v) - \alpha w. \end{aligned} \tag{1.1}$$

Here, $u(t)$, $v(t)$, and $w(t)$ represent susceptible, infected, and recovered (by treatment) populations at any time t respectively.

$' = \dfrac{d}{dt}$ denotes the time derivative of a function.

$a \geq 0$ is the rate of growth of the susceptible population, $b > 0$ denotes the interaction rate of infected with susceptible, d denotes the rate of susceptible individuals who are naturally immune to the infection and in no way get infected, $c > 0$ is the vaccination rate and the parameter $\alpha > 0$ is the rate at which a recovered person becomes susceptible again as he is not-vaccinated and re-exposed to infection. $0 < b_1 \leq b$ is the rate of conversion of susceptibles into infected, $d_1 > 0$ is the death rate of the infected population not at all treated or inadequately treated or beyond the treatment, $r > 0$ represents the treatment rate and also recovery rate. f denotes the infection function which shows how susceptible u are converted into infected v, $V(u)$ is the vaccination function (depends on susceptible population), and $P(v)$ is the recovery (by treatment) function of the infected individuals. All these functions are assumed to be continuous functions over the intervals of definitions.

It was claimed in [35] that several models on the SIR system become special cases of system (1.1). The model is quite general in this sense. System (1.1) includes a term that represents the treatment efforts in containing the spread of the disease (controlling the interaction of the infected population with the susceptible). This is a unique feature considering SIR models as most of the other studies concentrate on efforts of vaccination and ignore the influence of treatment. The reason could possibly be society worries more about epidemics than infectious diseases depending on the impacts they make. To elaborate, epidemics may not give enough time to treat, occur suddenly, and are impulsive in nature. On the other hand, infectious

diseases provide scope for study and examination. Thus, the roles of vaccination and treatment interchange in epidemics to infectious diseases. In the present scenario of Covid-19 also, it is useful to reconsider such models with treatment efforts to study their impact on containing the disease.

Little work is reported on the influence of treatment of the infected population. Studies of epidemics or disease models have focused on vaccination or measures based on clinical data etc. It is established in ([31, 32]) that vaccination alone cannot handle the spread of disease. It is important to observe that treatment as an in-patient is better than a quarantine, as it ensures both isolation for an infected person and treatment for the infection. A fully treated person has a little chance of reinfection and is no more infectious. Further, it is shown that a proper combination of treatment and vaccination provides a disease-free environment and neither of the efforts is completely efficient in eradicating the disease when applied alone.

There are different metrics used in understanding the spread of a disease and the most accepted one is the basic reproduction number (denoted by R_0) which is the number of secondary infections caused by a primary contact. Usually, $R_0 < 1$ implies that the spread of disease is not effective while $R_0 > 1$ implies the prevalence of disease. For mathematical modelers, it is a pleasure to study the stability aspects of equilibria: (i) stability of a disease-free equilibrium implies eradication of the disease and (ii) stability of disease equilibrium means the disease prevalence. Though an estimate of R_0 gives an idea of disease spread, it may not provide a complete picture of the dynamics. In [32], it is established that the control of disease is difficult even if $R_0 < 1$, for example, in the case of a co-infection due to a comorbidity such as diabetes. Local stability of equilibria is dependent on the initial conditions of the system. It helps understand conflicts or control of the disease environment, when the initial conditions (that is, the initial status of the disease) are, near the equilibria but it cannot be applied if the information provided is not near enough to the equilibrium state. On the other hand, the global stability conditions are applicable irrespective of the initial conditions (status of the beginning or initial spread of disease). Thus, the global stability of disease-free equilibrium shows that the disease will be eradicated how predominant the disease was initially, and the global stability of endemic equilibrium urges us to improve the measures to be taken.

In [35], only the local stability of equilibria is emphasized, the authors expressed the difficulty in providing conditions for global stability of system (1.1), as it is a very complex system with at least three nonlinear functions representing the interactions and conversions. Only one global asymptotic stability condition was obtained, that too for a special case of the model (1.1) in which all functional relations are assumed to be linear $f(u) = u, P(v) = v$ and $V(u) = u$. Though the model is very complex and involves too many terms, the study in system(1.1) hints that the system has some stabilizing terms in each equation. Moreover, global stability establishes the strength of vaccination, treatment, and controlling the spread of disease irrespective of the situation where it is identified. With this support, we wish to pursue the global asymptotic stability (GAS, for short) of equilibria of (1.1) in this article.

The paper is organized as follows. Different Lyapunov function(al)s and inequality analyses enable us to obtain several sufficient conditions for the global asymptotic stability of (1.1) in Section 2. We provide examples to illustrate the results and check for their independence in Section 3. We provide simulations using ODE23 of MATLAB to provide a pictorial representation of examples. A discussion

concludes the paper in Section 4.

2. GAS results

The term $f(u,v)$ that represents the conversion of susceptibles into infected is the main villain that hurdles any attempt to provide global stability results of (1.1). To simplify this, we let $f(u,v) = f(u)v$ as our first case. This type of assumption is quite common in biological models inferring that each infected v converts $f(u)$ of u. For the examples of $f(u)$ one may refer to [35,36]. Different functions popular in literature are presented in examples. We come back to the general function $f(u,v)$ a little later in this paper. With this assumption of f, we consider

$$\begin{aligned} u^{'} &= a - bf(u)v - du - cV(u) + \alpha w, \\ v^{'} &= b_1 f(u)v - rP(v) - d_1 v, \\ w^{'} &= rP(v) - \alpha w, \end{aligned} \tag{2.1}$$

with appropriate initial conditions.

Equilibria for this system are given by

$$\begin{aligned} a - bf(u^*)v^* - du^* - cV(u^*) + \alpha w^* &= 0, \\ b_1 f(u^*)v^* - rP(v^*) - d_1 v^* &= 0, \\ rP(v^*) - \alpha w^* &= 0. \end{aligned} \tag{2.2}$$

Clearly a solution of (2.2) is $(u^*, 0, 0)$, where u^* solves $du^* + cV(u^*) = a$. In [35], it is shown that a sufficient condition for the existence of such a disease-free equilibrium is $0 < V(a/d) < \infty$ so that the curves $a - du^*$ and $cV(u^*)$ meet, yielding a u^* satisfying the above equation.

Also (2.2) has a positive solution yielding an endemic equilibrium for (2.1) that represents a disease environment. Explicit expressions for equilibrium points are difficult to obtain at this stage in view of the presence of nonlinear functions in all the equations. However, we estimate these equilibria for the functions considered in the illustrative examples provided in a later section. Hence, we assume tacitly, hereafter, that the equilibria to system (2.1) do exist. Unless specified, we hereafter designate an equilibrium solution of (2.1) by (u^*, v^*, w^*) whether it is endemic or disease free.

Using (2.2) in (2.1), we get after rearrangement,

$$\begin{aligned} (u-u^*)^{'} &= -bf(u)(v-v^*) - bv^*(f(u) - f(u^*)) - d(u-u^*) \\ &\quad -c(V(u) - V(u^*)) + \alpha(w - w^*) \\ (v-v^*)^{'} &= b_1 f(u)(v-v^*) + b_1 v^*(f(u) - f(u^*)) - r(P(v) - P(v^*)) - d_1(v-v^*) \\ (w-w^*)^{'} &= r(P(v) - P(v^*)) - \alpha(w-w^*). \end{aligned} \tag{2.3}$$

We make the following assumptions on the functions. There exist positive constants L_1, L_2, M_1, M_2, N_1, and N_2 such that

$$L_1 \leq \frac{f(u) - f(u^*)}{u - u^*} \leq L_2; M_1 \leq \frac{V(u) - V(u^*)}{u - u^*} \leq M_2; N_1 \leq \frac{P(v) - P(v^*)}{v - v^*} \leq N_2 \tag{2.4}$$

respectively for $u \neq u^*, v \neq v^*$.

We further assume that f is bounded and is such that

$$f(u) < \frac{rN_1 + d_1}{b_1}, \forall u. \tag{2.5}$$

With these assumptions, we shall establish our results.

Theorem 2.1. *Assume that the functional relations in (2.1) satisfy conditions (2.4) and (2.5).The equilibrium solution (u^*, v^*, w^*) of (2.1) is globally asymptotically stable, provided the parameters satisfy the following inequalities,*
(i) $B^2 < 4p_1q_1AC$, *(ii)* $\alpha^2 < 4p_2\alpha_1 A$, *(iii)* $r^2N_2^2 \leq 4q_2\alpha_2 C$,
where $A = L_1bv^* + d + cM_1$, $B = \max\limits_{u\geq 0}\{b_1v^*L_2 - bf(u)\}$, $C = \min\limits_{u\geq 0}\{rN_1 + d_1 - b_1f(u)\}$, p_1, p_2, q_1, q_2 *and* α_1, α_2 *are positive constants, such that* $p_1 + p_2 = 1, q_1 + q_2 = 1$, *and* $\alpha_1 + \alpha_2 = \alpha$.

Proof. We consider the function

$$U(t) \equiv U(u, v, w) = \frac{1}{2}(u - u^*)^2 + \frac{1}{2}(v - v^*)^2 + \frac{1}{2}(w - w^*)^2.$$

Clearly, $U(u^*, v^*, w^*) = 0$ and $U(u, v, w) > 0$ for $(u, v, w) \neq (u^*, v^*, w^*)$. Now, along the solutions of (2.1) using (2.3), we have that the time derivative of U is given by

$$\begin{aligned}
U' =& (u - u^*)[-bf(u)(v - v^*) - bv^*(f(u) - f(u^*)) - d(u - u^*) \\
&- c(V(u) - V(u^*))v + \alpha(w - w^*)] + (v - v^*)[b_1f(u)(v - v^*) \\
&+ b_1v^*(f(u) - f(u^*) - r(P(v) - P(v^*)) - d_1(v - v^*)] \\
&+ (w - w^*)[r(P(v) - P(v^*)) - \alpha(w - w^*)] \\
=& - d(u - u^*)^2 - bv^*(f(u) - f(u^*))(u - u^*) - c(V(u) - V(u^*))(u - u^*) \\
&- bf(u)(u - u^*)(v - v^*) + \alpha(w - w^*)(u - u^*) - d_1(v - v^*)^2 + b_1f(u)(v - v^*)^2 \\
&- r(P(v) - P(v^*))(v - v^*) + b_1v^*(f(u) - f(u^*))(v - v^*) \\
&- \alpha(w - w^*)^2 + r(P(v) - P(v^*))(w - w^*) \\
=& - \Big[d + bv^*\frac{f(u) - f(u^*)}{u - u^*} + c\frac{V(u) - V(u^*)}{u - u^*}\Big](u - u^*)^2 - bf(u)(u - u^*)(v - v^*) \\
&+ \alpha(w - w^*)(u - u^*) - \Big[d_1 - b_1f(u) + r\frac{P(v) - P(v^*)}{v - v^*}\Big](v - v^*)^2 \\
&+ b_1v^*\frac{f(u) - f(u^*)}{u - u^*}(u - u^*)(v - v^*) - \alpha(w - w^*)^2 \\
&+ r\frac{P(v) - P(v^*)}{v - v^*}(v - v^*)(w - w^*) \\
\leq& - \big[d + bv^*L_1 + cM_1\big](u - u^*)^2 + \big[b_1v^*L_2 - bf(u)\big](u - u^*)(v - v^*) \\
&- \big[d_1 + rN_1 - b_1f(u)\big](v - v^*)^2 + \alpha(w - w^*)(u - u^*) \\
&+ rN_2(v - v^*)(w - w^*) - \alpha(w - w^*)^2 \\
\leq& - \big[p_1A(u - u^*)^2 - B(u - u^*)(v - v^*) + q_1C(v - v^*)^2\big] \\
&- \big[p_2A(u - u^*)^2 - \alpha(u - u^*)(w - w^*) + \alpha_1(w - w^*)^2\big] \\
&- \big[q_2C(v - v^*)^2 - rN_2(v - v^*)(w - w^*) + \alpha_2(w - w^*)^2\big].
\end{aligned} \tag{2.6}$$

Each term in the right hand side of the above inequality (2.6) is of the form $-\left[lx^2+mxy+ny^2\right]$. We know that the expression $lx^2+mxy+ny^2$ is positive definite if and only if $l>0, n>0$ and $m^2<4ln$ and correspondingly, $-\left[lx^2+mxy+ny^2\right]$ is negative definite. Letting $l=p_1A,\ m=-B,\ n=q_1C$ and $x=u-u^*,\ y=v-v^*$ and $z=w-w^*$,and observing that $A>0$ by assumptions on parameters and $C>0$ follows from (2.5), the first term on the right hand side of (2.6),that is,

$$-\left[p_1A(u-u^*)^2-B(u-u^*)(v-v^*)+q_1C(v-v^*)^2\right]$$

is negative definite by assumption (i) above. Similarly assumptions (ii) and (iii) ensure the negative definiteness of the second and third expressions of (2.6). Hence, the RHS of inequality (2.6) is negative definite, and hence it follows that $U'<0$ along the solutions of (2.1) (using (2.3)). Thus, U defined above is the Lyapunov function required and the rest of the argument follows from standard results (c.f., [22]). Hence, the equilibrium solution (u^*,v^*,w^*) is globally asymptotically stable. □

Remark 2.1. Consider the following rearrangement of (2.6).

$$\begin{aligned}U'\leq\ &-p_2A(u-u^*)^2+B(u-u^*)(v-v^*)-q_1C(v-v^*)^2\\ &-p_1A(u-u^*)^2+\alpha(u-u^*)(w-w^*)-\alpha_1(w-w^*)^2\\ &-q_2C(v-v^*)^2+rN_2(v-v^*)(w-w^*)-\alpha_2(w-w^*)^2.\end{aligned}$$

Then the negative definiteness of U' follows from the conditions on the parameters $(iv)\ B^2<4p_2q_1AC$, $(v)\ \alpha^2<4p_1\alpha_1A$, $(vi)\ r^2N_2^2\leq 4q_2\alpha_2C$.

Thus, (iv)-(vi) provide another set of sufficient conditions for global asymptotic stability of the equilibrium solution.

An interested reader may explore further combinations of terms to establish negative definiteness of U'. We provide a couple of such conditions as a matter of fact.

$(vii)\ B^2<4p_1q_2AC$, $(viii)\ \alpha^2<4p_1\alpha_1A$, $(ix)\ r^2N_2^2\leq 4q_1\alpha_2C$,
$(x)\ B^2<4p_2q_2AC$, $(xi)\ \alpha^2<4p_1\alpha_1A$, $(xii)\ r^2N_2^2\leq 4q_1\alpha_2C$.

We present one more result on stability.

Theorem 2.2. *Assume that the functions f,V,P satisfy (2.4) and (2.5). Further, the parameters satisfy*

$$\triangle\cong Min\left\{A-\frac{B}{2}-\frac{\alpha}{2},C-\frac{rN_2}{2}-\frac{B}{2},\frac{\alpha}{2}-\frac{rN_2}{2}\right\}>0, \tag{2.7}$$

where A,B,C are as in Theorem 2.1. Then the equilibrium solution (u^*,v^*,w^*) of (2.1) is globally asymptotically stable.

Proof. Employing the same Lyapunov functional U in Theorem 2.1 and proceeding, we have from (2.6) that

$$\begin{aligned}U'\leq\ &-A(u-u^*)^2+B(u-u^*)(v-v^*)+rN_2(v-v^*)(w-w^*)\\ &-C(v-v^*)^2+\alpha(u-u^*)(w-w^*)-\alpha(w-w^*)^2.\end{aligned} \tag{2.8}$$

Splitting the product term using $uv\leq\frac{1}{2}(u^2+v^2)$ and rearranging, we obtain

$$U'\leq-\left(A-\frac{B}{2}-\frac{\alpha}{2}\right)(u-u^*)^2-\left(C-\frac{rN_2}{2}-\frac{B}{2}\right)(v-v^*)^2$$

$$
\begin{aligned}
&- \left(\frac{\alpha}{2} - \frac{rN_2}{2}\right)(w-w^*)^2 \\
&\leq - \triangle U, \qquad (2.9)
\end{aligned}
$$

or $U^{'} + \triangle U \leq 0$, and the conclusion that $U \to 0$ as $t \to \infty$ follows from theory. Thus, $(u-u^*, v-v^*, w-w^*) \to (0,0,0)$ for large t. Therefore, (u^*, v^*, w^*) is globally asymptotically stable. □

Remark 2.2. Notice that Theorem 2.1 and Theorem 2.2 utilize the same Lyapunov functional and restriction on functional relations to provide two different sets of parametric conditions for global stability. Splitting of the product term into different combinations provides the scope for obtaining different sets of conditions on parameters. This may be seen below. We consider the following arrangements:

1. $B(u-u^*)(v-v^*) \leq \frac{B^2}{2}(u-u^*)^2 + \frac{1}{2}(v-v^*)^2$,
2. $B(u-u^*)(v-v^*) \leq \frac{1}{2}(u-u^*)^2 + \frac{B^2}{2}(v-v^*)^2$,
3. $rN_2(v-v^*)(w-w^*) \leq \frac{r^2N_2^2}{2}(v-v^*)^2 + \frac{1}{2}(w-w^*)^2$,
4. $rN_2(v-v^*)(w-w^*) \leq \frac{1}{2}(v-v^*)^2 + \frac{r^2N_2^2}{2}(w-w^*)^2$,
5. $rN_2(v-v^*)(w-w^*) \leq \frac{r^2}{2}(v-v^*)^2 + \frac{N_2^2}{2}(w-w^*)^2$,
6. $rN_2(v-v^*)(w-w^*) \leq \frac{N_2^2}{2}(v-v^*)^2 + \frac{r^2}{2}(w-w^*)^2$,
7. $\alpha(u-u^*)(w-w^*) \leq \frac{\alpha^2}{2}(u-u^*)^2 + \frac{1}{2}(w-w^*)^2$,
8. $\alpha(u-u^*)(w-w^*) \leq \frac{1}{2}(u-u^*)^2 + \frac{\alpha^2}{2}(w-w^*)^2$.

Using combinations of these terms, we obtain as many as eight types of sufficient conditions as listed below. We may notice that by utilizing combinations of these terms along with those present in Theorem 2.1 and 2.2, a large number of sufficient conditions are possible for global asymptotically stable of (2.1). The same is recorded as the following result.

Theorem 2.3. *Assume that the functions of (2.1) satisfy the conditions (2.4) and (2.5). Then the equilibrium solution (u^*, v^*, w^*) is globally asymptotically stable if any of the following conditions are satisfied.*

1. $\triangle_1 \cong Min\left\{A - \frac{B^2}{2} - \frac{\alpha}{2}, C - \frac{rN_2}{2} - \frac{1}{2}, \frac{\alpha}{2} - \frac{rN_2}{2}\right\} > 0;$
2. $\triangle_2 \cong Min\left\{A - \frac{1}{2} - \frac{\alpha}{2}, C - \frac{rN_2}{2} - \frac{B^2}{2}, \frac{\alpha}{2} - \frac{rN_2}{2}\right\} > 0;$
3. $\triangle_3 \cong Min\left\{A - \frac{B}{2} - \frac{\alpha}{2}, C - \frac{r^2N_2^2}{2} - \frac{B}{2}, \frac{\alpha}{2} - \frac{1}{2}\right\} > 0;$
4. $\triangle_4 \cong Min\left\{A - \frac{B}{2} - \frac{\alpha}{2}, C - \frac{1}{2} - \frac{B}{2}, \frac{\alpha}{2} - \frac{r^2N_2^2}{2}\right\} > 0;$

$$
\begin{aligned}
&5.\quad \triangle_5 \cong Min\left\{A-\frac{B}{2}-\frac{\alpha}{2}, C-\frac{r^2}{2}-\frac{B}{2}, \alpha-\frac{N_2^2}{2}\right\}>0;\\
&6.\quad \triangle_6 \cong Min\left\{A-\frac{B}{2}-\frac{\alpha}{2}, C-\frac{N_2^2}{2}-\frac{B}{2}, \alpha-\frac{r^2}{2}\right\}>0;\\
&7.\quad \triangle_7 \cong Min\left\{A-\frac{B}{2}-\frac{\alpha^2}{2}, C-\frac{rN_2}{2}-\frac{B}{2}, \alpha-\frac{1}{2}\right\}>0;\\
&8.\quad \triangle_8 \cong Min\left\{A-\frac{B}{2}-\frac{1}{2}, C-\frac{rN_2}{2}-\frac{B}{2}, \alpha-\frac{\alpha^2}{2}\right\}>0. \qquad (2.10)
\end{aligned}
$$

Proof. Employing the same Lyapunov functional as in Theorem 2.1, splitting the product term in (2.6) according to 1-8 as in Remark 2.2 and rearranging as in Theorem 2.2, one may establish the required negative definiteness of the Lyapunov functional. The rest of the proof is obvious. □

Remark 2.3. We remark that parametric conditions of Theorem 2.2 and Theorem 2.3 are further open to improvement. For example, employing the following inequality $ab \leq \eta a^2 + \frac{1}{4\eta}b^2$, for any $\eta > 0$, in place of $ab \leq \frac{1}{2}a^2 + \frac{1}{2}b^2$, we have that the parametric conditions of Theorem 2.3 may be modified as

$$
\triangle \cong Min\left\{A-B\eta_1-\alpha\eta_3, C-rN_2\eta_2-\frac{B}{4\eta_1}, \frac{\alpha}{4\eta_3}-\frac{rN_2}{4\eta_2}\right\}. \qquad (2.11)
$$

using

$$
\begin{aligned}
B(u-u^*)(v-v^*) &\leq B\left(\eta_1(u-u^*)^2+\frac{1}{4\eta_1}(v-v^*)^2\right),\\
rN_2(v-v^*)(w-w^*) &\leq rN_2\left(\eta_2(v-v^*)^2+\frac{1}{4\eta_2}(w-w^*)^2\right),\\
\alpha(u-u^*)(w-w^*) &\leq \alpha\left(\eta_3(u-u^*)^2+\frac{1}{4\eta_3}(w-w^*)^2\right).
\end{aligned}
$$

Clearly (2.10) is a special case of (2.11) for $\eta_1 = \eta_2 = \eta_3 = \frac{1}{2}$.

The advantage of this inequality is that basing on the strength of the parameters, we can choose the parameters $\eta' s$ for manipulating the stability of the equilibrium. In other words, the new parameter η helps explore more regions of stability for the system (2.1). This may be observed in examples to be presented in the next section.

We shall now present another couple of criteria for the stability of the equilibrium solution of (2.1). This time the Lyapunov functional is modified, and conditions on f, V, and P are assumed as follows.

For positive constants L_1, L_2, M_1, M_2, N_1 and N_2, we assume that

$$
\begin{aligned}
L_1|u-u^*| &\leq |f(u)-f(u^*)| \leq L_2|u-u^*|,\\
M_1|u-u^*| &\leq |V(u)-V(u^*)| \leq M_2|u-u^*|,\\
N_1|v-v^*| &\leq |P(v)-P(v^*)| \leq N_2|v-v^*| \qquad (2.12)
\end{aligned}
$$

hold respectively for $u \neq u^*, v \neq v^*$.

We are now in a position to state and prove.

Theorem 2.4. *Assume that the functional relations of (2.1)satisfy the conditions (2.12). Assume further that the parameters satisfy* $d + cM_1 + (b - b_1)L_1v^* > 0$ *and* $Min\{d_1 + (b - b_1)f(u)\} > 0$. *Then the equilibrium solution* (u^*, v^*, w^*) *is globally asymptotically stable.*

Proof. We employ the functional

$$U(u, v, w) = |u - u^*| + |v - v^*| + |w - w^*|.$$

Then along the solution of (2.1), the upper right derivative of U using (2.3) is given by

$$\begin{aligned}
D^+U \leq & - bf(u)|v - v^*| - bv^*|f(u) - f(u^*)| - d|u - u^*| - c|V(u) - V(u^*)| \\
& + \alpha|w - w^*| + b_1f(u)|v - v^*| + b_1v^*|f(u) - f(u^*)| - r|P(v) - P(v^*)| \\
& - d_1|v - v^*| + r|P(v) - P(v^*)| - \alpha|w - w^*| \\
\leq & - (b - b_1)v^*|f(u) - f(u^*)| - d|u - u^*| - c|V(u) - V(u^*)| \\
& - (b - b_1)f(u)|v - v^*| - d_1|v - v^*| \\
\leq & - (b - b_1)v^*L_1|u - u^*| - cM_1|u - u^*| - d|u - u^*| \\
& - (b - b_1)f(u)|v - v^*| - d_1|v - v^*| \\
\leq & - (d + cM_1 + (b - b_1)L_1v^*)|u - u^*| - (d_1 + (b - b_1)f(u))|v - v^*| \\
< & \ 0 \ , (\text{by hypothesis}) \qquad (2.13)
\end{aligned}$$

Therefore D^+U is negative definite, and the rest of the argument follows from earlier results. Thus, $U \to 0$ for large t. The proof is thus complete. □

We shall now consider the general case (1.1), which is (2.1) with $f(u, v)$ instead of $f(u)v$. To proceed with global stability, we need the following assumptions on f. Suppose that there exist two positive constants K_1, K_2 such that

$$|f(u_1, v_1) - f(u_2, v_2)| \leq K_1|u_1 - u_2| + K_2|v_1 - v_2|. \qquad (2.14)$$

We recall (1.1) for ready reference

$$\begin{aligned}
u^{'} &= a - bf(u, v) - du - cV(u) + \alpha w, \\
v^{'} &= b_1f(u, v) - rP(v) - d_1v, \\
w^{'} &= rP(v) - \alpha w. \qquad (2.15)
\end{aligned}$$

Suppose (u^*, v^*, w^*) is an equilibrium solution of (1.1). Then we have

$$\begin{aligned}
a &= bf(u^*, v^*) + du^* + cV(u^*) - \alpha w^*, \\
0 &= b_1f(u^*, v^*) - rP(v^*) - d_1v^*, \\
0 &= rP(v^*) - \alpha w^*. \qquad (2.16)
\end{aligned}$$

Using (2.16) in (2.15) we have

$$\begin{aligned}
(u - u^*)^{'} &= -b(f(u, v) - f(u^*, v^*)) - d(u - u^*) - c(V(u) - V(u^*)) + \alpha(w - w^*), \\
(v - v^*)^{'} &= b_1(f(u, v) - f(u^*, v^*)) - r(P(v) - P(v^*)) - d_1(v - v^*), \\
(w - w^*)^{'} &= r(P(v) - P(v^*)) - r(w - w^*). \qquad (2.17)
\end{aligned}$$

We shall establish as follows.

Theorem 2.5. *Assume that the interaction function f satisfies (2.14), the vaccination function V and recovery function P satisfy (2.12). Then the equilibrium solution of (u^*, v^*, w^*) of (1.1) is globally asymptotically stable provided the conditions*

$$(i).\ d + cM_1 > |b_1 - b|K_1 \quad and \quad (ii).\ d_1 > |b_1 - b|K_2$$

hold.

Proof. We employ the same functional as in Theorem 2.4. That is, we consider

$$U(u, v, w) = |u - u^*| + |v - v^*| + |w - w^*|.$$

Then along the solutions of (1.1), the upper right derivative of U using (2.17) is given by

$$\begin{aligned}
D^+U \leq & - b|f(u,v) - f(u^*,v^*)| - d|u - u^*| - c|V(u) - V(u^*)| + \alpha|w - w^*| \\
& + b_1|f(u,v) - f(u^*,v^*)| - r|P(v) - P(v^*))| - d_1|v - v^*| \\
& + r|P(v) - P(v^*)| - \alpha|w - w^*| \\
\leq & (b_1 - b)|f(u,v) - f(u^*,v^*)| - d|u - u^*| - c|V(u) - V(u^*)| - d_1|v - v^*| \\
\leq & |b_1 - b|[K_1|u - u^*| + K_2|v - v^*|] - d|u - u^*| - cM_1|u - u^*| - d_1|v - v^*| \\
\leq & - (d + cM_1 - |b_1 - b|K_1)|u - u^*| - (d_1 - |b_1 - b|K_2)|v - v^*| \\
< & 0(\text{by assumption}).
\end{aligned}$$

By $D^+U < 0$ and employing the standard arguments, one may complete the proof. Thus, $U \to 0$ for $t \to \infty$. In other words $(u, v, w) \to (u^*, v^*, w^*)$ as $t \to \infty$. The proof is complete. □

Remark 2.4. It may be observed that Theorem 2.4 gives a completely different set of parametric conditions for global stability compared to that of Theorem 2.1, Theorem 2.2 and Theorem 2.3. Thus, it offers a new stability region for the system (2.1). On the other hand, Theorem 2.5 provides GAS conditions for a general, complex system such as (1.1).

Remark 2.5. The behavior of a system depends on the parameters chosen and the functional relations among the interacting populations. It may be observed that Theorem 2.1 to Theorem 2.4 present several sets of sufficient conditions on parameters of system for the global asymptotic stability of the equilibria, of course, the conditions on functional relations are imposed through (2.4), (2.5), (2.12) or (2.14) as the case may be. One may notice through simple comparison that the restrictions on parameters are fewer in Theorem 2.1 when compared to those in Theorems 2.2 and 2.3. However, all these conditions define different regions of stability as defined by parametric spaces. Restrictions on parameters are further eased in Theorem 2.4 through a different Lyapunov path and modified conditions on functions. In fact, the conditions in Theorem 2.4 are vacuously true due to the assumptions made on functions and parameters b, b_1. Again, some strain on parameters is necessary in Theorem 2.5 due to the choice of a generalized conversion function. On the whole, the system may be regarded to have some in-built stability with properly chosen functional relations and parameters.

Having obtained various GAS conditions for systems (2.1) and (1.1), we illustrate these results with numerical examples in the next section.

3. Numerical simulations

In this section, we analyze how the results of Section 2 establish the GAS of equilibrium of systems (2.1) and (1.1) by using numerical examples and their simulations. Before presenting our examples, we observe that the parameter d accounts for the immunity strength of the susceptible community (d is the rate of removal from the system or the rate of escape from being infected!). Similarly, d_1 (removal rate of infected population) supports the term corresponding to non-infectious population who may either do not require any treatment or recover by themselves or be dead. Neither category contributes to spread of infection. Naturally, larger values of d and d_1 should signify a low infection state. Therefore d and d_1 are the dominating parameters here. The same is reflected by the parametric conditions in all the results discussed in the previous sections. Further observation of the conditions shows that the vaccination parameter c and treatment rate r support d and d_1 in establishing the stability of equilibria. Thus, our mathematical conditions reflect biological meanings. We have also noticed in Remark 2.5 that the functional relations f (the conversion function), V (the vaccination function) and P (the treatment function) are also contributing to the stability of the system. The following examples support our observations.

We shall first consider numerical examples for the system (2.1), where $f(u,v) = f(u)v$. Our first example studies the asymptotic stability of disease-free equilibrium and the second one deals with a disease prevailing environment.

Example 3.1. Consider the system

$$\begin{aligned} u' &= 18 - 2f(u)v - 5u - 3V(u) + w, \\ v' &= f(u)v - \frac{1}{2}P(v) - \frac{3}{2}v, \\ w' &= \frac{1}{2}P(v) - w. \end{aligned} \tag{3.1}$$

We choose the functions $f(u)$, $V(u)$ and $P(v)$ in such a way that they satisfy the inequality (2.4).

Case(i). Let us assume $f(u) = \dfrac{1}{1+e^{-u}}$, $V(u) = u$ and $P(v) = v$. For this choice of functions, we get $L_1 = 0.1531$, $L_2 = 0.1799$, $M_1 = 1$, $M_2 = 1$, $N_1 = 1$, $N_2 = 1$. Equilibrium solution for this system is $(2.248, 0, 0)$. Calculating the values of A, B and C from the Theorem 2.1, we get $A = 8$, $B = -1$ and $C = 1.3340$. By choosing $p_1 = p_2 = q_1 = q_2 = \alpha_1 = \alpha_2 = \dfrac{1}{2}$, it has been observed that the system (3.1) satisfies the parametric conditions of Theorem 2.1. Hence, by virtue of Theorem 2.1, the system is GAS, i.e., the solutions of the system (3.1) converge to the point $(2.248, 0, 0)$, which is a disease-free equilibrium state. The same may be observed from the simulations shown in Figure 1.

Case(ii). Choose $f(u) = \dfrac{1}{1+e^{-u}}$, $V(u) = \dfrac{u}{u+1}$ and $P(v) = v$. For this choice of functions, we get $L_1 = 0.1531$, $L_2 = 0.1799$, $M_1 = 0.1822$, $M_2 = 0.3079$, $N_1 = 1$, $N_2 = 1$. This system has an equilibrium solution as $(3.1448, 0, 0)$. The values of A, B and C from the Theorem 2.1 are $A = 5.5465$, $B = -1$ and $C = 1.3340$. Substituting these values in Theorem 2.2, we get $\Delta = 0.2500 > 0$. As the system (3.1) satisfies the condition of Theorem 2.2, the system (3.1) is GAS. Simulations of this system with chosen response functions may be seen in Figure 2.

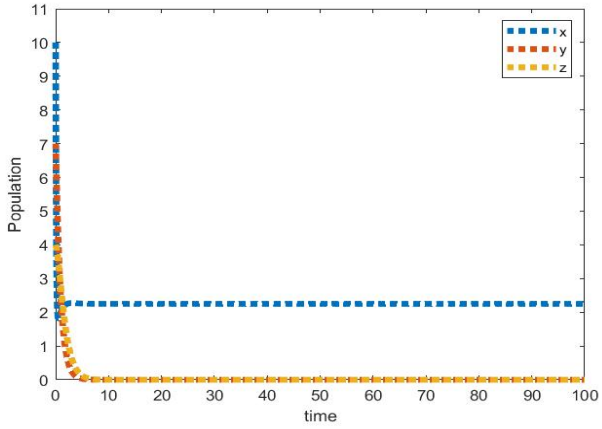

Figure 1. The Stability of disease-free equilibrium of (3.1) under high system immunity and vaccination efforts.

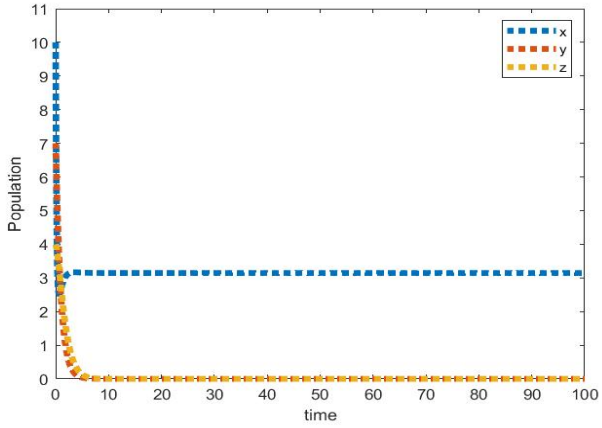

Figure 2. Populations approaching a disease free state though vaccination efforts are slowed down.

Remark 3.1. It is observed that the system (3.1) with the functions $f(u) = \dfrac{1}{1+e^{-u}}$, $V(u) = \dfrac{u}{u+1}$ and $P(v) = v$ satisfies all the conditions of Theorem 2.3 except $\Delta_3 > 0$ condition.

It is also observed that, for $\eta_1 = 2$, $\eta_2 = 2$ and $\eta_3 = 2$, this system does not satisfy the condition (2.11) of Remark 2.3 (as $\Delta = -0.67$). But as it satisfies at least one condition of Theorem 2.3 and also the condition of Theorem 2.2, the system is GAS. Therefore, the GAS conditions derived in Theorem 2.1, Theorem 2.2, Theorem 2.3, and Remark 2.3 are independent of each other.

Example 3.2.

$$u' = 22 - 3f(u)v - 3u - 7V(u) + w$$
$$v' = 3f(u)v - \frac{1}{2}P(v) - \frac{3}{2}v$$

$$w^{'} = \frac{1}{2}P(v) - w. \tag{3.2}$$

We shall choose the functions $f(u)$, $V(u)$ and $P(v)$ in such a way that they satisfy the inequality (2.12).

Case(i) If $f(u) = \dfrac{1}{1+e^{-u}}$,$V(u) = \dfrac{u}{u+1}$ and $P(v) = v$, then $L_1 = 0.0009$ $L_2 = 0.0516$, $M_1 = 0.2236$, $M_2 = 0.5904$, $N_1 = 1$ and $N_2 = 1$. Equilibrium point for this system is $(0.6923, 11.3705, 5.6850)$. From Theorem 2.5, $d+cM_1+(b-b_1)L_1v^* = 4.5655 > 0$ and $Min\{d_1 + (b-b_1)f(u)\} = 1.500 > 0$. By virtue of Theorem 2.4, system (3.2) is GAS and the simulations of this system with chosen functions can be seen in Figure 3.

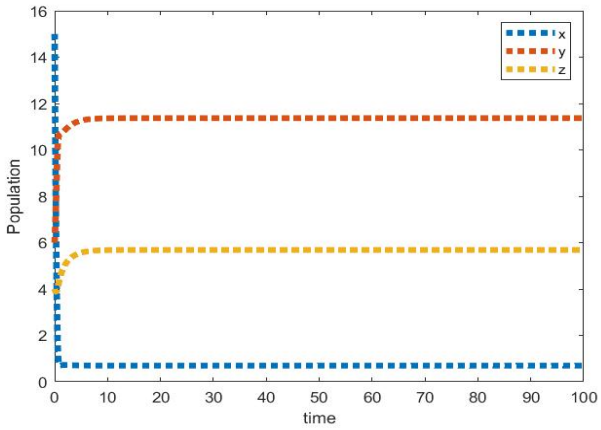

Figure 3. Prevalence of disease environment under high interaction with infected population and low community immunity.

Case(ii) By choosing $f(u) = \dfrac{u}{u+1}$, $V(u) = \dfrac{1}{1+e^{-u}}$ and $P(v) = \dfrac{v}{v+1}$, the values of Lipschitz constants will be $L_1 = 0.2418$ $L_2 = 0.4837$, $M_1 = 0.0033$, $M_2 = 0.0493$, $N_1 = 0$ and $N_2 = 0.1$. Here the equilibrium point is $(1.0675, 9, 0567, 0.4503)$. The value of $d + cM_1 + (b-b_1)L_1v^* = 3.0231 > 0$ and $Min\{d_1 + (b-b_1)f(u)\} = 1.500 > 0$. Therefore, by Theorem 2.4, system (3.2) with chosen functions is GAS. The simulations of this system can be noticed in Figure 4.

Now let us consider the general case of (1.1) where we consider $f(u, v)$ nstead of $f(u)v$.

Case(iii) If $f(u, v) = \dfrac{u}{u+v}$, $V(u) = u$ and $P(v) = v$, then Lipschitz constants will take the values $K_1 = 1$, $K_2 = 1$, $M_1 = 1$, $M_2 = 1$, $N_1 = 1$ and $N_2 = 1$. Equilibrium point for this system is $(2.0485, 1.0060, 0.5030)$.The value of $d+cM_1 + (b-b_1)K_1 = 10 > 0$ and $Min\{d_1 - (b_1-b)K_2\} = 1.500 > 0$. Therefore, by Theorem 2.5, system (3.2) with chosen functions is GAS. The simulations of this system can be noticed in Figure 5.

Remark 3.2. In the first example, we have considered the situation where only one-half of the contacted susceptible population is converted into infected ($b_1 = 1, b = 2$). Under reasonable rates of removal ($d = 5$) and vaccination ($c = 3$), the disease-free equilibria do exist and are stable in each case. A rise in susceptible population

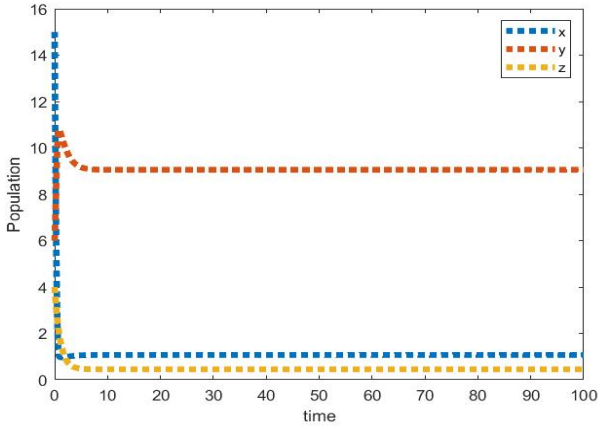

Figure 4. Simulations of the system (3.2) showing that infected populations rise due to reduced vaccination efforts.

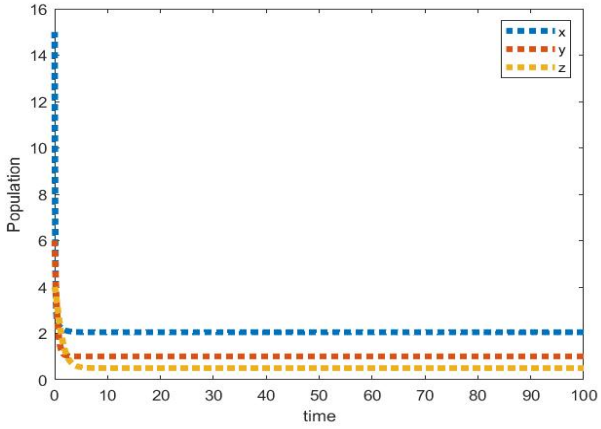

Figure 5. Stability of solutions to a reduced state of infection under high vaccination and treatment.

(from 2.248 to 3.1448) may be attributed to reduced vaccination efforts ($V(u) = u$ to $\dfrac{u}{u+1}$). In Example 3.2, all the susceptible population that is contacted by the infected ones are converted to infected ones ($b = b_1$) at higher rates than in the previous example. Further, the removal rate is reduced but vaccination efforts are increased now. A disease environment has prevailed as one may expect! The other parameters are kept the same in all cases. The conversion function and vaccination function are reversed in cases (i) and (ii) which resulted appropriate changes in susceptible population and infected population. A drastic fall in recovered population may be noticed due to a reduced treatment (linear to sub-linear)! Again a rise in vaccination and treatment efforts led to a rise in susceptible population, reducing infected population at the same time.

4. Conclusion

The interplay among a plethora of factors ranging from pathogen biological properties to environmental and socio-cultural behavioral conditions necessitates the development of sophisticated mathematical models for a robust representation of infectious diseases. A number of models have been proposed, which can broadly categorize as (i) statistical models, (ii) state-space models and (iii) machine learning models. The forecasting and non-casting capabilities of these models are explored, and the results are utilized in establishing effective control strategies and prevention policies. Even in most cases, the models built and studied concentrated more on vaccination efforts, often ignoring the treatment part.

In this paper, we consider an SIR model, which includes a term representing the treatment efforts in containing the spread of disease. The model is quite general in nature in the sense that many SIR models become special cases of this. The model equations are framed rigorously with proper assumptions, variables and parameters. Due to the complexity of the underlying interactions, the model is difficult to study and analyze. Only local stability aspects of the equilibrium are found in the literature. But the prediction of disease outbreaks and control strategies is effective when GAS of the equilibrium is established. In the present work, we focused on establishing the GAS of the endemic disease-free equilibrium.

We began with a particular case wherein the nonlinear function $f(u, v)$ which describes the interaction between susceptible and infected populations taken the form $f(u, v) = f(u)v$. By imposing gradient-type conditions on the response functions, two different sets of GAS conditions are derived. As many as eight sets of sufficient conditions for GAS are derived utilizing the same Lyapunov functional but manipulating the product terms. By changing the Lyapunov functional and suitably modifying the conditions on the functions, another set of sufficient conditions for the GAS is derived. It is observed that the stability regions obtained for each set of conditions are different. The general case is then considered providing GAS conditions for the complex system (1.1). Numerical examples are worked out to illustrate theorems and simulations are carried out for a pictorial representation of the system behavior. Parametric conditions are discussed in terms of biological phenomena and impact of vaccination and treatment on the disease dynamics are discussed.

We intend to link the model with real data, which is a particular utility towards the design of vaccination and treatment policies. We wish to conduct simulations and empirical analysis based on real-time data sets and also convey an extensive comparative investigation of this with the existing models. Having noticed the influence of parameters on disease dynamics, the estimation and optimization for desired results would be an interesting subject with large applications. All these aspects are reserved for our future study.

References

[1] I. Ahn, S. Heo, S. Ji et al., *Investigation of nonlinear epidemiological models for analyzing and controlling the mers outbreak in korea*, Journal of Theoretical Biology, 2018, 437, 17–28.

[2] L. J. Allen, *A primer on stochastic epidemic models: Formulation, numerical simulation, and analysis*, Infectious Disease Modelling, 2017, 2(2), 128–142.

[3] R. M. Anderson, C. Fraser, A. C. Ghani et al., *Epidemiology, transmission dynamics and control of sars: the 2002–2003 epidemic*, Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 2004, 359(1447), 1091–1105.

[4] E. Beretta, V. Capasso and D. G. Garao, *A mathematical model for malaria transmission with asymptomatic carriers and two age groups in the human population*, Mathematical Biosciences, 2018, 300, 87–101.

[5] J. Burton, L. Billings, D. A. Cummings and I. B. Schwartz, *Disease persistence in epidemiological models: The interplay between vaccination and migration*, Mathematical Biosciences, 2012, 239(1), 91–96.

[6] R. Casagrandi, L. Bolzoni, S. A. Levin and V. Andreasen, *The sirc model and influenza a*, Mathematical biosciences, 2006, 200(2), 152–169.

[7] N. Chitnis, J. M. Cushing and J. M. Hyman, *Bifurcation analysis of a mathematical model for malaria transmission*, SIAM Journal on Applied Mathematics, 2006, 67(1), 24–45.

[8] I. Cooper, A. Mondal and C. G. Antonopoulos, *Dynamic tracking with model-based forecasting for the spread of the covid-19 pandemic*, Chaos, Solitons & Fractals, 2020, 139, 110298.

[9] A. L. P. D. Costa, O. A. R. Neto and A. C. T. Silva-Júnior, *Conditioners of the infectious diseases dynamics*, Estação Científica (UNIFAP), 2019.

[10] S. L. de Souza, A. M. Batista, I. L. Caldas et al., *Dynamics of epidemics: Impact of easing restrictions and control of infection spread*, Chaos, Solitons & Fractals, 2021, 142, 110431.

[11] Y. Dumont and M. Tchuenche, *Mathematical studies on the sterile insect technique for the chikungunya disease and aedes albopictus*, Journal of mathematical biology, 2011, 65, 809–54.

[12] B. Emerenini and S. Inyama, *Mathematical model and analysis of transmission dynamics of hepatitis b virus*, F1000Research, 2017, 7.

[13] L. Esteva and C. Vargas, *A model for dengue disease with variable human population*, Journal of mathematical biology, 1999, 38, 220–40.

[14] S. Eubank, H. Guclu, S. Kumar et al., *Modeling disease outbreaks in realistic urban social networks*, Nature, 2004, 429, 180–4.

[15] S. Funk, M. Salathé and V. Jansen, *Modelling the influence of human behaviour on the spread of infectious diseases: A review*, Journal of the Royal Society, Interface / the Royal Society, 2010, 7, 1247–56.

[16] G. Giordano, F. Blanchini, R. Bruno et al., *Modelling the covid-19 epidemic and implementation of population-wide interventions in italy*, Nature medicine, 2020, 26(6), 855–860.

[17] F. C. Grassly NC, *Mathematical models of infectious disease transmission*, Nat Rev Microbiol, 2008, 6, 477–487.

[18] N. Hoertel, M. Blachier, C. Blanco et al., *A stochastic agent-based model of the sars-cov-2 epidemic in france*, Nature Medicine, 2020, 26, 1–5.

[19] A. Huppert and G. Katriel, *Mathematical modelling and prediction in infectious disease epidemiology*, Clinical Microbiology and Infection, 2013, 19(11), 999–1005.

[20] M. J. Keeling and L. Danon, *Mathematical modelling of infectious diseases*, British Medical Bulletin, 2009, 92(1), 33–42.

[21] N. A. Kudryashov, M. A. Chmykhov and M. Vigdorowitsch, *Analytical features of the sir model and their applications to covid-19*, Applied Mathematical Modelling, 2021, 90, 466–473.

[22] J. LaSalle, *The Stability of Dynamical Systems*, SIAM, Philadelphia, 1976.

[23] J. Lee, G. Chowell and E. Jung, *A dynamic compartmental model for the middle east respiratory syndrome outbreak in the republic of korea: A retrospective analysis on control interventions and superspreading events*, Journal of Theoretical Biology, 2016, 408, 118–126.

[24] Q. Lin, S. Zhao, D. Gao et al., *A conceptual model for the coronavirus disease 2019 (covid-19) outbreak in wuhan, china with individual reaction and governmental action*, International Journal of Infectious Diseases, 2020, 93, 211–216.

[25] M. Lipsitch, T. Cohen, B. Cooper et al., *Transmission dynamics and control of severe acute respiratory syndrome*, science, 2003, 300(5627), 1966–1970.

[26] X. Liu and P. Stechlinski, *Application of control strategies to a seasonal model of chikungunya disease*, Applied Mathematical Modelling, 2015, 39(12), 3194–3220.

[27] T. Mapder, S. Clifford, J. Aaskov and K. Burrage, *A population of bang-bang switches of defective interfering particles makes within-host dynamics of dengue virus controllable*, PLOS Computational Biology, 2019, 15, 1–24.

[28] S. Martorano Raimundo, M. Amaku and E. Massad, *Equilibrium analysis of a yellow fever dynamical model with vaccination*, Computational and mathematical methods in medicine, 2015, 2015.

[29] R. E. Morrison and A. Cunha, *Embedded model discrepancy: A case study of zika modeling*, Chaos, 2020, 30 5, 051103.

[30] F. Ndaïrou, I. Area, J. J. Nieto et al., *Fractional model of covid-19 applied to galicia, spain and portugal*, Chaos, Solitons & Fractals, 2021, 144, 110652.

[31] A. Omame, U. K. Nwajeri, M. Abbas and C. Onyenegecha, *A fractional order control model for diabetes and covid-19 co-dynamics with mittag-leffler function*, AEJ - Alexandria Engineering Journal, 2022, 61, 7619–7635.

[32] A. Omame, N. Sene, I. Nometa et al., *Analysis of covid-19 and comorbidity co-infection model with optimal control*, Optimal Control Applications and Methods, 2021, 42, 1568–1590.

[33] L. Opatowski, D. Guillemot, P.-Y. Boëlle and L. Temime, *Contribution of mathematical modeling to the fight against bacterial antibiotic resistance*, Current Opinion in Infectious Diseases, 2011, 24(3), 279–287.

[34] D. Prodanov, *Analytical parameter estimation of the sir epidemic model. applications to the covid-19 pandemic*, Entropy, 2020, 23(1), 59.

[35] P. R. S. Rao and M. N. Kumar, *A dynamic model for infectious diseases: The role of vaccination and treatment*, Chaos, Solitons & Fractals, 2015, 75, 34–49.

[36] P. R. S. Rao, K. V. Ratnam and S. R. Mushnuri, *Predictive dynamics of infectious diseases-a new technique*, World Journal of Modelling and Simulation, 2019, 15, 128–139.

[37] C. I. Siettos and L. Russo, *Mathematical modeling of infectious disease dynamics*, Virulence, 2013, 4, 295–306.

[38] J. P. Tian and J. Wang, *Global stability for cholera epidemic models*, Mathematical Biosciences, 2011, 232(1), 31–41.

[39] X. Wang, C. Wang and K. Wang, *Global dynamics of a novel deterministic and stochastic sir epidemic model with vertical transmission and media coverage*, Advances in Difference Equations, 2020, 2020.

[40] S. J. Weinstein, M. S. Holland, K. E. Rogers and N. S. Barlow, *Analytic solution of the seir epidemic model via asymptotic approximant*, Physica D: Nonlinear Phenomena, 2020, 411, 132633.

[41] J. S. Weitz and J. Dushoff, *Modeling post-death transmission of ebola: challenges for inference and opportunities for control*, Scientific reports, 2015, 5(1), 1–7.

[42] G. Zaman, I. H. Jung, D. F. M. Torres and A. Zeb, *Mathematical modeling and control of infectious diseases*, Computational and Mathematical Methods in Medicine, 2017, 2017, 1–1.

[43] M. Zhu and Y. Xu, *A time-periodic dengue fever model in a heterogeneous environment*, Mathematics and Computers in Simulation, 2019, 155, 115–129. International Conference on Mathematical Modeling and Computational Methods in Science and Engineering.