Control of Disease Dynamics Under Time Varying Vaccination and Treatment Rates

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Abstract
Vaccination and treatment are two major strategies in controlling or eradication of any contagious disease. Usually, both these factors are represented by fixed parameters in most of the studies. In the present work, an SIR (Susceptible-Infectious-Recovered) model of populations is considered with time-dependent vaccination and treatment rates and influence of these disease control strategies is studied. Besides establishing the boundedness of solutions, conditions are provided on asymptotic closeness of solutions. Upon further restrictions on vaccination and treatment, it is observed that the populations may be made to approach a pre-specified state affairs which the society could manage. Further study reveals that the system may approach eventually an equilibrium solution of a system with constant rates of vaccination and treatment. Illustrations are provided to understand the technique and its effectiveness.

Keywords: Infectious diseases, vaccination, treatment, convergence, stability.
MSC (2010) 37L45, 37D35, 34D23

1. Introduction
Human health has been widely affected by diseases which are broadly classified into infectious and non-infectious diseases. Amongst them the infectious diseases due to their dynamical behavior poses a major threat to the human population. This necessitates the need to understand its mechanisms which lead to the disease spread processes. One of the primary reasons for studying about dynamics of infectious diseases is to improve, control and ultimately to eradicate the infectious diseases from the population. Thus, modelling the dynamics of infectious diseases [11, 12, 13, 17] became a power tool in the approach of studying the patterns and suggesting ways to mitigate the diseases. Over the past many years various efforts and studies were made by several researchers and scientists from different fields to understand the disease dynamics [2, 5, 6, 7]. Their efforts are to make a global surveillance network that could confront the pandemics and re-emerging infectious diseases. To analyze the dynamics of such outbreaks mathematical modelling was developed, which helps not only to predict the possible causes for spread of an epidemic accurately but also assists to assess and develop control strategies for potential outbreaks [10, 13].

Various mathematical models [9, 13, 16] attempted not only to improve control measures with optimal use of limited resources but also to eradicate the infection from the affected population. Amongst them SIR model is the more sought-after model which subdivides the whole population into three categories namely susceptible, infected and recovered [3, 6, 10,12]. Many authors considered application of several kinds of control measures in their epidemiological models [4, 8, 15] to predict the impact of the viruses. With vaccination as the control measure several SIR epidemic models have been introduced. According to these models, vaccination as the major control variable could minimize the susceptible individuals and lead to prevention /eradication of the infectious diseases. But it was observed, vaccination alone cannot bring optimum control of the spread of infection from a community. Further, it is observed vaccination could only be a good choice for controlling the disease during early stages of the disease. Massive vaccination may not be possible when the population is very large. Sometimes vaccine resistant strains could emerge due to frequent or long-term vaccination, which could make recovery from diseases difficult [10, 14]. This leads to emergence of treatment, the other control variable.

Over the time it is seen that, whenever an epidemic occurs the immediate action to contain the disease is vaccinating the non-infected, susceptible population and the affected must undergo medical treatment. While the vaccine is being developed symptomatic treatment ropes in. Vaccine resistant strains stress the importance of treatment and proper vaccination reduces the stress on requirement of treatment. Vaccination has the role of preventing healthy people from getting infected by a disease, while treatment cures a disease and can also be used as a prophylactic. Thus, vaccination and treatment should work together in controlling the spread of diseases. SIR models using vaccination and treatment strategies came in, to obtain optimal result of containing the disease spread. Apart from vaccination, if treatment is considered in the control measures, then not only rapid reduction in the proportion of susceptible individuals but also an increase in recovered individuals was observed. Thus, epidemic models with vaccination and treatment become utmost priority. Thus, when these are used together, they can contain the disease spread more efficiently.

Now, vaccination depends on (a) the ability of the pharmaceutical companies and laboratories to produce suitable and enough quantity to meet the demand; (b) the actual requirement, that is, the number of susceptible at any particular point of time available for vaccination; and (c)availability of vaccine at the moment. On the whole, we can say as the spread of the disease varies over the time, corresponding should be the variation in vaccination. In other words, vaccination should vary with time and need not be constant always. Treatment, on the other hand restricts movement of infectious and infected population and works also as a quarantine. Secondly, it provides opportunity to understand the disease dynamics or behaviour by experts. Now treatment depends on (i)readiness of the society or facilities available in the society to start the treatment process; (ii) spread of the disease, that is, treatment rate varies according to the number of infected and (iii) availability of medical teams and medicines etc. Thus, situation (time) tells how the system requires vaccination and treatment and that vaccination and treatment need not be fixed constants but time varying.

Motivated by above observations, we consider here, an SIR model proposed in [12]. We introduce time varying vaccination and treatment rate functions and study their impact on the disease dynamics. In [9] it is observed that a proper interplay between vaccination and treatment rates (assumed to be constant fixed values) could drive the system to a desired state. The authors could provide only an algebraic technique and numerical examples to illustrate this. In the present, we shall provide a theoretical support to this concept. For any mathematical model describing the dynamics of infectious diseases, basic aim would be to establish conditions under which the spread of disease is under control. This we study in terms of boundedness of solutions, convergence to a known situation or stability of equilibrium solutions etc. In the present work, we follow the same method, employing the flexibility to vary the vaccination and treatment rates.

The strategy is as follows:

a) To establish the boundedness and asymptotic closeness of solutions of the system- prerequisite that the system is controllable
b) To establish conditions on parameters, functional relations with suitably restricted vaccination and treatment rates to make the system converge to a pre-specified, desired state of disease environment
c) To establish the stability of our non-autonomous system in terms of the stability of the equilibrium solution of a system with constant vaccination and treatment rates.

The paper is organized as follows. In Section 2, we describe the model and establish to provide estimates on vaccination and/or treatment functions so that the solutions of the model are non-negative and might be bounded as well. In Section 3, a predefined set of constant values are chosen from the space of solutions of the system and conditions are established on the system parameters and functions, for the asymptotic stability of these predefined values as an assumed equilibrium. Numerical examples with simulations are provided here for an illustration of the technique employed and the results obtained. In Section 4, we consider the autonomous system with constant vaccination and treatment rates as a special case which admits an equilibrium solution and provide conditions on our time varying vaccination and treatment functions so that the solutions of non-autonomous system approaches this equilibrium solution asymptotically. Conclusion follows in Section 5.

2. The Model and Basic Properties

We consider the model

$$\begin{aligned} x' &= a - bf(x,y) - dx + \alpha z - cV(t), \\ y' &= b_1 f(x,y) - r(t)P(y) - d_1 y, \\ z' &= r_1 P(y) - \alpha z. \end{aligned} \tag{1}$$

In (1) x, y, z denotes the susceptible, infected and recovered populations respectively and $' = \frac{d}{dt}$ denotes the time derivative. Here $a \geq 0$ is rate of growth of susceptible population, $b > 0$ is interaction rate between susceptibles and infected ones, d is rate of susceptible individuals who are naturally immune to the infection and in no way get infected, $\alpha > 0$ is rate at which a recovered person becomes susceptible again, $c > 0$ is vaccination rate, the parameter $0 < b_1 \leq b$ is the rate of conversion of susceptible into infected, and $d_1 > 0$ denotes the death rate of infected population which is not treated well or inadequately treated or beyond the treatment. V is the vaccination function assumed to be a function of time variable t. The time variant function r(t) is the treatment rate, f denotes infection function which shows how susceptible x are converted into infected y and P is the recovery function of infected by treatment. The positive constant r_1 is the recovery rate.

The vaccination and treatment functions are assumed to be non negative functions with $V(0) = 0$, $r(0) > 0$. Further assumptions on these functions will be made in the due course. The conversion function $f(x, y)$ is assumed to satisfy $f(0, y) \equiv 0$, $f(x, 0) \equiv 0$ and $f(x, y) > 0$ for all other x, y. Thus, there is no conversion in the absence of either of susceptible or infected ones. Similarly, we assume $P(0) = 0$ and $P(y) > 0$ for $y > 0$. Further assumptions on functions will be made depending on the requirements there. For more details of such functions, we refer the readers to [12].

We shall now establish that the solutions are non-negative. This complies with basic requirement for a biological model such as (1), representing populations.

Theorem 2.1. All the solutions of (1) are non-negative in the domain of definition, provided the vaccination function satisfies the condition $V(t) \leq \frac{a}{c}$ $\forall$ t.

Proof. We shall start with the non-negativity of the recovery population z.
Before taking negative values, z(t) by its continuity should assume the value 'z'. Suppose there exists $t_1 > 0$ such that at $t = t_1$, $z(t_1) = 0$. Then, from the third equation of [12], $z'(t_1) = r_1 P(y(t_1))$.
By our assumption $P(y) \geq 0$ $\forall$ y, we have $z'(t_1) \geq 0$. Thus, at $t = t_1$, $z(t_1) = 0$, $z'(t_1)$ is non-decreasing. Hence, z is not going beyond '0'. Hence $z(t) \geq 0$, $\forall$t.

Similarly, using the assumption $f(x,0) = 0$ and $P(0) = 0$ and arguing as above, we can establish that if $y(t_2) = 0$ at $t = t_2$ then $y'(t_2) = 0$ implying that y is non-decreasing or is not taking negative values [12].

Now consider the susceptible population. Assume that there exists a $t_3 > 0$ such that $x(t_3) = 0$. Now from the first equation of (1), we have $x'(t_3) = a - cV(t_3) + \alpha z(t_3)$, using $f(0, y) = 0$, $\forall$y. Clearly $x'(t_3) \geq 0$ by the assumptions on 'V' and that $z(t) \geq 0$, $\forall$t. Again, x is non-decreasing at $t = t_3$ which means that x is non-negative in a neighbourhood around $t = t_3$. Running similar argument for all such ' t_3', one may correlate that $x(t) \geq 0$, $\forall$t. Thus, all the solutions of (1) are non-negative in the domains of definition.

Our next results establish that the solutions of (1) are eventually close to each other, in the sense that if (x, y, z) and $(\bar{x}, \bar{y}, \bar{z})$ are two solutions of (1) then for $t \to \infty, (x, y, z) \to (\bar{x}, \bar{y}, \bar{z})$, under certain conditions.

Theorem 2.2. Assume that the functions f and P satisfy the conditions (3) and the parameters of the system (1) satisfy

$$(i)d > (b - b_1)L_1 \text{ and } (ii)d_1 + r_1 M_2 + b_1 L_2 > r(t)M_1 + L_2 b \tag{2}$$

in which L_1, L_2 and $M_1 > 0$ are such that

$$|f(x,y) - f(\bar{x}, \bar{y})| \leq L_1|x - \bar{x}| + L_2|y - \bar{y}| \text{ and } |P(y) - P(\bar{y})| \leq M_1|y - \bar{y}| \tag{3}$$

Then, for $t \to \infty, (x, y, z) \to (\bar{x}, \bar{y}, \bar{z})$ for any pair of solutions (x, y, z) and $(\bar{x}, \bar{y}, \bar{z})$ of (1).

Proof. We employ the functional

$$W = |x - \bar{x}| + |y - \bar{y}| + |z - \bar{z}|$$

Then the upper Dini derivatives of W along the solutions of (1) is given by

$$\begin{aligned} D^+W &\leq -b|f(x,y)-f(\bar{x},\bar{y})|-d|x-\bar{x}|+\alpha|z-\bar{z}|+b_1|f(x.y)-f(\bar{x},\bar{y})|-r(t)|P(y)-P(\bar{y})| \\ &\quad -d_1|y-\bar{y}|+_{r_1}|P(y)-P(\bar{y})|-\alpha|z-\bar{z}| \\ &\leq -d_1|x-\bar{x}|-(b-b_1)|f(x,y)-f(\bar{x},\bar{y})|-d_1|y-\bar{y}|-(r(t)-)P(y)-P(\bar{y})t(r(t)-r_1)M_1|y-\bar{y}| \\ &= -(d-(b-b_1)L_1|x-\bar{x}|-(d_1-(r(t)-r_1)M_1-(b-b_1)L_2)|y-\bar{y}|| \\ &< 0, \{\text{by assumptions on parameters.}\} \end{aligned}$$

By definition

$W(t) = W(x, y, z) \geq 0$ and $W = 0$ at $x = \bar{x}, y = \bar{y}$ and $z = \bar{z}$.

Thus, W is the required Lyapunov functional and employing standard arguments [12], it may be shown that W(t) → 0 for large 't'.

Hence, $(x, y, z) \to (\bar{x}, \bar{y}, \bar{z})$ as $t \to \infty$.

Thus, all the solutions are coming close to each other eventually.

So far, we have shown that the solutions of (1) are non-negative (minimum requirement to represent a biological situation) and are close to each other under conditions (which means that if the behaviour of one solution is known, the behaviour of others can be assessed). In what follows, we establish conditions under which the solutions could be bounded so that all the solutions could be close to such bounded solutions so as to predict/control the behaviour of the system.

Theorem 2.3. All the solutions of (1) are bounded provided the vaccination rate satisfies the integral condition $\int_0^t |a - cV(t)|\, dt < \infty, \forall t$.

Proof. We employ the functional, $W(t) = W(x, y, z) = x + y + z$.

Then the time derivative of W along the solutions of (eq1) is given by

$$W'(t) \leq a - (b - b_1)\big(f(x, y) - f(\bar{x}, \bar{y})\big) - dx - (r(t) - r_1)p(y) - d_1 y - cV(t)$$
$$\leq a - cV(t) - dx - d_1 y$$
$$\Rightarrow W'(t) + dx + d_1 y \leq a - cV(t).$$

Integrating on both sides w.r.t 't' from 0 to 't', we get

$$W(t) + \int_0^t [dx(t) + d_1 y(t)]\, dt \leq \int_0^t [a - cV(t)]\, dt + W(0) \qquad (4)$$

Since the righthand side of the above inequality is finite by assumptions, boundedness of W = x + y + z follows. Since x, y, and z are all non-negative, each should be bounded. Thus, the conclusion follows.

Remark 2.4. Notice that a function such as $V(t) = \frac{a}{c}(1 + e^{-t})$ or $V(t) = \frac{a}{c}\big(1 + \sin t(t)\big)$, etc satisfies the above condition. Hence, our assumptions on V(t) in Theorem 2.3 are not unrealistic.

Remark 2.5. Now we may infer that under the parametric conditions of Theorem 2.2 and vaccination satisfying the condition in Theorem 2.3, all the solutions of (1) are bounded and are close to each other. It is now clear that the system behaviour is predictable/controllable. Our next question is whether the solutions of system (1) converge to finite values within the regions of parameters and functional relations, vaccination rate defined by above two results. In other words, can we find some constant values in the region of definitions of solutions of (1) to which the solutions approach? The following section answers this question.

3. Convergence to a Desired State

We are studying a model that represents disease dynamics. One usual way is to find where the solutions are going under the impact of vaccination and treatment. We take the converse path here. We shall first define a state which the society feels comfortable or tolerable with regards to disease environment. We shall then estimate our two control measures V and r with which this defined state of environment is reached. Mathematically, we assume that (η, δ, ζ) is the state of disease (Susceptible, Infected and Recovered populations respectively) desired by the society. Then we shall establish conditions on the vaccination and treatment functions under which the solutions (x, y, z) of (1) approach (η, δ, ζ) for sufficiently large values of t, of course, within the purview of other parameters and functional relations of the system.

Assume that η, δ and ζ are all fixed non negative constants that exist in the regions of definition of the solutions of (1).

Clearly Clearly $\frac{d\eta}{dt} = \eta' = 0, \delta' = 0$ and $\zeta' = 0$.

Consider the following rearrangement of equations (1).

$$x' = (x - \eta)' = a - cV(t) - b\big(f(x, y) - f(\eta, \delta)\big) - d(x - \eta) + \alpha(z - \zeta) - bf(\eta, \delta) - d\eta + \alpha\zeta$$
$$y' = (y - \delta)' = b_1\big(f(x, y) - f(\eta, \delta)\big) - r(t)[P(y) - P(\delta)] - d_1(y - \delta) + (b_1 f(\eta, \delta) - r(t)P(\delta) - d_1\delta)$$
$$z' = (z - \zeta)' = r_1\big(P(y) - P(\delta)\big) - \alpha(z - \zeta) + (r_1 P(\delta) - \alpha\zeta) \qquad (5)$$

We shall assume that $r_1P(\delta) - \alpha\zeta = 0$, ($\delta$, ζ satisfy the condition).

We shall now estimate a result to obtain sufficient conditions under which all solutions of (1) approach (η, δ, ζ).

Theorem 3.1. Assume that the conditions of Theorem 2.2 and the condition of V(t) in Theorem 2.3 hold good and also there exist η, δ, ζ such that $r_1P(\delta) - \alpha\zeta = 0$ and

$$\begin{aligned} &\text{(i) } p(t) = [a - cV(t) - b\, f(\eta,\delta) - d\eta + \alpha\zeta] \to 0 \text{ for } t \to \infty \text{ and} \\ &\text{(ii) } q(t) = b1f(\eta,\delta) - r(t)p(\delta) - d_1\delta \to 0 \text{ for } t \to \infty \text{ or} \\ &\text{(iii) } \int_0^\infty p(t)\, d(t) < \infty \text{ and } \int_0^\infty q(t)\, d(t) < \infty. \end{aligned} \tag{6}$$

hold good. Then all the solutions of (1) satisfy, $\lim_{t\to\infty}(x, y, z) = (\eta, \delta, \zeta)$

Proof. We employ the functional

$$W(t) = W(x, y, z) = |x - \eta| + |y - \delta| + |z - \zeta|. \tag{7}$$

The upper right derivative of W along the solutions of (5) is given by

$$\begin{aligned} D^+W &\le -b|\, f(x,y) - f(\eta,\delta)\,| - d|\, x - \eta| + \alpha|z - \zeta| + |a - cV(t) - bf(\eta,\delta) - d\eta + \alpha\zeta| \\ &\quad + b_1|\, f(x,y) - f(\eta,\delta)| - r(t)|\, P(y) - P(\delta)\,| - d_1|y - \delta| + |b_1f(\eta,\delta) - r(t)P(\delta) - d_1\delta \\ &\le -(d - (b - b_1)L_1)|x - \eta| - (d_1 - (r(t) - r_1)M_1 - (b - b_1)L_2|y - \delta| + |p(t)| + |q(t)|. \end{aligned}$$

Then the negative definiteness of D^+W, follows from the assumptions on p(t) and q(t) for large 't'. Observing that $W(\eta, \delta, \zeta) = 0$ and $W(t) \ge 0, \forall\, t,$, it may be noticed that W defined above is the required Lyapunov functional. The rest of the argument follows employing standard arguments [12].

Hence, the conclusion follows as $t \to \infty$.

Remark 3.2. Observe that the assumptions on p(t) and q(t) provide new conditions on the vaccination rate and treatment rate. In other words, if $V(t) \to \frac{1}{c}[a - bf(\eta,\delta) - d\eta + \alpha\zeta]$ and $r(t) \to \frac{1}{p(\delta)}[bf(\eta,\delta) - d_1\delta]$, then the solutions of $(x, y, z) \to (\eta, \delta, \zeta)$, provided other conditions on parameters and functions are satisfied.

Upon further forcing V(t) from the condition in Theorem 2.3 and the treatment rate staying around $\frac{b_1f(\eta,\delta) - d_1\delta}{p(\delta)}$, the system approaches any predefined desired constant set of values that could be reasonable to estimate.

We shall now present a couple of examples to illustrate our results and help estimate the vaccination and treatment rates to reach a desired state of populations.

Example 3.3.

$$\begin{aligned} x' &= 20 - \frac{4x}{x+y} - 2x + \alpha z - 3V(t), \\ y' &= \frac{4x}{x+y} - r(t)y - 2y, \\ z' &= y - \alpha z \end{aligned} \tag{8}$$

Let $\eta = 4, \delta = 1, \zeta = 2$.

Clearly $\alpha = \frac{1}{2}$ we have to satisfy $r_1\delta - \alpha\zeta = 0$

Since $b=b_1$, condition (i) of Theorem 2.2 is vacuously true.

Clearly $\frac{x}{x+y} - \frac{\bar{x}}{\bar{x}+\bar{y}} = \frac{x(\bar{y}-y)+y(x-\bar{x})}{(x+y)(\bar{x}+\bar{y})} \le \frac{1}{(x+y)}(y - \bar{y}) + \frac{1}{\bar{x}+\bar{y}}(x - \bar{x}) < (y - \bar{y}) + (x - \bar{x})$

Hence $L_1=1$ and $L_2=1$. And as P(y)=y, $M_1=1$here. Hence $d_1+r_1 > r(t)$ would satisfy condition(ii) of Theorem 2.2 i.e. r(t) < 3.

$$\begin{aligned} &d_1 = 2,\ r_1 = 1, p(\delta) = \delta = 1 \\ &r(t) = \frac{bf(\eta,\delta) - d_1\delta}{p(\delta)} = \left[\frac{4\eta}{\eta+\delta} - 2\delta\right][1 - e^{-t}] \\ &= \left[\frac{16}{5} - 2\right][1 - e^{-t}] = \frac{6}{5}(1 - e^{-t}) \\ &V(t) = \frac{1}{c}[a - bf(\eta,\delta) - d\eta + \alpha\zeta] = \frac{1}{3}\left[20 - \frac{16}{5} - 8 + 1\right][1 - e^{-t}] = \frac{9\cdot8}{3}(1 - e^{-t}) \end{aligned}$$

Then (x, y, z) → (4, 1, 2) as shown in figure 1.

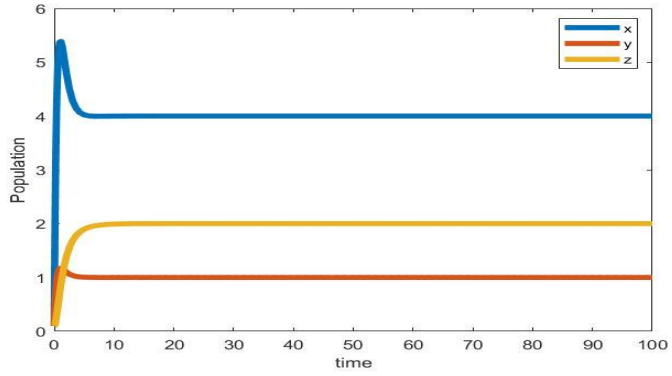

Figure1 : Letting $\alpha = \frac{1}{2}, V(t) = \frac{9\cdot8}{3}(1 - e^{-t})$ and $r(t) = \frac{9\cdot8}{3}(1 - e^{-t})$, one may notice that the solutions of (8) converging to the pre-specified values (4,1,2) of populations.

Example 3.4.

$$\begin{aligned} x' &= 10 - 3xy - x + \alpha z - 2V(t), \\ y' &= 2.7xy - r(t)y - 3y, \\ z' &= 2.5y - \alpha z. \end{aligned} \tag{9}$$

Let $\eta = 2\delta = 1, \zeta = 1$.

From $r_1\delta - \alpha\zeta = 0$, we get $\alpha = 2.5$.

Clearly $|xy - \bar{x}\bar{y}| = |xy - x\bar{y} + x\bar{y} + \bar{x}\bar{y}| = |x(y - \bar{y})| + |y(x - \bar{x})| \leq \max(y)|x - \bar{x}| + \max(y)|x - \bar{x}|$.

Here $L_1 = \max(y) = 1.1745$ and $L_2 = \max(x) = 5.3887$. And as $p(y) = y$, $M_1 = 1$.

As $d-(b-b_1)L_1 = 0.65 > 0$. Condition (i) of Theorem 2.2 is satisfied.

By the condition (ii) of this Theorem 2.2, $r(t) < \frac{d_1 + r_1 M_1 + b_1 L_2 - L_2 b}{M1} = 3.88$.

$r(t) = \frac{bf(\eta,\delta) - d_1\delta}{p(\delta)} = 2.4[1 - e^{-t}]$.

$V(t) = \frac{1}{c}[a - bf(\eta,\delta) - d\eta + \alpha\zeta] = \frac{4.5}{2}(1 - e^{-t})$

Then (x, y, z) → (2,1,1) as shown in Figure 2.

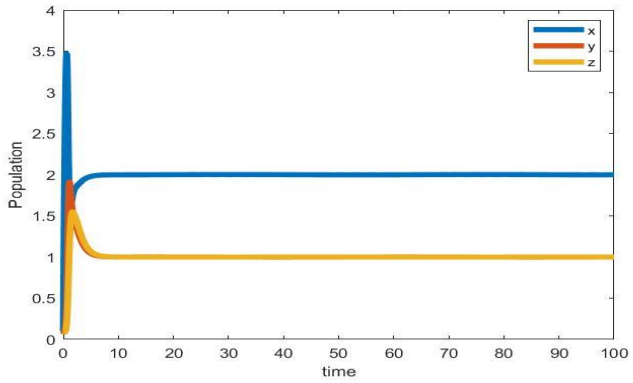

Figure 2. Solutions of (9) approaching the desired state of disease (2,1,1) with $\alpha = 2.5, V(t) = \frac{4.5}{2}(1 - e^{-t})$ and $r(t) = 2.4(1 - e^{-t})$ as specified by Theorem 3.1.

4 A Special Case

In this section we consider the particular situation where both the vaccination and treatment rates are fixed constants. This may be the case where the society is in a position to apply both vaccination and treatment at fixed rates irrespective of demand/requirement.

Mathematically, we let $V(t) \equiv V$, $r(t) \equiv r$, fixed constants in (1). Thus, we consider

$$\begin{aligned} x' &= a - bf(x,y) - dx + \alpha z - cV \\ y' &= b_1 f(x,y) - rP(y) - d_1 y \\ z' &= r_1 P(y) - \alpha z \end{aligned} \tag{10}$$

Few numerical examples are provided to estimate on the vaccination rate (V), treatment rate (r) and recovery rate (α), all constants, to make the system approach a desired (predefined) state of disease environment.

However, no theoretical support is provided by the authors in [11]. One might have noticed that the present work fills this gap and also deals with a more general case of time varying/ situation depending on remedial measures.

We shall now understand the behaviour of solutions of (1) with those of (10). In fact, (10) being an autonomous system, it could have constant equilibria unlike (1). Equilibria, being constant solutions of the system, if stable would establish the stability of the system. We further try to explore the possibility of solutions of (1) approaching the equilibria of (10).

We have already established that under these conditions of Theorem 2.2, any pair of solutions of (1) are asymptotically close. We shall now try to verify similar closeness may be obtained among the solutions of (1) and (10). For this we now let (x, y, z) of the solution of (1) and $(\bar{x}, \bar{y}, \bar{z})$, as the solution of (10) and obtain conditions for $(x, y, z) \to (\bar{x}, \bar{y}, \bar{z})$ for sufficiently large 't'. Since $(\bar{x}, \bar{y}, \bar{z})$ is the solution of (11) we have

$$\begin{aligned} \bar{x}' &= a - bf(\bar{x}, \bar{y}) - d\bar{x} + \alpha\bar{z} - cV \\ \bar{y}' &= b_1 f(\bar{x}, \bar{y}) - rP(\bar{y}) - d_1\bar{y} \\ \bar{z}' &= r_1 P(\bar{y}) - \alpha\bar{z} \end{aligned} \tag{11}$$

Subtracting (11) from (1), we have

$$\begin{aligned} (x - \bar{x})' &= -b[f(x, y) - f(\bar{x}, \bar{y})] - d[x - \bar{x}] + \alpha(z - \bar{z}) - c[V(t) - V] \\ (y - \bar{y})' &= b_1[f(x, y) - f(\bar{x}, \bar{y})] - r(t)[P(y) - P(\bar{y})] - (r(t) - r)P(\bar{y}) - d_1(y - \bar{y})) \\ (z - \bar{z})' &= r_1[P(y) - P(\bar{y})] - \alpha(z - \bar{z}) \end{aligned} \tag{12}$$

We shall assume that there exist constants p_1, p_2 such that

$$0 \le p_1 \le P(y) \le p_2 < \infty, \ \forall\, y \tag{13}$$

We shall now establish the conditions for asymptotic closeness of (x, y) and $(\bar{x}, \bar{y})$.

Theorem 4.1. Assume that the functions of f and P satisfy the conditions (3) and also (13) holds good. Assume that the parameters of the system satisfy

$$(i) d > (b - b_1)L_1 \qquad \text{and} \qquad (ii) d_1 + r_1M_1 + b_1L_2 > rM_1 + bL_2$$

Further assume that the functions V(t) and r(t) satisfy either of the conditions

$$(iii) \int_0^\infty |V(t) - V|\, dt < \infty \text{ and } \int_0^\infty |r(t) - r| < \infty$$

or

$$\lim_{t\to\infty} |V(t) - V| = 0 \text{ and } \lim_{t\to\infty} |V(t) - r| = 0$$

Then for $t \to \infty$, $(x, y, z) \to (\bar{x}, \bar{y}, \bar{z})$ for any solution (x, y, z) and $(\bar{x}, \bar{y}, \bar{z})$ of (1) and (10) respectively.

Proof. We employ the same functional and proceed as in Theorem 2.2. We consider

$W(t) = |x - \bar{x}| + |y - \bar{y}| + |z - \bar{z}|$

The upper Dini derivative of W w.r.t 't' along the solutions of (12) after a rearrangement is given by

$$D^+W \le -(b - b_1)|f(x, y) - f(x^-, \bar{y})| - d|x - \bar{x}| - (r - r_1)|P(y) - P(\bar{y})| - d_1|y - \bar{y}| - (r(t) - r)P(\bar{y}) + c|V(t) - V|$$

$$\le -(d - (b - b_1)L)|x - \bar{x}| + (d - (r - r_1)M_1 - (b - b_1)L_2)|y - \bar{y}| + |r(t) - r|p_2 + c|V(t) - V|.$$

Negative definiteness of D^+W follows from assumptions $|r(t) - r| \to 0$ and $|V(t) - V| \to 0$ and for sufficiently large 't'. Alternately, we have

$$D^+W + [d - (b - b_1)L]|x - \bar{x}| + [d - (r - r_1)M_1 - (b - b_1)L_2]|y - \bar{y}| \le p_2|r(t) - r| + C|V(t) - V|$$

Integrating on both sides from 0 to t with respect to t, we get

$$W(t) + \int_0^t [d - (b - b_1)L]|x(t) - \bar{x}|\, dt + \int_0^t [d - (r - r_1)M_1 - (b - b_1)L_2]|y(t) - \bar{y}|\, dt \le W(0) + p_2 \int_0^t |r(t) - r|\, dt + c \int_0^t |V(t) - V|\, dt$$

Now the conclusion follows from the integral conditions on V(t) and r(t) and assumptions on the other parameters. For detailed arguments one may refer to (14). Thus, $(x, y, z) \to (\bar{x}, \bar{y}, \bar{z})$ for large t'.

Remark 4.2. It is clear from Theorem 4.1 that under the conditions specified, the solutions of (1) could be close to the solutions of (10). Now (10) being an autonomous system and may possess a constant equilibrium solution say (x*, y*, z*) of (10). Then in such a case letting $(\bar{x}, \bar{y}, \bar{z}) = (x^*, y^*, z^*)$ in Theorem 4.1, we may conclude that all the solutions of (1) approach this (x^*, y^*, z^*) of (10). Thus, the system (1) is asymptotically stable under the conditions of Theorem 4.1.

Example 4.2. We shall now re-examine check Example 3.4 with constant vaccination and treatment rates. That is, we consider

$$\begin{aligned} x' &= 10 - 3xy - x + 2.5z - 2V \\ y' &= 2.7xy - ry - 3y \\ z' &= 2.5y - 2.5z \end{aligned} \qquad (14)$$

where V = 2.25 and r = 2.4. It is easy to see that the endemic equilibrium solution of this system is (2,1,1). Now by the choice of V(t)= 2.25 (1- e^{-t}) and r(t)= 2.4(1- e^{-t}) (as in Example 3.4) we observe that all the conditions of Theorem 4.1 are satisfied and hence, all the solutions of the system (1) approach the equilibrium (2,1,1) of (14), as already established in Example 3.4.

Remarks 4.3. The reason for choosing already studied Example 3.4 is to draw the attention of the readers to the observation that the predefined state (desired) (η, δ, ζ) of section 3 is nothing but an equilibrium solution of a system with constant parameters V, r such as (10) or (14). The boundedness and convergence of solutions of (1) make it a controllable system and we may notice that this is as good as a system with constant parametric values provided the time varying functions satisfy conditions such as those prescribed here. Thus, within the space of parameters, the system (1) and system (10) behave similarly.

5 Conclusion

The primary interest in investigating the infectious diseases is to understand the pandemic/epidemic situation and propose a framework to predict, assess and develop control strategies for such potential outbreaks. Mathematical modelling is one such tool.

In this study we considered a modified SIR model wherein the two control measures vaccination and treatment are regarded as time-dependent functions and studied its dynamics. Both vaccination and treatment are crucial in containing the spread of disease as the world has already witnessed in several cases including the latest pandemic COVID-19. Need, demand and availability of these measures make them time dependent rather than simple, fixed constant parameters. At the same time, they should go hand-in-hand but are not simple, independent measures. Thus, estimation of vaccination and treatment efforts help bring the situation under control. This is exactly what is followed in this work. Initially, in Theorem 2.1, conditions are obtained on vaccination function so that all solutions of the system are at least non negative and thus, represent a biological situation. It is established under specified conditions on parameters and functional relations that the solutions are close to each other. Once a bounded solution is obtained, Theorem 2.2 ensures that no solution (situation) is violent or beyond control. Thus, boundedness of solutions is important as it is not hard to handle such situations by the society. Theorem 2.3 assures this. Even boundedness is not a comfortable state - a situation could be oscillatory and needs further efforts to control it. To avoid such complications, we have studied the asymptotic behaviour of solutions.

Mathematically, a non autonomous system such as (1) does not possess an equilibrium solution to study its stability. To overcome this, we proposed an assumed or put forth a desired set of values for populations to approach this eventually. This may be regarded as an assumed equilibrium for the system. Conditions are now obtained on the parameters, functional relations so that this assumed constant equilibrium is within the range of the solution space of the system and this equilibrium comes out to be stable by virtue of Theorem 3.1. Thus, vaccination and treatment functions are estimated to bring the system to a desired state of disease. Further contemplation reveals that the pre-defined, fixed values of the populations could be equilibria of systems with constant vaccination and treatment rates. Thus, stability of non-autonomous system is derived in terms of equilibria of an autonomous system. Examples establish that our estimates are possible at least numerically bringing the populations to a predefined state and that they may be applied to real time problems.

The results and the remarks presented in Sections 3 and 4 infer that the disease dynamics may be controlled equally well either through variable rates of vaccination and treatment or for fixed rates of administration of them. The Choice is of the society basing on its preparedness or availability of resources.

The work done in this paper, provides estimates on the vaccination and treatment efforts to be made by a society in order to fight any contagious or pandemic situation and bring it to desired state. Testing the present results on a real time situation or practical (experimental or clinical) data is the next step to make this study more realistic and applicable. A proper balance of vaccination and treatment as suggested in this study could lead the society to proper utilization of its resources. Further exploration is needed in this direction. Similar behaviour of solutions

of non- autonomous systems and autonomous as studied in this paper needs a further probe for generalization of results and may be taken up by enthusiastic researchers.

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