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Disease control through removal of population using Z-control approach

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ABSTRACT

Present study considers the situation where the removal of population is adopted as a prevention measure for isolating the susceptible population from an infected region to reduce the disease prevalence. To investigate the scenario, a dynamic error based method, Z-type control is applied in an SI type disease model with the aim of achieving a predetermined disease prevalence. The controlled system is designed by introducing a new compartment (the population in an infection-free region) in the uncontrolled system to capture the removal of susceptible population from the infected region to an infection free region. By performing numerical simulations, our study shows that using Z-control mechanism, the removal of susceptible to an infection free region can effectively achieve a predetermined disease prevalence. The removal rates required for achieving a specific reduction in infected population for different levels of disease endemicity are quantified. Furthermore, the global sensitivity analysis (PRCC) is also performed to have a more clear insights on the correlations of the control parameter with the model parameters.

1. Introduction

Recurrence of the diseases that have already persisted and also the appearance of newly invaded diseases make the public health authorities and policy makers more vigilant about the control and prevention. Variations in ecological and climatic factors enhance the possibility of the emergence of new pathogens [1]. Moreover, the evolution of pathogens accelerates the emergence of the disease and worsens the predictability of disease invasion [2]. The diseases like HIV, Small pox, Rabies, Measles, Dengue, Cholera, etc. have been emerged since decades whereas Zika, Ebola, Chikungunya, MERS-CoV, etc. are recently invaded and spread worldwide within a short period of time. Communicable diseases become a potential burden to the socio-economic condition of developing and under developed countries [3]. Some neglected tropical diseases cause physical disabilities and even premature death to human which consequently slow down the economic productivity of a country [4,5]. Not only human, infectious diseases also victimize the animals, birds causing depletion in economic and agricultural growth. Diseases like avian influenza, foot and mouth disease, viral haemorrhagic septicaemia virus in fish, etc. cause huge economic losses in food, agriculture and aquaculture every year [6]. Moreover, the transmission of diseases among animals, birds, etc. create the possibility of infecting the human population. With the

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growing advancements in the modern transportation technology, infectious diseases spread in the distant parts of the world very quickly and become a global concern [7,8].

Due to the infeasibility of performing experiments and the lack of disease related data, mathematical models become popular to analyse the disease transmission mechanism as well as to investigate the consequences of the application of control measures. Several modelling frameworks such as deterministic, stochastic, agent based model, chain binomial model, spatial model, etc. have been employed to depict the disease transmission [9]. However, among these approaches, mathematical modelling in a deterministic setting gained considerable attentions perhaps because of its modelling and computational simplicity. In this approach, usually a set of ordinary differential equations are constructed with the assumption that the population under consideration is homogeneously mixed.

The investigation of the consequences of interventions is one of the major aspect in the context of infectious disease modelling. Incorporation of different intervention strategies into the model can be executed in different ways. For instance, to model the behavioural change such as awareness [10,11], isolation [12,13] or to study the impact of vaccination [14], an extra compartment is usually introduced in the model. On the other hand, in the context of vector borne disease modelling, incorporation of self protection such as use of bed net, application of vector repellent on skin, etc. [15] can be accomplished by introducing a control parameter to capture the reduction in the transmission rate. The application of different vector control strategies, treatment, etc. [16] can also be encapsulated by using a control parameter to capture the increase in the respective rates (mortality rate of vector and recovery rate). To quantify the efficiency as well as the outcomes of the control strategies mainly two popular techniques: optimal control, impulsive control have been applied in numerous studies [17,18]. In optimal control technique, usually one can seek for a time dependent control parameter for which infection burden and the costs associated with the intervention of the disease is minimized [19,20]. On the other hand, using impulsive control technique, the effect of non-continuous interventions such as weekly/monthly vector control, spraying of insecticides, etc. are evaluated [21,22]. These techniques are very useful for the assessment of effectiveness of different intervention strategies in lowering or even eliminating the disease. However, the above mentioned methods are not so useful to analyse the situations where the key objective is to achieve a predetermined infected population after applying suitable control. From epidemiological point of view, attaining a predetermined disease prevalence is an important aspect for public health organizations. World Health Organization (WHO) has adopted proper strategies to achieve targeted disease prevalence for several emerging diseases. For instance, WHO implemented strategies: Stop TB and End TB to achieve targets of 50% reduction in the disease prevalence and disease induced mortality by 2015 and 95% reduction in TB deaths between 2015 and 2035 respectively in India [23–25].

From a dynamical system's point of view, the problem of achieving a pre-decided infected population can be addressed by adopting Z-type dynamic control method proposed by Zhang et al. [26]. In Z-type control, an exogenous control is introduced in the controlled system and the control mechanism is designed in such a way that the difference between actual system's output and targeted output is forced to converge to zero.

Though initially Z-type control method has been applied in the field of neural network [27–30], recently some studies have applied this control mechanism to different ecological and eco-epidemiological models to explore the dynamics of the systems [31–34]. In the context of infectious disease modelling [35] applied Z-type dynamic control in a simple SI model and analysed the dynamics of the system. The author considered isolation of susceptible individuals through migration as the control measure and explored that the rate of migration can be designed by using Z-control method to control infectious disease. In contrast, Lacitignola et al. [36] recently studied the control of backward bifurcation phenomena using Z-type control mechanism in an SIR disease model, where they considered isolation of a portion of susceptible population by using suitable prevention measures such as masks, hand-washing, gargling, vaccination, etc. However, in the present study we consider a different kind of prevention measure: removal of susceptible population from infected region to a neighbouring infection-free region to control the disease spread. We consider a simple SI model and design a Z-type controlled system aiming to explore the disease dynamics and quantify the rate of removal of susceptible to maintain a specific disease prevalence.

Remaining parts of the manuscript are organized as follows: Section 2 describes a brief description of the model under consideration, Section 3 is devoted in analysing the long-term temporal behaviour of the uncontrolled system, design of controlled system incorporating Z-type control is presented in Section 4. The results of our study are presented in Section 5 with the help of numerical simulation. The manuscript is ended with conclusion (Section 6).

2. Description of model

We consider a simple deterministic SI-type compartmental model. The demography of the population is considered in the model in order to study the long term behaviour of the system. Total population is partitioned into two compartments: susceptible(S) and infected(I) depending on the health condition of the individuals. Susceptible population is assumed to be recruited via birth, immigration, etc. at a constant rate Λ. It is also assumed that population is decreased due to natural death at a rate μ. To model the transition from susceptible to infected we consider non-linear incidence rate. There are several studies where non-linear incidence rate has been used to capture the saturated contacts or "psychological effect" of the population [37–39]. Following the above mentioned literatures, we consider the incidence rate as $\frac{\beta SI}{a+I}$, which essentially captures more restrained increase in incidence than that of bilinear incidence and exclude the possibility of

unrestricted contact rate. Here β represents the transmission rate and the parameter a is used to capture the saturation factor. We consider the following set of ordinary differential equation to represent the disease transmission mechanism:

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \frac{\beta SI}{a+I} - \mu S \\ \frac{dI}{dt} &= \frac{\beta SI}{a+I} - \mu I, \end{aligned} \tag{2.1}$$

together with the initial conditions $S(0) > 0$ and $I(0) > 0$.

3. Basic dynamical properties

In this section, we will explore some basic dynamical behaviours of the proposed model by using standard methods of non-linear dynamics. One of the key quantity in epidemiology, the basic reproduction number ($\mathcal{R}_0$) is derived by following next generation matrix approach and based on this quantity the conditions for local and global stability of disease free equilibrium as well endemic equilibrium are derived.

Lemma 1. *Consider the compact set $\Omega = \{(S, I) : S \geq 0, I \geq 0, S + I \leq \frac{\Lambda}{\mu}\}$. Then the set Ω is positively invariant and all the forward solutions of the system (2.1) are ultimately bounded.*

Proof. Let us denote the total population by $H(t)$,

$$H(t) = S(t) + I(t). \tag{3.1}$$

We take time derivative of Eq. (3.1) along the solution of our system (2.1),

$$\begin{aligned} \frac{dH}{dt} &= \frac{dS}{dt} + \frac{dI}{dt} \\ &= \Lambda - \mu H. \end{aligned} \tag{3.2}$$

Solving the linear differential equation (3.2) we have,

$$H(t) = \frac{\Lambda}{\mu} + (H(0) - \frac{\Lambda}{\mu})e^{-\mu t}.$$

From the above equation it follows that, if $H(0) \leq \frac{\Lambda}{\mu}$, then $H(t) \leq \frac{\Lambda}{\mu}$. Therefore, the compact set Ω is positively invariant with respect to the system (2.1). Any solution with initial conditions within Ω will stay in Ω for all t and therefore bounded. □

The basic reproduction number, $\mathcal{R}_0$ measures the potential of disease invasion in a entirely susceptible population. By applying the next generation matrix approach [40], it follows that the basic reproduction number for the system (2.1) is

$$\mathcal{R}_0 = \frac{\beta \Lambda}{a\mu^2}.$$

3.1. Equilibrium and stability analysis

The system (2.1) has two equilibrium points: (*i*) disease-free equilibrium (DFE), $\mathcal{E}_0 = (\frac{\Lambda}{\mu}, 0)$, and (*ii*) the endemic equilibrium $\mathcal{E}^* = (S^*, I^*)$, where

$$\begin{aligned} S^* &= \frac{\mu a(\beta + \mu\mathcal{R}_0)}{\beta(\beta + \mu)}, \\ I^* &= \frac{\mu a(\mathcal{R}_0 - 1)}{\beta + \mu}. \end{aligned}$$

Here the endemic equilibrium $\mathcal{E}^*$ is feasible only if $\mathcal{R}_0 > 1$.

3.1.1. Disease free equilibrium and its stability

Lemma 2. *The disease free equilibrium (DFE), $\mathcal{E}_0$ for the system (2.1) is locally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. To perform local stability analysis of DFE, the corresponding Jacobian matrix $J_{\mathcal{E}_0}$ of the system (2.1) at the point $\mathcal{E}_0$ is computed as follows,

$$J_{\mathcal{E}_0} = \begin{bmatrix} -\mu & -\frac{\Lambda\beta}{\mu a} \\ 0 & \frac{\Lambda\beta}{\mu a} - \mu \end{bmatrix}.$$

The eigenvalues of $J_{\mathcal{E}_0}$ are $-\mu$ and $\frac{\beta\Lambda}{\mu a} - \mu$. Therefore, the DEF is locally asymptotically stable if $\frac{\beta\Lambda}{\mu a} - \mu < 0$, i.e. $\frac{\beta\Lambda}{\mu^2 a} < 1$. This implies if $\mathcal{R}_0 < 1$, then the DFE is locally asymptotically stable. □

Lemma 3. *The disease free equilibrium (DFE), $\mathcal{E}_0$ for the system (2.1) is globally asymptotically stable if $\mathcal{R}_0 < 1$.*

Proof. It is already shown that the disease free equilibrium (DFE), $\mathcal{E}_0$ is the only equilibrium for the system (2.1) in the compact set $\Omega = \{(S, I) : S \geq 0, I \geq 0, S + I \leq \frac{\Lambda}{\mu}\}$ if the basic reproduction number $\mathcal{R}_0 < 1$.

From the second equation of (2.1), we get

$$\begin{aligned} \frac{dI}{dt} &= \frac{\beta SI}{a+I} - \mu I \\ &\leq \frac{\beta \Lambda I}{\mu(a+I)} - \mu I \\ &\leq (\frac{\beta \Lambda}{\mu a} - \mu) I \\ &\leq \mu(\frac{\beta \Lambda}{\mu^2 a} - 1) I \\ &\leq \mu(\mathcal{R}_0 - 1) I. \end{aligned} \tag{3.3}$$

From the above inequality, it follows that, $\frac{dI}{dt} < 0$ if $\mathcal{R}_0 < 1$ and consequently $I(t)$ tends to zero as t approaches to $+\infty$. This proves that the disease free equilibrium (DFE), $\mathcal{E}_0$ for the system (2.1) is globally asymptotically stable if $\mathcal{R}_0 < 1$. □

3.1.2. Endemic equilibrium and its stability

Lemma 4. *The endemic equilibrium, $\mathcal{E}^*$ for the system (2.1) is locally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. The Jacobian matrix $J_{\mathcal{E}^*}$ of the system (2.1) at the endemic equilibrium $\mathcal{E}^*$ is given by,

$$J_{\mathcal{E}^*} = \begin{bmatrix} -\frac{\beta I^*}{a+I^*} - \mu & -\frac{a\beta S^*}{(a+I^*)^2} \\ \frac{\beta I^*}{a+I^*} & \frac{a\beta S^*}{(a+I^*)^2} - \mu \end{bmatrix}.$$

The trace (tr) and determinant (det) of the Jacobian matrix $J_{\mathcal{E}^*}$ are given by,

$$\begin{aligned} trJ_{\mathcal{E}^*} &= -\frac{\beta I^*}{a+I^*} - \mu + \frac{a\beta S^*}{(a+I^*)^2} - \mu, \\ detJ_{\mathcal{E}^*} &= (-\frac{\beta I^*}{a+I^*} - \mu)(\frac{a\beta S^*}{(a+I^*)^2} - \mu) + \frac{a\beta S^*}{(a+I^*)^2}\frac{\beta I^*}{a+I^*}. \end{aligned}$$

Substituting the values of S^* and I^* in the above expressions we get simplified form of $trJ_{\mathcal{E}^*}$ and $detJ_{\mathcal{E}^*}$ in terms of $\mathcal{R}_0$ and other model parameters as follows:

$$\begin{aligned} trJ_{\mathcal{E}^*} &= \frac{\mu^2 - \frac{2\beta\Lambda}{a} - \frac{\beta^2\Lambda}{a\mu}}{\beta + \mu\mathcal{R}_0}, \\ detJ_{\mathcal{E}^*} &= \frac{\mu^2(\beta+\mu)(\mathcal{R}_0 - 1)}{(\beta + \mu\mathcal{R}_0)^2}(\mu + \beta). \end{aligned}$$

The endemic equilibrium for the system (2.1) is locally asymptotically stable if $trJ_{\mathcal{E}^*} < 0$ and $detJ_{\mathcal{E}^*} > 0$. Now $detJ_{\mathcal{E}^*} > 0$ if $\mathcal{R}_0 > 1$. The condition $\mathcal{R}_0 > 1$ implies $\mu^2 < \frac{\beta\Lambda}{a}$. Putting this condition in the expression of $trJ_{\mathcal{E}^*}$, we see that $trJ_{\mathcal{E}^*}$ becomes negative. Therefore, the endemic equilibrium is locally asymptotically stable for $\mathcal{R}_0 > 1$. □

Lemma 5. *The endemic equilibrium for the system (2.1) is globally asymptotically stable if $\mathcal{R}_0 > 1$.*

Proof. Since we have considered a two-dimensional epidemic model, Dulac–Bendixson criterion can be applied to investigate the existence of periodic orbit (closed orbit) in susceptible–infected plane.

Let $f_1(S, I)$, $f_2(S, I)$ represent the two functions on the right hand side of system (2.1). We choose the Dulac function $B(S, I) = \frac{1}{SI}$.

Now we consider the following expression

$$D = \frac{\partial}{\partial S}(f_1 B) + \frac{\partial}{\partial I}(f_2 B).$$

On simplification we get $D = -(\frac{\Lambda}{S^2 I} + \frac{\beta}{(a+I)^2}) < 0$ for $(S, I) \in R_+^2$.

Therefore, by the Dulac–Bendixson theorem [41], there is no periodic orbit in R_+^2 for the system (2.1). Moreover, since $\mathcal{E}^*$ is the unique positive equilibrium in R_+^2 if $\mathcal{R}_0 > 1$, every positive solution will converge to $\mathcal{E}^*$. Combining the above argument with the local stability proved in Lemma 4 implies that $\mathcal{E}^*$ is globally asymptotically stable if $\mathcal{R}_0 > 1$. □

4. Design of Z-type control system

To design a Z-type control system, (*i*) extrinsic control, and (*ii*) targeted output variable are the two main quantities which are required to be specified [31,32]. The extrinsic control acts as control system's input which drives the actual system to achieve its targeted output state.

Z-type control is an error-based method and the difference between the actual state and the targeted state is defined to be the tracking error of the corresponding control system. The control scheme is considered to be successful if the error approaches to zero.

The Z-control method can be applied in a dynamical system in two ways: direct method and indirect method. The fundamental difference between these two methods is that in direct method the extrinsic control is applied to the corresponding system component whose desired state is targeted to be achieved whereas in indirect method, the control is applied to the system component other than the corresponding state variable whose desired state is aimed to be achieved [31,32].

It is to be noted that application of Z-control mechanism in ecological, epidemiological and eco-epidemiological systems implies isolation/removal and recruitment of population [31–34]. However, in epidemic situation if the Z-controller is applied in susceptible population then the update parameter is likely to be positive [35,36] which implies isolation/removal of susceptible population from the region of epidemic. In the present study, we consider a situation where an infectious disease is prevalent in a region. To lower the disease prevalence, susceptible population is removed from the infected region and moved to an accessible region free from infection. We intend to study the temporal dynamics of the infected population as well as the dynamics of the population in the infection-free region with the help of Z-type control mechanism. The primary aim is to reduce the level of disease endemicity and achieve a targeted infection prevalence by removing susceptible population. Here, we introduce a new compartment consisting of the population of an infection free region to design the Z-controlled system. The susceptible individuals removed from the infected region enter the new compartment and increase the total population of the infection-free region. Our designed Z-control system is given as follows:

$$\begin{aligned} \frac{dS}{dt} &= \Lambda - \frac{\beta SI}{a+I} - \mu S - u(t)S \\ \frac{dI}{dt} &= \frac{\beta SI}{a+I} - \mu I \\ \frac{dN}{dt} &= \Lambda_N - \mu N + u(t)S. \end{aligned} \tag{4.1}$$

Here $N(t)$ denotes the total population of the infection-free region and Λ_N represents the constant recruitment rate of the population in that region. The natural death rate of the population in the infection-free region is taken to be same as that of the population in the infected region. This assumption is quite reasonable as the variation in demographic factor is negligible between two neighbouring regions. Here $u(t)$ denotes the time-dependent removal or recruitment rate. It is to be noted that the removal or recruitment is always considered to be dependent on the number of susceptible population of the infected region, not on the number of population in the infection-free region. To control the spread of infection or to eradicate the disease, we indirectly control the abundance of susceptible individuals by means of restricted migration depending on the abundance susceptible population in the region of infection. Such restricted migration (extrinsic control) is designed by indirect Z-control parameter.

We are to derive an analytical expression for $u(t)$ from Eq. (4.1) so that the actual number of infected population $I(t)$ is converged to the desired number of infected population $I_d(t)$. Following the procedure as described in [31] for indirect method, we introduce two error functions v_1 and v_2. The design formulas for v_1 and v_2 are given by,

$$\begin{aligned} v_1 &= I(t) - I_d(t) \\ \dot{v_1} &= -\lambda v_1 \\ v_2 &= \dot{v_1} + \lambda v_1 \\ \dot{v_2} &= -\lambda v_2. \end{aligned} \tag{4.2}$$

Here λ is called the design parameter which is always positive and measures the rate of convergence of the method. Combining the Eqs. (4.1) and (4.2) we have

$$\ddot{I}(t) - \ddot{I_d}(t) + \lambda(\dot{I}(t) - \dot{I_d}(t)) = -\lambda(\dot{I}(t) - \dot{I_d}(t)) + \lambda(I(t) - I_d(t)).$$

Now substituting $\dot{I}(t)$ and $\ddot{I}(t)$ in the above equation we get the following equation,

$$\frac{\beta\left(a\dot{S}I + aS(\frac{\beta SI}{a+I} - \mu I) + \dot{S}I^2\right)}{(a+I)^2} - \mu\left(\frac{\beta SI}{a+I} - \mu I\right) - \ddot{I_d} = -2\lambda\left(\frac{\beta SI}{a+I} - \mu I - \dot{I_d}\right) - \lambda^2\left(I - I_d\right).$$

Solving for $\dot{S}$ we have,

$$\dot{S} = \frac{f(S,I) - \beta aS(\frac{\beta SI}{a+I} - \mu I)}{\beta(aI + I^2)},$$

where,

$$f(S,I) = (a+I)^2\Big(\ddot{I}_d - 2\lambda(\frac{\beta SI}{a+I} - \mu I - \dot{I}_d) + \mu(\frac{\beta SI}{a+I} - \mu I) - \lambda^2(I - I_d)\Big).$$

Let us denote $g(S,I) = \frac{f(t)-\beta aS(\frac{\beta SI}{a+I}-\mu I)}{\beta(aI+I^2)}$. Using this expression we finally obtain the explicit expression for $u(t)$ as follows:

$$u(t) = \frac{1}{S(t)}\left[\Lambda - \frac{\beta S(t)I(t)}{a+I(t)} - \mu S(t) - g(S,I)\right]. \tag{4.3}$$

It is also noted that theoretically the expression of $u(t)$ allows the possibility that any instant of time t, $u(t)$ can take both positive and negative values. Positive value of $u(t)$ indicates the removal of susceptible population from the infected region to infection-free region whereas the negative value represents the converse situation i.e the recruitment of the susceptible to the infected region. However, from the point of view of disease eradication, we are likely to get positive value of $u(t)$.

Theorem 1. *The tracking error v_1 of the Z-controlled system (4.1) equipped with the controller $u(t)$, initiating from a positive initial condition $[S(0), I(0), N(0)]^T$ converges to zero exponentially for a continuously differentiable and bounded desired state $I_d(t)$.*

Proof. From the Z-type control design formula (4.2) we have,

$$v_2 = \dot{v_1} + \lambda v_1.$$

Substituting the above equality into $\dot{v_2} = -\lambda v_2$ we get,

$$\ddot{v_1} + 2\lambda\dot{v_1} + \lambda^2 v_1 = 0. \tag{4.4}$$

Solving (4.4), we obtain

$$v_1 = (c_1 + c_2 t)e^{-\lambda t}, \forall t \geq 0,$$

where c_1 and c_2 are arbitrary constants. Using the initial conditions, we can obtain the arbitrary constants as

$$c_1 = I(0) - I_d(0) \text{ and } c_2 = \dot{I}(0) - \dot{I}_d(0) + \lambda(I(0) - I_d(0)).$$

From Lemma 1 in [42], there exist $\hat{c} > 0$, $\hat{\lambda} > 0$ such that $v_1 \leq \hat{c}e^{-\hat{\lambda}t}$. This implies that the tracking error v_1 converges to zero exponentially with rate $\hat{\lambda}$ and consequently the infected population $I(t)$ goes to the targeted infected population $I_d(t)$. □

4.1. Equilibria and local stability analysis of Z-controlled system

In this section, using standard techniques of linear stability analysis, the stability properties of the equilibrium of the system (4.1) are explored. We replace $u(t)$ in the system (4.1) by the expression given in (4.3) and we now have the following Z-controlled system

$$\begin{aligned} \frac{dS}{dt} &= g(S,I) \\ \frac{dI}{dt} &= \frac{\beta SI}{a+I} - \mu I \\ \frac{dN}{dt} &= h(S,I,N). \end{aligned} \tag{4.5}$$

The expression of $g(S,I)$ is already given previously and the expression of $h(S,I,N)$ is given by,

$$h(S,I,N) = \Lambda_N + \Lambda - \mu N - \frac{\beta SI}{a+I} - \mu S - g(S,I).$$

It is worthy to note here that the expressions of $g(S,I)$ and $h(S,I,N)$ do not include 't' explicitly. Therefore the system (4.5) is an autonomous system and we can apply the standard linearization technique to study the dynamical properties. Here we consider the number of targeted infected population to be constant, $I_d(t) = I_d = constant$. The equilibrium point of Z-controlled system (4.6) can be obtained by solving the following equations:

$$\begin{aligned} & g(S_c, I_c) = 0 \\ & \frac{\beta S_c I_c}{a+I_c} - \mu I_c = 0 \\ & h(S_c, I_c, N_c) = 0. \end{aligned} \tag{4.6}$$

Solving the above equation we get a unique equilibrium (S_c, I_c, N_c), where $S_c = \frac{\mu(a+I_d)}{\beta}$, $I_c = I_d$ and $N_c = \frac{\beta(\Lambda_N+\Lambda)-a\mu^2-(\mu^2+\beta\mu)I_d}{\beta\mu}$.

For a biologically feasible equilibrium point, N_c should be always non-negative. Therefore we have,

$$\frac{\beta(\Lambda_N + \Lambda) - a\mu^2 - (\mu^2 + \beta\mu)I_d}{\beta\mu} \geq 0.$$

On simplifying the above inequality, we get an upper bound of the desired state I_d as:

$$I_d \leq \frac{\beta\Lambda_N + a\mu^2(\mathcal{R}_0 - 1)}{\mu(\mu + \beta)}.$$

From the expression of $u(t)$ provided in (4.3), it is evident that $u(t)$ is independent of the parameters related to the newly introduced compartment $N(t)$ (i.e the population in the infection-free region). Therefore, instead of considering the Z-controlled system (4.1), if we apply Z-control to the two compartments *SI* model (2.1), the overall dynamics of these two controlled systems would not be changed in terms of achieving a desired abundance of infected. However, the inclusion of the new compartment, $N(t)$ in our Z-controlled system helps to identify the differences between the isolation of susceptible individuals by using protecting masks, bed net, vaccine, etc. and the isolation of individuals through migration. In the new Z-control model (SIN) the preventive measure (spatial isolation/removal of a portion of susceptible population) can be incorporated more accurately. After introduction of the compartment $N(t)$, we obtain an upper bound of the desired prevalence I_d for which the biological feasibility of the equilibrium is preserved. If we wish to achieve a desired infected abundance below the threshold value then the Z-control method can be applied successfully. However, if the desired infected state is greater than that threshold, then the Z-control method will not work (will not preserve the positivity of the solution trajectories of the controlled system).

Theorem 2. *The unique equilibrium point $\mathcal{E}_c = (S_c, I_c, N_c)$ of the Z-controlled system (4.5) is locally asymptotically stable.*

Proof. The Jacobian matrix at the interior equilibrium point $\mathcal{E}_c = (S_c, I_c, N_c)$ of the Z-controlled system (4.5) is

$$J(\mathcal{E}_c) = \begin{bmatrix} a_{11} & a_{12} & 0 \\ a_{21} & a_{22} & 0 \\ a_{31} & a_{32} & -\mu \end{bmatrix},$$

where $a_{11} = -2\lambda + \frac{\mu I_d}{a+I_d}$, $a_{12} = \frac{2a\mu\lambda I_d + 2\mu\lambda I_d^2 - \mu^2 I_d^2 - \lambda^2(a+I_d)^2}{\beta I_d(a+I_d)}$, $a_{21} = \frac{\beta I_d}{a+I_d}$, $a_{22} = \frac{a\mu}{a+I_d} - \mu$, $a_{31} = -\frac{\beta I_d}{a+I_d} - \mu + 2\lambda - \frac{\mu I_d}{a+I_d}$, $a_{32} = \frac{a\mu}{a+I_d} - \frac{2a\mu\lambda I_d + 2\mu\lambda I_d^2 - \mu^2 I_d^2 - \lambda^2(a+I_d)^2}{\beta I_d(a+I_d)}$.

The corresponding characteristic equation is

$$(-\mu - x)(x^2 - (a_{11} + a_{22})x + a_{11}a_{22} - a_{21}a_{12}) = 0,$$

It is to be noted that $-\mu(< 0)$ is turned out to be an eigenvalue of the Jacobian matrix. The condition for the negativity (negative or negative real part) of the remaining eigenvalues is $(a_{11} + a_{22}) < 0$ and $a_{11}a_{22} - a_{21}a_{12} > 0$. On simplifying, we get

$$(a_{11} + a_{22}) = -2\lambda < 0 \text{ and } a_{11}a_{22} - a_{21}a_{12} = \lambda^2 > 0.$$

Therefore, the equilibrium $\mathcal{E}_c = (S_c, I_c, N_c)$ of Z-controlled system is locally asymptotically stable. □

4.2. Positiveness of the solution

We have the following analytical expression of $I(t)$ by solving (4.4),

$$I(t) = I_d + c_1 e^{-\lambda t} - (c_2 - \lambda c_1)te^{-\lambda t} \tag{4.7}$$

where,

$$c_1 = I(0) - I_d, c_2 = I(0)(\mu - \tfrac{\beta S(0)}{a+I(0)}). \tag{4.8}$$

To study the positivity of infected population, $I(t)$, we present the following theorems.

Theorem 3. *Suppose the desired infected state $I_d(t) = I_d$ is positive for all $t \geq 0$. If the inequality: $(\mu - \frac{\beta S(0)}{a+I(0)}) \leq 0$ or $\lambda \geq (\mu - \frac{\beta S(0)}{a+I(0)}) > 0$ holds then $I(t) \geq 0$, $\forall t \geq 0$.*

Proof. From Eq. (4.7) it is clear that $I(t) > 0$, if

$$I_d(t) > (c_2 - \lambda c_1)t - c_1.$$

Let us consider $X(t) = I_d e^{\lambda t}$ and $Y(t) = (c_2 - \lambda c_1)t - c_1$. Consequently, if the slope of $Y(t)$ is less than the value of the derivative $\dot{X}(0) = \lambda I_d$, i.e.

$$c_2 - \lambda c_1 - \lambda I_d = c_2 - \lambda I(0) \leq 0. \tag{4.9}$$

Then the above inequality holds true for $t \geq 0$ and $I(t)$ is strictly positive for all $t \geq 0$. From Eq. (4.8), it is clear that if $(\mu - \frac{\beta S(0)}{a+I(0)}) < 0$, then $c_2 \leq 0$. Also the inequality (4.9) holds for all $\lambda > 0$. Again, if the condition: $(\mu - \frac{\beta S(0)}{a+I(0)}) > 0$ holds then the inequality (4.9) is satisfied provided $\lambda \geq (\mu - \frac{\beta S(0)}{a+I(0)})$. □

Theorem 4. *Suppose $I_d > 0$ and $(\mu - \frac{\beta S(0)}{a+I(0)}) > 0$. If $0 < \lambda_T \leq \lambda < (\mu - \frac{\beta S(0)}{a+I(0)})$, λ_T satisfy the following equation $\log(\frac{c_2-\lambda_T c_1}{\lambda_T I_d}) - \frac{c_2}{c_2-\lambda_T c_1} = 0$, then $I(t) \geq 0$, $\forall t \geq 0$.*

Proof. We consider a positive time T such that $\dot{X}(T) = \dot{Y}(T)$. For $\lambda < (\mu - \frac{\beta S(0)}{a+I(0)})$, the inequality $(\frac{c_2-\lambda c_1}{\lambda_T I_d}) > 1$ can be easily verified. Therefore, the time $T = \frac{1}{\lambda} log(\frac{c_2-\lambda c_1}{\lambda I_d})$ is positive if $(\frac{c_2-\lambda c_1}{\lambda I_d}) > 1$, i.e. $\lambda < (\mu - \frac{\beta S(0)}{a+I(0)})$. Now we want to keep the function $X(t)$ above the straight line $Y(t)$, for all $t > 0$. This can be done by decreasing the value of λ until the value λ_T which represents the case when $Y(t)$ overlaps the tangent line to $X(t)$ at T where $X(T) = Y(T)$. In such a case, the value of λ_T satisfies the equation

$$log(\frac{c_2 - \lambda_T c_1}{\lambda_T I_d}) - \frac{c_2}{c_2 - \lambda_T c_1} = 0. \quad \square$$

Theorem 5. *Suppose $I(0), I_d \in [A, B] \subset R_+$ and*
$\lambda > \frac{I(0)(\mu - \frac{\beta S(0)}{a+I(0)})}{I(0)-A}$, if $(\mu - \frac{\beta S(0)}{a+I(0)}) > 0$
$\lambda > -\frac{I(0)(\mu - \frac{\beta S(0)}{a+I(0)})}{B-I(0)}$, if $(\mu - \frac{\beta S(0)}{a+I(0)}) < 0$
then $I(t) \in [A, B]$ for all $t \geq 0$.

Proof. Let $X_A(t) = (I_d - A)e^{\lambda t}$, $X_B(t) = (I_d - B)e^{\lambda t}$, and $Y(t) = (c_2 - \lambda c_1)t - c_1$. For the assurance of the fact that $I(t) \in (A, B)$, we should verify the following condition:

$$X_A(t) < Y(t) < X_B(t), \quad for \quad all \quad t \geq 0. \tag{4.10}$$

Following the procedure described in Theorem 3, we have

$$X_B(0) = I_d - B < I_d - I(0) = Y(0) < I_d - A = X_A(0).$$

In order to satisfy Eq. (4.10), it should be verified that the slop of $Y(t)$ is bounded, having the upper bound and lower bound as $\dot{X}_B(0) = \lambda(I_d - B)$, and $\dot{X}_A(0) = \lambda(I_d - A)$ respectively. That means the slop of $Y(t)$ is bounded if the following two conditions are satisfied:

$$c_2 - \lambda(c_1 + I_d - A) = c_2 - \lambda(I(0) - A) < 0, \tag{4.11}$$

$$\lambda(c_1 + I_d - B) - c_2 = -c_2 - \lambda(B - I(0)) < 0. \tag{4.12}$$

It can be observed that if $c_2 < 0$, then the condition (4.11) holds true. On the other hand, if $c_2 > 0$, then we have $\lambda > \frac{c_2}{I(0)-A}$. In a similar manner, the condition (4.12) holds if $c_2 > 0$ and $\lambda > \frac{c_2}{B-I(0)}$ if $c_2 < 0$. Hence, we can get bound for λ according to the sign of c_2. □

Theorem 6. *Suppose $I(0), I_d \in [A, B] \subset R_+$ and*
$\lambda_{T_A} \leq \lambda < \frac{I(0)(\mu - \frac{\beta S(0)}{a+I(0)})}{I(0)-A}$, if $(\mu - \frac{\beta S(0)}{a+I(0)}) > 0$
$\lambda_{T_B} \leq \lambda < -\frac{I(0)(\mu - \frac{\beta S(0)}{a+I(0)})}{B-I(0)}$, if $(\mu - \frac{\beta S(0)}{a+I(0)}) < 0$
where λ_{T_A} and λ_{T_B} satisfy the equations

$$log(\frac{c_2-\lambda_{T_A} c_1}{\lambda_{T_A}(I_d-A)}) - \frac{c_2}{c_2-\lambda_{T_A} c_1} = 0 \tag{4.13}$$

$$log(\frac{c_2-\lambda_{T_B} c_1}{\lambda_{T_B}(I_d-B)}) - \frac{c_2}{c_2-\lambda_{T_B} c_1} = 0 \tag{4.14}$$

with $T_A, T_B \geq 0$ satisfying
$(I_d - A)e^{\lambda_{T_A} T_A} = -c_1 + (c_2 - \lambda_{T_A} c_1)T_A$
$(I_d - A)e^{\lambda_{T_B} T_B} = -c_1 + (c_2 - \lambda_{T_B} c_1)T_B$
then $I(t) \in [A, B]$ for all $t \geq 0$.

Proof. We first consider the case $(\mu - \frac{\beta S_1(0)}{a+I_1(0)}) > 0$. For the values of $\lambda > \frac{I(0)(\mu - \frac{\beta S(0)}{a+I(0)})}{I(0)-A}$, there exists a positive time T_A where $\dot{X}_A(T_A) = \dot{Y}(T_A)$. This gives $T_A = \frac{1}{\lambda} log(\frac{c_2 - \lambda c_1}{\lambda(I_d - A)})$.

Similarly, in case of $(\mu - \frac{\beta S(0)}{a+I(0)}) < 0$, there exists a positive time T_B, where

$$T_B = \frac{1}{\lambda} log(\frac{c_2 - \lambda c_1}{\lambda(I_d - B)}) \text{ for } \lambda < -\frac{I(0)(\mu - \frac{\beta S(0)}{a+I(0)})}{I(0)-A}.$$

Now we want to keep the function $X_A(t)$ and $X_B(t)$ above and below the straight line $Y(t)$, for all $t > 0$. This can be done by decreasing the value of λ until $Y(t)$ overlaps the tangent line to $X_B(t)$ and $X_A(t)$ at T_B and T_A where $X_A(T_A) = Y(T_A)$ and $X_B(T_B) = Y(T_B)$. In such a case, the value of λ_{T_A} and λ_{T_B} satisfy the following equations:
$log(\frac{c_2 - \lambda_{T_A} c_1}{\lambda_{T_A}(I_d - A)}) - \frac{c_2}{c_2 - \lambda_{T_A} c_1} = 0$
and
$log(\frac{c_2 - \lambda_{T_B} c_1}{\lambda_{T_B}(I_d - B)}) - \frac{c_2}{c_2 - \lambda_{T_B} c_1} = 0.$ □

Theorem 7. *Consider $S(0), I(0), N(0) > 0$ and let*
(i) $I(0) > I_d > 0$
(ii) $(\mu - \frac{\beta S(0)}{a+I(0)}) > 0$
(iii) $\lambda > (\mu - \frac{\beta S(0)}{a+I(0)})$
(iv) $\frac{\beta S(0) I(0)}{a+I(0)} - \mu I_d > 0$ and $(\lambda - \mu)[I(0)(\mu - \frac{\beta S(0)}{a+I(0)}) - \lambda(I(0) - I_d)] > 0$.
Then $S(t) \geq 0$, $I(t) > 0$ for all $t \geq 0$.

Proof. By considering the assumptions of this theorem and also from Theorem 3, it follows that $I(t) > 0$ for all $t \geq 0$. From the Z-controlled system (4.1), the susceptible population $S(t)$ can be expressed as follows

$$S(t) = \frac{a+I}{\beta}(\frac{\dot{I}}{I} + \mu).$$

By using Eq. (4.7) in the above expression, we obtain

$$S(t) = \frac{a+I}{\beta}(\frac{(\lambda - \mu)(c_2 - \lambda c_1)t + c_1\mu - c_2 + I_d e^{\lambda t}\mu}{I_d e^{\lambda t} + c_1 - (c_2 - \lambda c_1)t}).$$

Since $I(t) > 0$, we see that the denominator of the above expression is positive. The sufficient conditions for the numerator be positive are

$$c_1\mu - c_2 > 0 \text{ and } (\lambda - \mu)(c_2 - \lambda c_1) > 0.$$

After simplification we have the following conditions for positiveness of $S(t)$:

$$(\mu - \frac{\beta S(0)}{a + I(0)}) > 0 \text{ and } (\lambda - \mu)[I(0)(\mu - \tfrac{\beta S(0)}{a+I(0)}) - \lambda(I(0) - I_d)] > 0. \quad \square$$

From Eq. (4.5), we get

$$\begin{aligned} \tfrac{dN}{dt} + \mu N &= \Lambda_N + \Lambda - \tfrac{\beta SI}{a+I} - \mu S + \tfrac{aS}{a+I}(\tfrac{\beta S}{a+I} - \mu) \\ &- \tfrac{(a+I)}{\beta I}\left[(\mu - 2\lambda)(\tfrac{\beta SI}{a+I} - \mu I) - \lambda^2(I - I_d)\right]. \end{aligned} \tag{4.15}$$

Substituting $S(t)$ by $\frac{a+I}{\beta}(\frac{\dot{I}}{I} + \mu)$ in Eq. (4.15) we have:

$$\begin{aligned} \tfrac{dN}{dt} + \mu N &= \Lambda_N + \Lambda + \tfrac{a+I}{\beta I}\left[(\lambda - \mu)^2 I - \lambda^2 I_d\right] \\ &+ \tfrac{(\dot{I} + \mu I)}{\beta I^2}\left[a(\dot{I} + \mu I) + 2a(\lambda - \mu)I + 2(\lambda - \mu)I^2 - a\mu I - \beta I^2\right]. \end{aligned}$$

Solving the above linear differential equation in N, we get

$$\begin{aligned} N(t) &= \tfrac{\Lambda_N + \Lambda}{\mu} + e^{-\mu t}\int \Bigg[e^{\mu\tau}\tfrac{a+I}{\beta I(\tau)}\left[(\lambda - \mu)^2 I(\tau) - \lambda^2 I_d\right] \\ &+ \tfrac{(\dot{I(\tau)} + \mu I(\tau))}{\beta I^2(\tau)}\left[\, a(\dot{I(\tau)} + \mu I(\tau)) + 2a(\lambda - \mu)I(\tau)\right. \\ &+ \left. 2(\lambda - \mu)I^2(\tau) - a\mu I(\tau) - \beta I^2(\tau)\,\right] \Bigg] d\tau. \end{aligned} \tag{4.16}$$

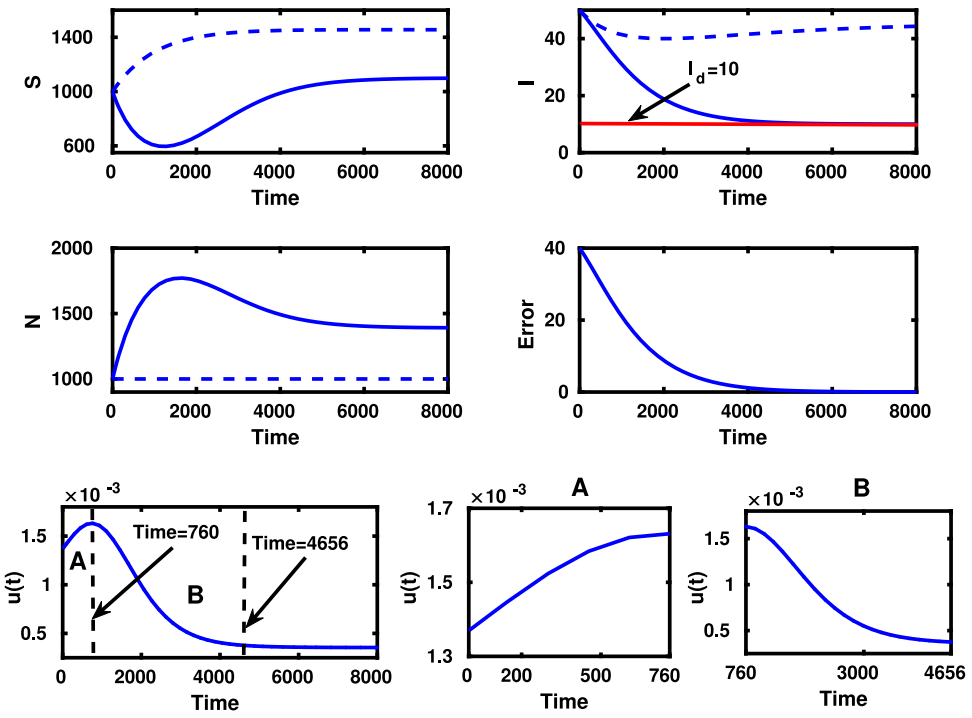

Fig. 1. Temporal variation of each compartment of the system (4.1). The desired number of infected population is fixed as $I_d = 10$. The other parameters are $\mu = 0.001$, $\beta = 0.0001$, $\Lambda = 1.5$, $\Lambda_N = 1$, $a = 100$, $\lambda = 0.00125$ and the corresponding basic reproduction number ($\mathcal{R}_0$) is 1.5. The dashed line indicates the trajectory of the uncontrolled system and the solid line represents the trajectory of the controlled system. The temporal variation of $u(t)$ for the time intervals [0,760] (A) and [761,4656] (B) are presented separately.

Regarding the positivity of the compartment $N(t)$, we do not find any simple parametric condition for which $N(t)$ remains positive for all $t \geq 0$. However, in Section 5, the positivity of $N(t)$ is verified numerically for a given set of parameter values.

5. Results

In this section extensive numerical simulations are performed to demonstrate the impact of population removal/recruitment and its effectiveness through Z-control mechanism by considering several situations like: (i) achieving a predetermined disease prevalence, (ii) disease eradication, (iii) biological feasibility of Z-control method, (iv) sensitivity between control parameter and other model parameters, (v) quantification of control parameter for different levels of disease endemicity.

5.1. Achievement of a targeted disease prevalence

We investigate the disease dynamics and also the temporal variation of the control $u(t)$ when a predefined disease prevalence I_d is targeted. For example, we consider an epidemic situation ($\mathcal{R}_0 = 1.5$) with the initial populations $(S, I, N) = (1000, 50, 1000)$. In such a situation, we fix $I_d = 10$ and simulate the system (4.5) along with the update parameter $u(t)$ given in Eq. (4.3) using the in-built function *ode45* in MATLAB (Mathworks, R2014a). From Fig. 1, it is observed that by applying Z-control, the system (4.5) approaches towards the controlled equilibrium $(S_c, I_c, N_c) = (1100, 10, 1390)$. The control parameter $u(t)$ assumes positive values throughout the specified time interval (see Fig. 1). Positive value of $u(t)$ indicates the removal of susceptible population from infected region to the infection-free region which is indeed practically feasible. Fig. 1 shows that removal of susceptible population from infected region to infection-free region can effectively achieve the targeted disease prevalence. Initially, 0.14% susceptible population should be removed and the percentage of removal increases from 0.14% to 0.16% between the time interval $[0, 760]$. In the subsequent time interval ($[761, 4656]$), the rate of removal decreases and achieve the desired infected population. It is to be noted that 0.04% population should be removed to maintain the targeted disease prevalence (see Fig. 1).

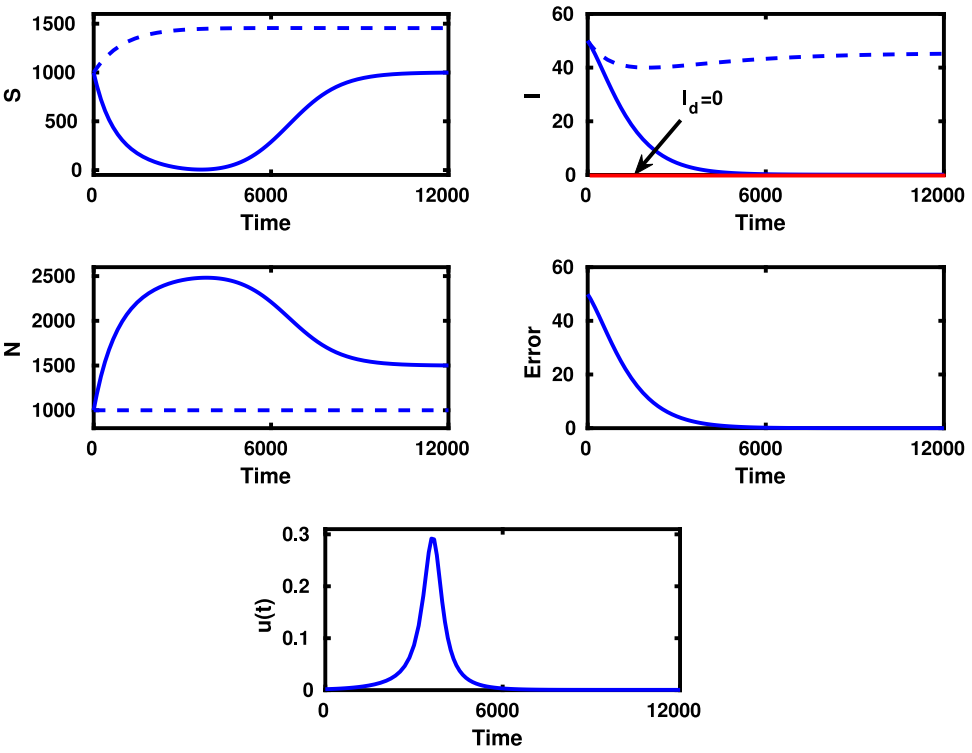

Fig. 2. Temporal variation of each compartment of the system (4.1). The desired state is fixed as $I_d = 0$. The other parameters are same as given in Fig. 1. The dashed line indicates the trajectory of the uncontrolled system and the solid line represents the trajectory of the controlled system.

5.2. Disease eradication

We analyse the possibility of the eradication of disease in the infected region through the removal of susceptible population. For the case of disease eradication we set $I_d = 0$ in system (4.5) with the initial condition $(S, I, N) = (1000, 50, 1000)$. We see from the Fig. 2 that the system (4.5) asymptotically converges to the controlled equilibrium $(S_c, I_c, N_c) = (1000, 0, 1500)$. This implies that the disease eradication is possible by removing the susceptible population from the infected region to an infection-free region. Similar to the case described earlier, the removal rate gradually increases at the initial time period and attains the maximum value 0.3 and in the subsequent time it decreases and converges to zero (see Fig. 2). It is observed that in order to eradicate the disease stronger control effort ($u(t)$) is required. It is to be noted that, once the infected population become zero, in the subsequent time there is no requirement of removal of susceptible population to maintain the disease free state.

5.3. Biological feasibility of Z-control method

It is already proved in Theorem 1 that Z-control method drives the system to the desired state for any positive initial condition. However, this control method sometimes fails to capture the biological feasibility though the desired state is achieved analytically [32,36]. Depending on the initial conditions one or more state variables of the controlled system may traverse through negative values while approaching to the desired state, which is unrealistic from biological point of view. In Fig. 3 it is shown that all the state variables remain positive while approaching to the controlled equilibrium $(S_c, I_c, N_c) = (1000, 0, 1500)$ for the initial condition (900, 40, 1000).

On the other hand, Fig. 4 shows that for a different initial condition (400, 90, 1200), the susceptible population becomes negative in the transient period while approaching to the desired equilibrium $(S_c, I_c, N_c) = (1000, 0, 1500)$.

We further demonstrate the role of the design parameter λ in determining the range of initial conditions for which the Z-controlled system approaches the desired equilibrium maintaining the biological feasibility. In Fig. 5, the basins of attraction for the controlled equilibrium $(S_c, I_c, N_c) = (1000, 0, 1500)$ are plotted in $S - I$ plane for increasing values of the design parameter λ. From Fig. 5, it is observed that the basin of attraction for analytically as well as biologically successful Z-control approach (i.e. the blue region) expands when the design parameter λ is increased (i.e for $\lambda = 0.0003; 0.0004; 0.0006$) up to a threshold value λ^*. If the value of λ exceeds the threshold value then the basin of attraction for successful Z-control approach gradually squeezes (i.e for $\lambda = 0.00125; 0.0013$). Finally the basin of

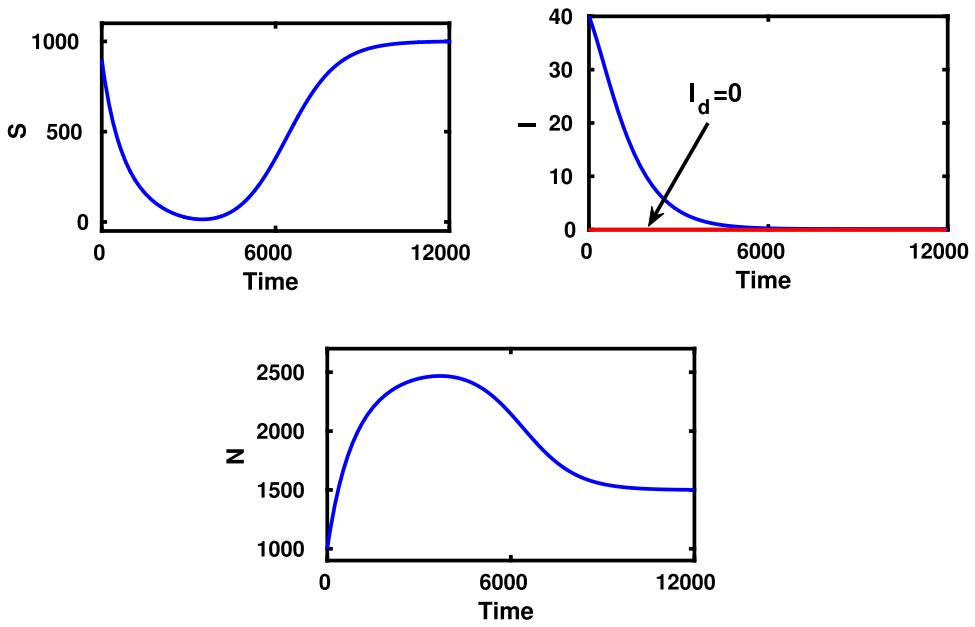

Fig. 3. Time series of all the compartments of the system (4.5). All the state variables assume non-negative values throughout the specified time interval. The desired state is fixed as $I_d = 0$. The other parameters are same as in Fig. 1. The initial conditions are taken as (900, 40, 1000). All the other parameters are fixed as in Fig. 1.

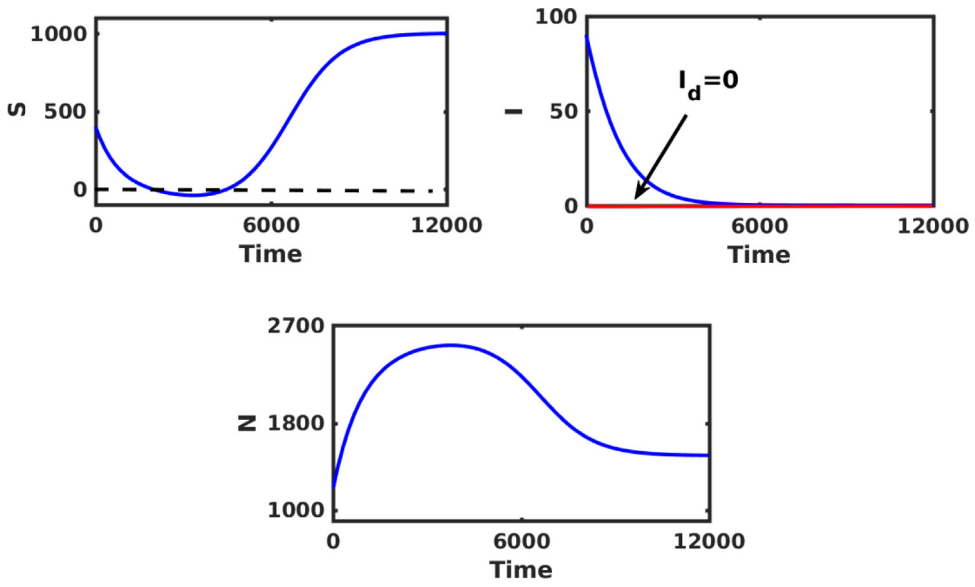

Fig. 4. Time series of all the compartments of the system (4.5) with initial conditions (400, 90, 1200). The desired state is fixed as $I_d = 0$. The susceptible population becomes negative for some time interval. All the other parameters are fixed as in Fig. 1.

attraction completely disappears when the value of λ is increased further (i.e for $\lambda = 0.0015$). Therefore, to make the Z-control successful for a broader range of initial conditions, an intermediate value of the design parameter λ should be chosen. Similar kind of observation has also been reported by Lacitignola et al. [36] in the context of epidemic model.

5.4. Sensitivity analysis

From the expression of $u(t)$ in (4.3), it is clear that the control parameter $u(t)$ depends on several model parameters and also the design parameter of the Z-control system. Sensitivity analysis is performed to measure the contribution of input parameters in the uncertainty of the output parameter [43]. Several techniques for performing sensitivity analysis are

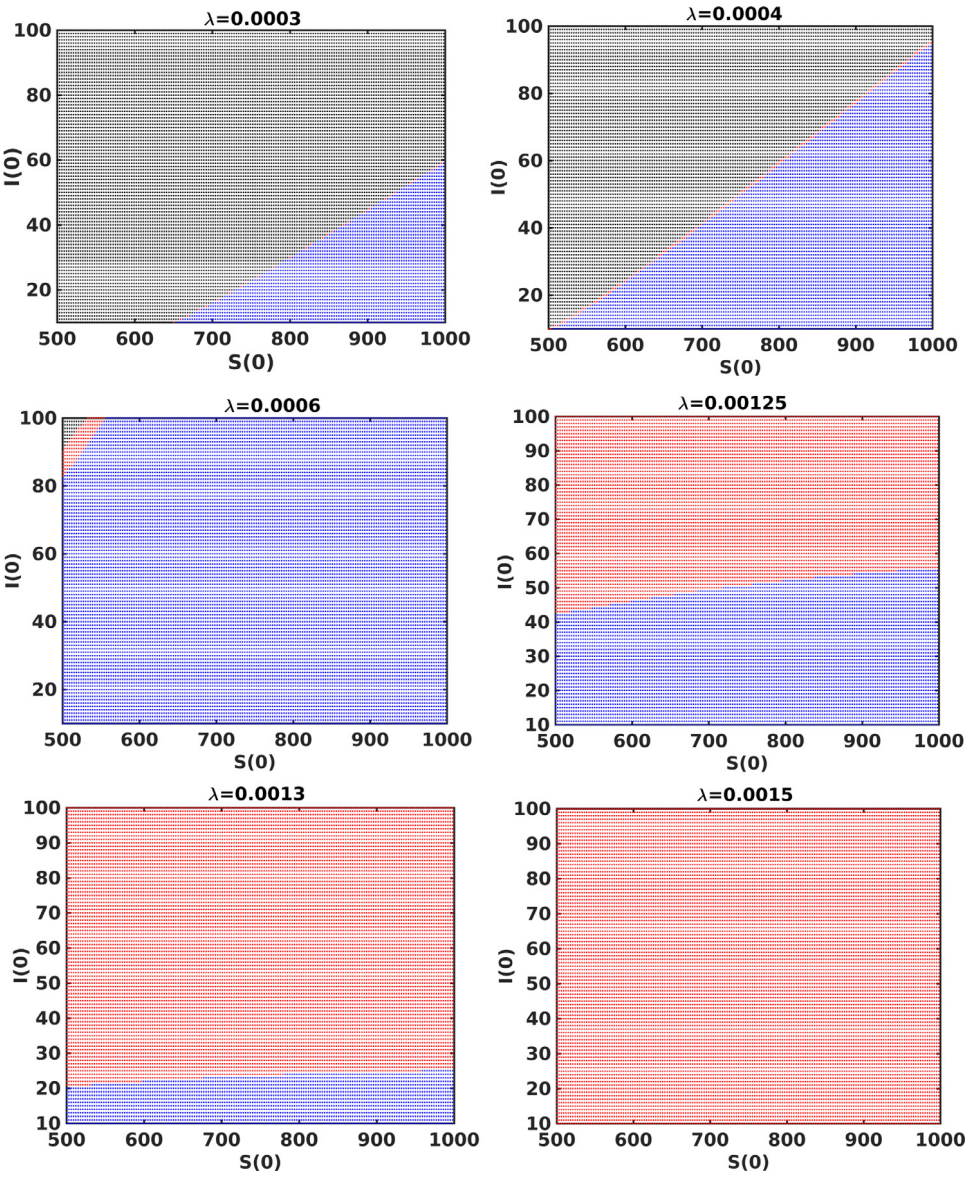

Fig. 5. Basins of attraction of the Z-controlled equilibrium point $(S_c, I_c.N_c) = (1000, 0, 1500)$ for increasing values of the design parameter λ: $\lambda = 0.0003; 0.0004; 0.0006; 0.00125; 0.0013; 0.0015$ respectively. The blue region denotes the set of all initial conditions for which the Z-control is successful and all the corresponding trajectories always preserve the positiveness while approaching the Z-controlled equilibrium. The black region represents the set of all initial conditions for which the Z-control fails to achieve the desired equilibrium. The red region represents the set of all initial conditions for which the Z-control is successful but fails to preserve the positiveness of the trajectories. All the other parameters are same as in Fig. 1.

available. Here we adopt partial rank correlation coefficients (PRCC), a sample based approach to quantify the sensitivity between $u(t)$ and the model parameters. A correlation coefficient between the input $x_i (i = 1, 2, \ldots, M)$ and output y is defined by,

$$\rho_{x_i,y} = \frac{\sum_{k=1}^{N}(x_{ik} - \bar{x})(y_k - \bar{y})}{\sqrt{\sum_{k=1}^{N}(x_{ik} - \bar{x})^2 \sum_{k=1}^{N}(y_k - \bar{y})^2}}.$$

The correlation coefficient $\rho_{x_i,y}$ lies between -1 and $+1$. If the data x_i and y are rank transformed then the partial rank correlation coefficient (PRCC) between x_i and y is measured as the correlation coefficient between the residuals $(x_i - \hat{x}_i)$ and $(y - \hat{y})$, where $\hat{x}_i$ and $\hat{y}$ follow some linear regression models [44]. By calculating PRCC, one can identify the influential parameters and investigate how they are correlated with the output.

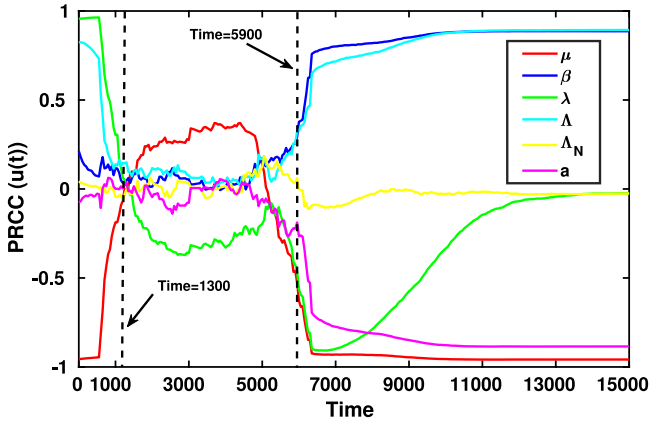

Fig. 6. Temporal variation of PRCC of control profile $u(t)$ with respect to different parameters.

We consider $u(t)$ as output and evaluate PRCC by taking all the model parameters and design parameter as input. Since $u(t)$ is a dynamic quantity, we calculate the PRCC over the time period [0, 15000] to get insights on how the correlations between $u(t)$ and other parameters vary over time.

To perform sensitivity analysis, we adopt Latin Hypercube Sampling (LHS) technique to generate samples for each input parameter [44]. For each parameter 1000 samples are drawn from uniform distribution from a biologically relevant interval. The dynamics of the PRCC values between $u(t)$ and the input parameters are depicted in Fig. 6. The temporal variations of the PRCCs are represented in three time intervals: (*i*) at initial time interval, (*ii*) the time interval when transitions occur and (*iii*) the time interval when system stabilizes (see Fig. 6). It is noted that $u(t)$ and the natural death rate μ are negatively correlated at the beginning and become positively correlated in the transition time and subsequently the correlation becomes negative. The transmission rate is positively correlated with $u(t)$ throughout the time interval and specifically during the stabilization period the correlation becomes very high. Increase in transmission rate implies higher disease incidence therefore in higher endemicity situation the rate of removal ($u(t)$) should be higher to achieve the targeted disease state. This might be a possible reason for this positive correlation between β and $u(t)$. The design parameter λ is positively correlated with $u(t)$ initially and the correlation becomes negative during transient period and ultimately becomes uncorrelated as the system stabilizes. The recruitment rate of susceptible population in the infected region is always positively correlated with $u(t)$. Since recruitment of susceptible increases the possibility of disease incidence and therefore the removal rate should be kept high to maintain a specified disease state. However the recruitment rate of susceptible in the infection free region does not possess any correlation with $u(t)$. This observation is quite obvious since the rate of susceptible removal from infected region should not be dependent on how much population is recruited in the infection free region. The parameter a is negatively correlated and the correlation becomes highly negative when the system has achieved the desired state.

5.5. Quantification of removal rate in different levels of endemicity

From Figs. 1 and 2 we can see that in order to achieve a desired prevalence the removal rate ($u(t)$) initially increases and attains the maximum value and in the subsequent time $u(t)$ gradually decreases and asymptotically approaches to a fixed value when the desired state of the infected population is achieved. Here we quantify the maximum value of $u(t)$ (see Fig. 7(A)) and the final value of $u(t)$ (see Fig. 7(B)) while achieving the desired infected density. We vary the force of infection and compute the basic reproduction number ($\mathcal{R}_0$) of the uncontrolled system which indicates the endemicity of the current epidemic. Then we vary the density of the targeted infected density and calculate the percentage of change among infected population and also note down the maximum value of update parameter $u(t)$ and the end value of the update parameter when the Z-control is successful. The percentage of reduction in infection (i.e. relative cases reduction) for a successful implementation of Z-controller can be more informative than that of absolute value of reduction in infection. Now we use contour plot of the maximum value of $u(t)$ and the end value of $u(t)$. In X-axis we vary the target i.e. percentage of reduction in infected density and in Y-axis we vary the $\mathcal{R}_0$ (i.e. endemicity/infectiousness). This picture can give a better idea for application of Z-control method in various endemic situations (for different disease transmission rate) with different targets such as controlling up to a desired/predetermined disease prevalence. From Fig. 7(A) it is seen that if the required percentage of infection reduction increases then the maximum value of the removal rate ($u(t)$) increases quite expectedly to achieve the desired disease prevalence. In particular, say for $\mathcal{R}_0 = 5$ to achieve up to 40% case reduction maximum 0.05% susceptible population should be removed (see Fig. 7(A)). Further it is observed that to reduce 80% infection, maximum 0.25% susceptible population should be removed. It is also noted that to achieve comparatively low cases reduction say up to 30%, in different levels of endemicity (i.e. for different values of $\mathcal{R}_0$), the maximum value

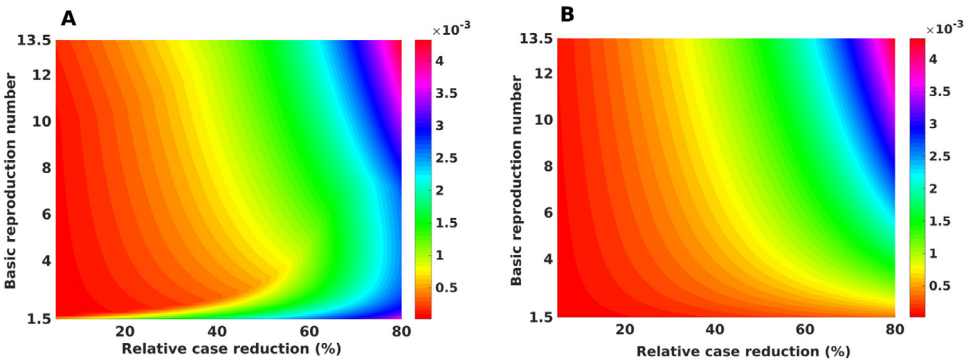

Fig. 7. (A) The colour bar represents the maximum value of the rate of removal ($u(t)$) during the whole time interval for achieving particular relative cases reduction for different values of $\mathcal{R}_0$. The value of $\mathcal{R}_0$ is obtained by varying the transmission rate β. (B) The colour bar represents the stabilized value of $u(t)$ after achieving particular relative cases reduction for different values of $\mathcal{R}_0$.

of the removal rate does not vary much. On the other hand, from Fig. 7(B) we observe that for a particular value of $\mathcal{R}_0$, if the required percentage of infected cases reduction increases then the end value of $u(t)$ also increases. Similar to the case of maximum value of $u(t)$ to achieve comparatively low cases reduction for different values of $\mathcal{R}_0$, a little variation in the end value of the removal rate is observed.

6. Conclusion

Implementation of different efficient and novel control strategies becomes essential to curb the rapid invasion of infectious diseases. Depending on the mode of transmission of the disease, the corresponding control strategies are designed to reduce the current disease prevalence as well as to restrain future outbreaks. Different mathematical and computational approaches have been employed by the researchers to capture the disease transmission scenario more realistically and also assess the impact of applying control strategies in lowering the disease prevalence.

In this study, we considered the isolation of a suitable portion of susceptible population as a control strategy to achieve a pre-determined disease prevalence. Isolation of susceptible population essentially reduces the contacts between infected and susceptible and consequently slows down the disease transmission process. Effective contacts between susceptible and infected can be lowered by the usage of suitable prevention measures such as use of masks, vaccination, hand-washing, etc. Lacitignola et al. [36] have referred the above mentioned prevention measures as extrinsic controls in a Z-type controlled system. However, in our study we have considered the spatial isolation of susceptible population, i.e., the removal of susceptible population from the infected region to a neighbouring infection-free region is considered as the prevention measure. We considered that a portion of susceptible population is removed from the region of infection which resulted lower contacts between susceptible and infected individuals. In the context of epidemic outbreak, our study considered a different kind of control measure on susceptible population and analysed various epidemiological queries using Z-control method.

Our analysis showed that removal of susceptible population from infected region to the infection free region can effectively achieve the predetermined disease prevalence. It has also been shown that the Z-control approach can be applied for the elimination of the disease. Moreover, introduction of a new compartment in our Z-controlled system not only captures the whereabouts of the removed susceptible population but also provides an upper bound of the desired prevalence for which the biological feasibility of the equilibrium is preserved for the controlled system. Therefore, if the desired infected abundance is below a threshold value, then the Z-control method can be applied successfully, otherwise Z-control method will fail to achieve the target.

We have demonstrated that the violation of biological feasibility of the solution of the controlled system may be observed due to the change in the initial conditions. Further numerical investigation suggested that intermediate value of the design parameter λ should be chosen to have a broader set of biologically feasible basin of attraction.

Sensitivity analysis between the removal rate and other parameters provides the clue that how different epidemiological and demographic factors influence the removal rate of the susceptible population which might help the policy makers and public health authorities in designing the control measures. Our study also provides the insights on the rate of removal to achieve a particular percentage of reduction in infected population for different levels of disease endemicity. This quantified removal rate serves as essential information about the portion of susceptible population should be removed to an infection free region to lower or even eliminate the disease.

The indirect Z-control approach can be successfully applied in severe disease outbreak situations. Since it is not always manageable to provide medicines or vaccines in disease outbreak, the removal of susceptible population to safe region might be beneficial in such a situation. The control mechanism described in our study can be applied not only to the fatal human diseases like Ebola, MERS CoV, etc. but also to the diseases which infect animals, birds, fishes, etc. Therefore, we

believe that the application of Z-control mechanism to disease dynamics can provide fruitful insights in designing suitable disease control strategy.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] S.J. Schrag, P. Wiener, Emerging infectious disease: what are the relative roles of ecology and evolution? Trends Ecol. Evol. 10 (8) (1995) 319–324.
[2] H. Chabas, S. Lion, A. Nicot, S. Meaden, S. van Houte, S. Moineau, et al., Evolutionary emergence of infectious diseases in heterogeneous host populations, PLoS Biol. 16 (9) (2018) e2006738.
[3] K. Jones, N. Patel, M.A. Levy, A. Storeygard, D. Balk, J.L. Gittleman, P. Daszak, Global trends in emerging infectious diseases, Nature 451 (7181) (2008) 990.
[4] C.D. Mathers, M. Ezzati, A. Lopez, Measuring the burden of neglected tropical diseases: the global burden of disease framework, PLoS Negl. Trop. Dis. 1 (2) (2007) e114.
[5] L. Conteh, T. Engels, D. Molyneux, Socioeconomic aspects of neglected tropical diseases, Lancet 375 (9710) (2010) 239–247.
[6] EPIZONE, Animal diseases, http://www.epizone-eu.net/en/Home/Animal-diseases.html.
[7] V. Colizza, A. Barrat, M. Barthélemy, A. Vespignani, The role of the airline transportation network in the prediction and predictability of global epidemics, Proc. Natl. Acad. Sci. USA 103 (7) (2006) 2015–2020.
[8] A.J. Tatem, D.J. Rogers, S.I. Hay, Global transport networks and infectious disease spread, Adv. Parasit. 62 (2006) 293–343.
[9] N.C. Grassly, C. Fraser, Mathematical models of infectious disease transmission, Nat. Rev. Microbiol. 6 (6) (2008) 477.
[10] S. Funk, M. Salathé, V.A.A. Jansen, Modelling the influence of human behaviour on the spread of infectious diseases: a review, J. R. Soc. Interface 7 (50) (2010) 1247–1256.
[11] S. Samanta, S. Rana, A. Sharma, A.K. Misra, J. Chattopadhyay, Effect of awareness programs by media on the epidemic outbreaks: A mathematical model, Appl. Math. Comput. 219 (12) (2013) 6965–6977.
[12] Y. Chen, B. Wen, Z. Teng, The global dynamics for a stochastic SIS epidemic model with isolation, Physica A 492 (2018) 1604–1624.
[13] M.A. Safi, A.B. Gumel, Qualitative study of a quarantine/isolation model with multiple disease stages, Appl. Math. Comput. 218 (5) (2011) 1941–1961.
[14] M.J. Keeling, M.E.J. Woolhouse, R.M. May, G. Davies, B.T. Grenfell, Modelling vaccination strategies against foot-and-mouth disease, Nature 421 (6919) (2003) 136.
[15] R.K. Gupta, L.C. Rutledge, Role of repellents in vector control and disease prevention, Am. J. Trop. Med. Hyg. 50 (6_Suppl.) (1994) 82–86.
[16] A.M. Kilpatrick, S.E. Randolph, Drivers, dynamics, and control of emerging vector-borne zoonotic diseases, Lancet 380 (9857) (2012) 1946–1955.
[17] R.M. Anderson, R.M. May, Infectious Diseases of Humans: Dynamics and Control, Oxford University Press, 1991.
[18] M.J. Keeling, P. Rohani, Modeling Infectious Diseases in Humans and Animals, Princeton University Press, 2011.
[19] H.R. Joshi, S. Lenhart, M.Y. Li, L. Wang, Optimal control methods applied to disease models, Contemp. Math. 410 (2006) 187–208.
[20] S. Lenhart, J.T. Workman, Optimal Control Applied to Biological Models, Chapman and Hall/CRC, 2007.
[21] L. Mailleret, V. Lemesle, A note on semi-discrete modelling in the life sciences, Philos. Trans. A Math. Phys. Eng. Sci. 367 (1908) (2009) 4779–4799.
[22] D.D. Bainov, P.S. Simeonov, Impulsive Differential Equations: Asymptotic Properties of the Solutions, Vol. 28, World Scientific, 1995.
[23] S. Mandal, V.K. Chadha, R. Laxminarayan, N. Arinaminpathy, Counting the lives saved by DOTS in India: a model-based approach, BMC Med. 15 (1) (2017) 47.
[24] World Health Organization (WHO), The stop TB strategy, 2006, http://apps.who.int/iris/bitstream/10665/69241/1/WHO-HTM-STB-2006.368-eng.pdf, (Accessed 1 March 2019).
[25] World Health Organization (WHO), End WHO, Strategy TB. Global strategy and targets for tuberculosis prevention, care and control after 2015, 2015, http://www.who.int/tb/strategy/en/, (Accessed 1 March 2019).
[26] Y. Zhang, Z. Li, Zhang neural network for online solution of time-varying convex quadratic program subject to time-varying linear-equality constraints, Phys. Lett. A. 373 (18–19) (2009) 1639–1643.
[27] Y. Zhang, C. Yi, Zhang Neural Networks and Neural-Dynamic Method, Nova Science Publishers, Inc., 2011.
[28] B. Liao, Y. Zhang, Different complex ZFs leading to different complex ZNN models for time-varying complex generalized inverse matrices, IEEE Trans Neural Netw. Learn. Syst. 25 (9) (2013) 1621–1631.
[29] D. Guo, Y. Zhang, Neural dynamics and Newton–Raphson iteration for nonlinear optimization, ASME J. Comput. Nonlinear Dyn. 9 (2) (2014) 021016.
[30] Y. Zhang, D. Jiang, J. Wang, A recurrent neural network for solving Sylvester equation with time-varying coefficients, IEEE Trans. Neural Netw. 13 (5) (2002) 1053–1063.
[31] Y. Zhang, X. Yan, B. Liao, Y. Zhang, Y. Ding, Z-type control of populations for Lotka–Volterra model with exponential convergence, Math. Biosci. 272 (2016) 15–23.
[32] D. Lacitignola, F. Diele, C. Marangi, A. Provenzale, On the dynamics of a generalized predator–prey system with Z-type control, Math. Biosci. 280 (2016) 10–23.
[33] S.S. Nadim, S. Samanta, N. Pal, I.M. ELmojtaba, I. Mukhopadhyay, J. Chattopadhyay, Impact of predator signals on the stability of a Predator–Prey System: A Z-control approach, Differ. Equ. Dyn. Syst. (2018) 1–17.

[34] A. Alzahrani, A.S. Alshomrani, N. Pal, S. Samanta, Study of an eco-epidemiological model with Z-type control, Chaos Solitons Fractals 113 (2018) 197–208.
[35] S. Samanta, Study of an epidemic model with Z-type control, Int. J. Biomath. 11 (07) (2018) 1850084.
[36] D. Lacitignola, F. Diele, On the Z-type control of backward bifurcations in epidemic models, Math. Biosci. (2019) 108215.
[37] V. Capasso, G. Serio, A generalization of the Kermack–McKendrick deterministic epidemic model, Math. Biosci. 42 (1–2) (1978) 43–61.
[38] W. Liu, S.A. Levin, Y. Iwasa, Influence of nonlinear incidence rates upon the behavior of SIRS epidemiological models, J. Math. Biol. 23 (2) (1986) 187–204.
[39] S. Ruan, W. Wang, Dynamical behavior of an epidemic model with a nonlinear incidence rate, J. Differ. Equ. 188 (1) (2003) 135–163.
[40] P.V.d. Driessche, J. Watmough, Reproduction numbers and sub-threshold endemic equilibria for compartmental models of disease transmission, Math. Biosci. 180 (1–2) (2002) 29–48.
[41] L. Perko, The Stability of Dynamical Systems, Springer, 2006.
[42] Z. Zhang, Y. Zhang, Design and experimentation of acceleration-level drift-free scheme aided by two recurrent neural networks, IET Control Theory Appl. 7 (1) (2013) 25–42.
[43] A. Saltelli, K. Chan, E.M. Scott, Wiley series in probability and statistics, in: Sensitivity Analysis, Wiley, 2000.
[44] S. Marino, I.B. Hogue, C.J. Ray, D.E. Kirschner, A methodology for performing global uncertainty and sensitivity analysis in systems biology, J. Theoret. Biol. 254 (1) (2008) 178–196.