

Backward bifurcation and optimal control of a vector borne disease

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Abstract: This paper deals with a simple mathematical model for the transmission dynamics of a vector-borne disease that incorporates both direct and indirect transmission. The model is analyzed using dynamical systems techniques and it reveals the backward bifurcation to occur for some range of parameters. In such cases, the reproduction number does not describe the necessary elimination effort of disease rather the effort is described by the value of the critical parameter at the turning point. The model is extended to assess the impact of some control measures, by re-formulating the model as an optimal control problem with density-dependent demographic parameters. The optimality system is derived and solved numerically to investigate that there are cost effective control efforts in reducing the incidence of infectious hosts and vectors.

Keywords: Epidemic model, Backward bifurcation, Optimal control, Pontryagin's Maximum Principle.

1. Introduction

Vector-borne disease such as dengue fever, West Nile virus, viral encephalitis and malaria result from an infection transmitted to humans and other animals by blood-feeding arthropods. The arthropods (insects or arachnids) that most commonly serve as vectors include blood sucking insects such as, mosquitoes, ticks, lice, and biting flies [2]. The majority of vector-borne diseases survive in nature by utilizing animals as their vertebrate hosts, and are therefore zoonoses. For a small number of zoonoses, such as malaria and dengue, humans are the major host, with no significant animal reservoirs. The vector receives the pathogen from an infected host and transmits it either to an intermediary host or directly to the human host. Vector-borne diseases are prevalent in the tropics and subtropics and are relatively rare in temperate zones, although climate change could create conditions suitable for outbreaks of diseases such as lyme disease, malaria, dengue fever, and viral encephalitis in temperate regions. The literature dealing with the mathematical theory on vector-borne diseases is quite

extensive. To date, many mathematical models of vector-borne disease have been developed in the literature [6–8]

Recently, the phenomenon of the backward bifurcations has arisen the interests in disease control (see [10, 11]). In this case, the basic reproduction number cannot describe the necessary disease eradication effort any more. Backward bifurcation in models, reveals that it is not sufficient to consider the dynamics based only on the basic reproduction number. Control measures for vector-borne diseases are important because most are zoonoses that are maintained in nature in cycles involving wild animals and are not amenable to eradication. Therefore, control methods generally focus on targeting the arthropod vector. These include undertaking personal protective measures by establishing physical barriers such as house screens and bed nets; wearing appropriate clothing (boots, apparel that overlap the upper garments, head nets, etc.); and using insect repellents. A lot of effort on controlling the diseases with administration of antiviral treatment and vaccination has been taken up over the years. Mathematical models have been used to help understanding the dynamics of infec-

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tion and its control (see [3, 12]). We obtain the backward bifurcations results by an elementary approach and avoid the center manifold theorem. However, the center manifold approach remains essential for more complicated models because of the technical complications of an elementary approach.

In this paper, a basic model [1] is considered to incorporate some important epidemiological features. Analysis of the model reveals that the model exhibits the phenomenon of backward bifurcation with standard incidence. Then the model is further extended taking into account the density-dependent demographic parameters and control functions to assess the impact of some control measures by using optimal control techniques. The model will then be used to determine cost-effective strategies for combatting the spread of vector borne infection in a given community. Finally, the optimality is taken to be to minimize the number of infected hosts and the total number of vectors population. In order to do this, we first show the existence of an optimal control for the optimal control problem and then we derive the optimality system. The optimality system is solved numerically by using an efficient numerical method.

The paper is organized as follows. In Section 2, we present a formulation of the mathematical model. The existence of backward bifurcation is analyzed in Section 3. In Section 4, the control problem is formulated. The necessary conditions for an optimal control and the corresponding states are derived using Pontryagin's Maximum Principle in Section 5. In Section 6, we solve the resulting optimality system numerically. Finally, the conclusions are summarized in Section 7.

2. Model frame work

The total population sizes at time t for the humans hosts and mosquitoes vector are denoted by $N_h(t)$ and $N_v(t)$, respectively. The population of size $N_h(t)$ is divided into three distinct classes: the susceptible population of size $S_h(t)$, the infectious population of size $I_h(t)$ and the recovered (or removed) population of size R_h . Thus $N_h(t) = S_h(t) + I_h(t) + R_h(t)$. The mosquitoes vector population $N_v(t)$ has the subclasses denoted by $S_v(t)$, and $I_v(t)$ for the susceptible and infected classes, respectively. Thus, $N_v(t) = S_v(t) + I_v(t)$. The compartmental deterministic mathematical model can be represented analytically by

the following nonlinear system of five ordinary differential equations:

$$\begin{aligned}\frac{dS_h}{dt} &= b_1 - \frac{\beta_1 S_h I_h}{N_h} - \frac{\beta_2 S_h I_v}{N_h} - \mu_h S_h, \\ \frac{dI_h}{dt} &= \frac{\beta_1 S_h I_h}{N_h} + \frac{\beta_2 S_h I_v}{N_h} - \gamma_h I_h - \delta_h I_h - \mu_h I_h, \\ \frac{dR_h}{dt} &= \gamma_h I_h - \mu_h R_h, \\ \frac{dS_v}{dt} &= b_2 - \frac{\beta_3 S_v I_h}{N_h} - \mu_v S_v, \\ \frac{dI_v}{dt} &= \frac{\beta_3 S_v I_h}{N_h} - \delta_v I_v - \mu_v I_v,\end{aligned}\quad (1)$$

with initial conditions

$$S_h(0) \geq 0, I_h(0) \geq 0, R_h(0) \geq 0, S_v(0) \geq 0, I_v(0) \geq 0. \quad (2)$$

The human host population is recruited (assumed susceptible) at a constant birth rate b_1 , β_1 is the rate of direct transmission of the disease, β_2 is the vector mediated transmission rate, μ_h is the natural mortality rate of human. Infectious humans recover at a rate γ_h and suffer disease-induced death at a rate δ_h . It is assumed that recovered individuals acquire lifelong immunity against re-infection. Similarly b_2 is the constant recruitment rate of susceptible vectors population by birth and susceptible mosquitoes become infected by biting infected humans at a rate β_3 , μ_v is the natural mortality rate of vectors population. Infectious vectors die due to disease at a rate δ_v [3].

The model (1) extends the model studied in [1] by including the disease-induced mortality in humans and vectors populations denoted by the parameters δ_h and δ_v respectively, and standard incidence rate represented in the system (1).

As $S_h + I_h + R_h = N_h$, so for convenience in calculations we consider the following system of differential equation for further analysis:

$$\begin{aligned}\frac{dS_h}{dt} &= b_1 - \frac{\beta_1 S_h I_h}{N_h} - \frac{\beta_2 S_h I_v}{N_h} - \mu_h S_h, \\ \frac{dI_h}{dt} &= \frac{\beta_1 S_h I_h}{N_h} + \frac{\beta_2 S_h I_v}{N_h} - \gamma_h I_h - \delta_h I_h - \mu_h I_h, \\ \frac{dN_h}{dt} &= b_1 - \mu_h N_h - \delta_h I_h, \\ \frac{dS_v}{dt} &= b_2 - \frac{\beta_3 S_v I_h}{N_h} - \mu_v S_v, \\ \frac{dI_v}{dt} &= \frac{\beta_3 S_v I_h}{N_h} - \delta_v I_v - \mu_v I_v,\end{aligned}\quad (3)$$

and determining R_h from $R_h = N_h - S_h - I_h$ or from $\frac{dR_h}{dt} = \gamma_h I_h - \mu_h R_h$.

Thus, in our proposed model the host and vector populations satisfy the following linear equations

$$\frac{dN_h}{dt} = b_1 - \mu_h N_h - \delta_h I_h, \quad (4)$$

and

$$\frac{dN_v}{dt} = b_2 - \mu_v N_v - \delta_v I_v. \tag{5}$$

It follows from (4) and (5) that

$$\frac{dN_h}{dt} \leq b_1 - \mu_h N_h, \quad \frac{dN_v}{dt} \leq b_2 - \mu_v N_v. \tag{6}$$

Then

$$\lim_{t \rightarrow \infty} Sup N_h \leq \frac{b_1}{\mu_h} \quad \text{and} \quad \lim_{t \rightarrow \infty} Sup N_v \leq \frac{b_2}{\mu_v}. \tag{7}$$

Thus the feasible region for the system (3) is

$$\Omega = \{(S_h, I_h, N_h, S_v, I_v) \in R_+^5, N_h \leq \frac{b_1}{\mu_h}, N_v \leq \frac{b_2}{\mu_v}\}.$$

Furthermore, the model (3) is well-posed epidemiologically and mathematically. Hence, it is sufficient to study the dynamics of this basic model in Ω . The disease-free equilibrium for the system (3) is, $E_f = (\frac{b_1}{\mu_h}, 0, \frac{b_1}{\mu_h}, \frac{b_2}{\mu_v}, 0)$.

In epidemiological models, the basic reproduction number denoted by R_0 is a key concept and is defined as the average number of secondary infection arising from a single infected individual introduced into the susceptible class during its entire infectious period in a totally susceptible population [9]. The dynamics of the model (3) is analyzed by R_0 given by

$$R_0 = \frac{\mu_h b_2 \beta_2 \beta_3}{\mu_v b_1 (\delta_v + \mu_v) (\gamma_h + \delta_h + \mu_h)} + \frac{\beta_1}{\gamma_h + \delta_h + \mu_h}. \tag{8}$$

The threshold quantity R_0 is the basic reproduction number of the disease. It can be derived from the Jacobian matrix of the system (3) at the disease-free equilibrium E_f together with the assumption of local asymptotical stability of E_f .

3. The endemic equilibria and backward bifurcation

In order to find positive solutions of the system (3), the following steps are taken. Let $E_1 = (S_h^*, I_h^*, N_h^*, S_v^*, I_v^*)$ represents any arbitrary endemic equilibrium of the model (3). Solving the equations in (3) at steady state gives,

$$S_h^* = \frac{b_1 - (\gamma_h + \delta_h + \mu_h) I_h^*}{\mu_h}, \quad N_h^* = \frac{b_1 - \delta_h I_h^*}{\mu_h},$$

$$S_v^* = \frac{b_2 (b_1 - \delta_h I_h^*)}{\mu_h \beta_3 I_h^* + \mu_v (b_1 - \delta_h I_h^*)},$$

$$I_v^* = \frac{\mu_h b_2 \beta_3 I_h^*}{(\mu_v + \delta_v) (\mu_h \beta_3 I_h^* + \mu_v (b_1 - \delta_h I_h^*))},$$

where $K_1 = (\gamma_h + \delta_h + \mu_h)$ and $K_2 = (\mu_v + \delta_v)$.

Substituting S_h^* , N_h^* and I_v^* into the second equation of the system (3) to give an equation of the form

$$g(I_h) = AI_h^{*2} + BI_h^* + C = 0, \tag{9}$$

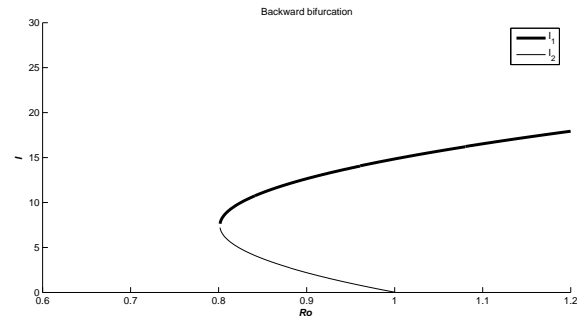


Figure 1 Bifurcation diagram of (1) showing a backward bifurcation. We consider $b_1 = 6$, $\beta_1 = 0.01$, $\beta_3 = 0.00072$, $\mu_h = 0.1$, $\gamma_h = 0.0004$, $\delta_h = 0.01$, $b_2 = 50$, $\mu_v = 0.02$, and $\delta_v = 0.001$ for numerical simulation.

with

$$A = K_1 K_2 (\mu_h \beta_3 (\beta_1 - \delta_h) + \mu_v \delta_h (\delta_h - \beta_1)),$$

$$B = K_1 K_2 (\mu_v b_1 \beta_1 - 2\mu_v b_1 \delta_h + \mu_v b_1 \beta_3) + K_2 b_1 \beta_1 (\mu_v \delta_h - \mu_h \beta_3) + K_1 \mu_h b_2 \beta_2 \beta_3, \tag{10}$$

$$C = \mu_v b_1^2 K_1 K_2 (1 - R_0).$$

We note that $C < 0$ if $R_0 > 1$, $C = 0$ if $R_0 = 1$, and $C > 0$ if $R_0 < 1$. If $R_0 = 1$, then $C = 0$ and there is a unique nonzero solution of (9) $I_h = -B/A$ which is positive if and only if $A > 0$ and $B < 0$ or $A < 0$ and $B > 0$. Now, depending upon the signs of A , B and C , we may have unique, two or no positive roots. Thus, the following result is established.

Theorem 2.1 The system (3) has a backward bifurcation at $R_0 = 1$ if and only if $A > 0$ and $B < 0$ provided $B^2 - 4AC > 0$.

If $C > 0$ and either $B \geq 0$ or $B^2 < 4AC$, there are no positive solutions of (9) and thus there are no endemic equilibria. Equation (9) has two positive solutions, corresponding to two endemic equilibria, if and only if $C > 0$, or $R_0 < 1$, and $B < 0$, $A > 0$, $B^2 > 4AC$.

4. Optimal control of extended model

In this section, we extend the model (1) by including density-dependent mortality rates in the vector and host populations, defined by $\mu_h = \mu_1 + \mu_2 N_h$ and $\mu_v = \mu_3 + \mu_4 N_v$, where $\mu_1 \geq 0$ and $\mu_3 \geq 0$ are density-independent death rates in the host and the vector populations, respectively, and using mass action type incidence rate. Also, $\mu_2 \geq 0$ and $\mu_4 \geq 0$ are proportionality constants. These types of per capita death rates are used in [5].

Similarly, the recruitment rate in each susceptible population is modified to include density effects. To do this, we replace the previous recruitment rates by $b_1 \rightarrow b_1 + \alpha_h N_h$ and $b_2 \rightarrow b_2 N_v$, where α_h is the proportionality

constant showing the impact of density on the recruitment rate. In general, the inclusion of density-dependent recruitment and death rates in population models tend to result in different dynamical features. Average recruitment and death rates are considered in most cases to reduce complications while analyzing the resulting models [15].

In the human host population, the associated forces of infection are reduced by factors of $(1 - u_1(t))$ and $(1 - u_2(t))$, respectively, where $u_1(t)$ measures a basic-practice blood-donation procedure that disallows the donations of infected donors and $u_2(t)$ measures the level of successful prevention efforts. The control $u_1(t)$ represents the implementation of a basic-practice blood-donation procedure that disallows the donations of infected donors [4]. The control $u_2(t)$ represents the use of alternative preventive measures to minimize or eliminate mosquito-human contacts (such as the use of insect repellents or bed nets). In most cases, vectors, such as, mosquitoes use favorable climatic conditions to flourish [13]. Combating efforts of vector-borne diseases are more effective and economical if they are in phase with climatic changes. Thus, a time-dependent mosquito control, preferably applied in seasons favorable for mosquito outbreak, is considered. The control function $u_3(t)$ represents the level of larvicide and adulticide used for mosquito control administered at mosquito breeding sites to eliminate specific breeding areas. Consequently, the reproduction rate of the mosquito population is reduced by a factor of $(1 - u_3(t))$ [14]. Also, it is assumed that the mortality rate of vectors population increases at a rate proportional to $u_3(t)$, where $r_0 > 0$ is a rate constant. Taking into account the above assumptions and extensions, we formulate an optimal control model for a vector-borne disease in order to derive optimal prevention and treatment strategies with minimal implementation cost. The dynamics of the system (1) are governed by the following system of five equations:

$$\begin{aligned} \frac{dS_h}{dt} &= b_1 + \alpha_h N_h - \beta_1 S_h I_h (1 - u_1) \\ &\quad - \beta_2 S_h I_v (1 - u_2) - (\mu_1 + \mu_2 N_h) S_h, \\ \frac{dI_h}{dt} &= \beta_1 S_h I_h (1 - u_1) + \beta_2 S_h I_v (1 - u_2) - \gamma_h I_h \\ &\quad - \delta_h I_h - (\mu_1 + \mu_2 N_h) I_h, \\ \frac{dR_h}{dt} &= \gamma_h I_h - (\mu_1 + \mu_2 N_h) R_h, \\ \frac{dS_v}{dt} &= b_2 N_v (1 - u_3) - \beta_3 S_v I_h (1 - u_2) \\ &\quad - (\mu_3 + \mu_4 N_v) S_v - r_0 u_3 S_v, \\ \frac{dI_v}{dt} &= \beta_3 S_v I_h (1 - u_2) - \delta_v I_v - (\mu_3 + \mu_4 N_v) I_v \\ &\quad - r_0 u_3 I_v, \end{aligned} \quad (11)$$

with initial conditions (2). Our objective functional for the above state system is given by

$$J(u_1, u_2, u_3) = \int_0^T (A_1 I_h + A_2 N_v + \frac{1}{2} (B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)) dt, \quad (12)$$

subject to the state system given by (11). In the objective functional A_1 , represents the weight constant of infected human and A_2 represents the weight constant of the total vectors population. B_1 , B_2 and B_3 are weight constants for blood donor screening, personal protection (reduction of vectors and human contacts) and vector control, respectively. The terms $1/2 B_1 u_1^2$, $1/2 B_2 u_2^2$ and $1/2 B_3 u_3^2$ describe the costs associated with the blood donor screening, prevention of vector-host contacts and vector control, respectively. The main objective in this optimal control problem is to minimize the number of people who become infected, the total number of vectors and the cost of implementing the control by using possible minimal control variables u_i for $i = 1, 2, 3$. The cost associated with the first control could come from donor screening systems. Similarly, the cost associated with second control could come from costs of vaccination, mosquito repellents, and supply of basic needs. The cost associated with third control could come from applying pesticides. We assume that the costs are proportional to the square of the corresponding control function. Our aim is to find control functions such that

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in U} J(u_1, u_2, u_3),$$

subject to the system (11), where the control set is defined as

$$U = \{(u_1, u_2, u_3) | u_i(t) \text{ is Lebesgue measurable on } [0, 1], 0 \leq u_i(t) \leq 1, i = 1, 2, 3\}. \quad (13)$$

In order to find an optimal solution, first we should find the Lagrangian and Hamiltonian for the optimal control problem (11) – (12). The Lagrangian of the optimal problem is given by

$$L = A_1 I_h + A_2 N_v + 1/2 (B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2).$$

We seek for the minimal value of the Lagrangian. To accomplish this, we define the Hamiltonian H for the control problem as follows:

$$H = L(I_h, N_v, u_1, u_2, u_3) + \lambda_1 \frac{dS_h}{dt} + \lambda_2 \frac{dI_h}{dt} + \lambda_3 \frac{dR_h}{dt} + \lambda_4 \frac{dS_v}{dt} + \lambda_5 \frac{dI_v}{dt}. \quad (14)$$

We prove the existence of an optimal control for system (11) and then derive the optimality system.

5. Existence of control problem

For the existence of our control problem we state and prove the following theorem.

Theorem 5.1 There exists an optimal control $u^* = (u_1^*, u_2^*, u_3^*) \in U$ such that

$$J(u_1^*, u_2^*, u_3^*) = \min_{(u_1, u_2, u_3) \in U} J(u_1, u_2, u_3),$$

subject to the control system (11) with the initial conditions (2).

Proof. To prove the existence of an optimal control pair we use the result in [16]. Note that the control and the state variables are nonnegative values. In this minimizing problem, the necessary convexity of the objective functional in u_1, u_2 and u_3 are satisfied. The set of all the control variables $(u_1, u_2, u_3) \in U$ is also convex and closed by definition. The optimal system is bounded which determines the compactness needed for the existence of the optimal control. In addition, the integrand in the functional (12), $A_1 I(t) + A_2 N_v(t) + 1/2(B_1 u_1^2 + B_2 u_2^2 + B_3 u_3^2)$ is convex on the control set U . Also we can easily see that, there exist a constant $\rho > 1$ and positive numbers ω_1, ω_2 such that

$$J(u_1, u_2, u_3) \geq \omega_1(|u_1|^2 + |u_2|^2 + |u_3|^2)^{\rho/2} - \omega_2,$$

because, the state variables are bounded, which completes the existence of an optimal control.

To find the optimal solution, we apply Pontryagin's Maximum Principle [17] to the hamiltonian (14), such that if (x, u) is an optimal solution of an optimal control problem, then there exists a non trivial vector function $\lambda = (\lambda_1, \lambda_2, \dots, \lambda_n)$ satisfying the following inequalities.

$$\begin{aligned} \frac{dx}{dt} &= \frac{\partial H(t,x,u,\lambda)}{\partial \lambda}, \\ 0 &= \frac{\partial H(t,x,u,\lambda)}{\partial u}, \\ \lambda' &= -\frac{\partial H(t,x,u,\lambda)}{\partial x}. \end{aligned} \tag{15}$$

Now we apply the necessary conditions to the Hamiltonian H in (14).

Theorem 5.2 Let $S_h^*, I_h^*, R_h^*, S_v^*$, and I_v^* be optimal state solutions with associated optimal control variables (u_1^*, u_2^*, u_3^*) for the optimal control problem (11)-(12). Then there exist adjoint variables λ_i , for $i=1, 2, \dots, 5$, satisfying

$$\begin{aligned} \lambda_1' &= -\alpha_h \lambda_1 + (\lambda_1 - \lambda_2)(\beta_1(1 - u_1)I_h + \beta_2(1 - u_2)I_v) \\ &\quad + (\mu_1 + \mu_2 N_h)\lambda_1 + \mu_2 \lambda_1 S_h + \mu_2 \lambda_2 I_h + \lambda_3 \mu_2 R_h, \\ \lambda_2' &= -\alpha_h \lambda_1 - A_1 + \beta_1(\lambda_1 - \lambda_2)(1 - u_1)S_h + \mu_2 \lambda_1 S_h \\ &\quad + (\gamma_h + \delta_h)\lambda_2 + (\mu_1 + \mu_2 N_h)\lambda_2 + \mu_2 \lambda_2 I_h - \gamma_h \lambda_3 \\ &\quad + \mu_2 \lambda_3 R_h + \beta_3(\lambda_4 - \lambda_5)(1 - u_2)S_v, \\ \lambda_3' &= -\alpha_h \lambda_1 + \mu_2 \lambda_1 S_h + \mu_2 \lambda_2 I_h + (\mu_1 + \mu_2 N_h)\lambda_3 \\ &\quad + \mu_2 \lambda_3 R_h, \\ \lambda_4' &= -A_2 - b_2 \lambda_4(1 - u_3) + \beta_3(\lambda_4 - \lambda_5)(1 - u_2)I_h \\ &\quad + (\mu_3 + \mu_4 N_v)\lambda_4 + \mu_4 \lambda_4 S_v \\ &\quad + \gamma_0 \lambda_4 u_3 + \mu_4 \lambda_5 I_v, \\ \lambda_5' &= -A_2 + \beta_2(\lambda_1 - \lambda_2)(1 - u_2)S_h - b_2 \lambda_4(1 - u_3) \\ &\quad + \mu_4 \lambda_4 S_v + \lambda_5 \delta_v + (\mu_3 + \mu_4 N_v)\lambda_5 + \mu_4 \lambda_5 I_v \\ &\quad + r_0 \lambda_5 u_3. \end{aligned}$$

with transversality conditions (or boundary conditions)

$$\lambda_i(T) = 0, \quad i = 1, 2, \dots, 5. \tag{17}$$

Furthermore, optimal controls u_1^*, u_2^* , and u_3^* are given as follows:

$$u_1^* = \max\{\min\{\frac{\beta_1(\lambda_2 - \lambda_1)S_h^* I_h^*}{B_1}, 1\}, 0\}, \tag{18}$$

$$u_2^* = \max\{\min\{\frac{\beta_2(\lambda_2 - \lambda_1)S_h^* I_v^* + \beta_3(\lambda_5 - \lambda_4)S_v^* I_h^*}{B_2}, 1\}, 0\}, \tag{19}$$

$$u_3^* = \max\{\min\{\frac{b_2 \lambda_4 N_v^* + r_0(\lambda_4 S_v^* + \lambda_5 I_v^*)}{B_3}, 1\}, 0\} \tag{20}$$

Proof. To determine the adjoint equations and the transversality conditions we use the Hamiltonian (14). From setting $S_h(t) = S_h^*(t), I_h(t) = I_h^*(t), R_h(t) = R_h^*(t), S_v(t) = S_v^*(t),$ and $I_v(t) = I_v^*(t),$ and differentiating the Hamiltonian (14) with respect to $S_h, I_h, R_h, S_v,$ and $I_v,$ respectively, we obtain (16). By solving the equations

$$\frac{\partial H}{\partial u_1} = 0, \quad \frac{\partial H}{\partial u_2} = 0 \quad \text{and} \quad \frac{\partial H}{\partial u_3} = 0, \tag{21}$$

on the interior of the control set and using the optimality conditions and the property of the control space U we can derive (18)-(20).

Here we call formulas (18)-(20) for $u^* = (u_1^*, u_2^*, u_3^*)$ the characterization of the optimal control. The optimal control and the state are found by solving the optimality system, which consists of the state system (11), the adjoint system (16), boundary conditions (1) and (17), and the characterization of the optimal control (18)-(20). To solve the optimality system we use the initial and transversality conditions together with the characterization of the optimal control (u_1^*, u_2^*, u_3^*) given by (18)-(20). In addition, the second derivative of the Lagrangian with respect to u_1, u_2 and $u_3,$ respectively, are positive, which shows that the optimal problem is minimum at controls u_1^*, u_2^* and $u_3^*.$

6. Numerical results and discussion

In this section we use an iterative method to find the numerical solution of our control problem. The numerical algorithm presented below is a semi-implicit finite difference method. We discretize the interval $[t_0, t_f]$ at the points $t_i = t_0 + il$ ($i = 0, 1, \dots, n$), where l is the time step such that $t_n = t_f$. Next, we define the state and adjoint variables $S_h(t), I_h(t), R_h(t), S_v(t), I_v(t), \lambda_1(t), \lambda_2(t), \lambda_3(t), \lambda_4(t), \lambda_5(t)$ and the controls $u_1(t), u_2(t), u_3(t)$ in terms of nodal points $S_h^i, I_h^i, R_h^i, S_v^i, I_v^i, \lambda_1^i, \lambda_2^i, \lambda_3^i, \lambda_4^i, \lambda_5^i, u_1^i, u_2^i$ and $u_3^i.$ Now a combination of forward and backward difference approximation is used as follows :

The method, developed by [18] and presented in [19-22], to adapt the numerical solution of our optimal control problem is given by:

$$\frac{S_h^{i+1} - S_h^i}{l} = b_1 + \alpha_h(S_h^{i+1} + I_h^i + R_h^i)$$

$$\begin{aligned}
 & -\beta_1 S_h^{i+1} I_h^i (1 - u_1^i) - \beta_2 S_h^{i+1} I_v^i (1 - u_2^i) \\
 & - [\mu_1 + \mu_2 (S_h^{i+1} + I_h^i + R_h^i)] S_h^{i+1}, \\
 \frac{I_h^{i+1} - I_h^i}{l} &= \beta_1 S_h^{i+1} I_h^{i+1} (1 - u_1^i) + \beta_2 S_h^{i+1} I_v^i (1 - u_2^i) \\
 & - \gamma_h I_h^{i+1} - \delta_h I_h^{i+1} - [\mu_1 + \mu_2 (S_h^{i+1} \\
 & + I_h^{i+1} + R_h^i)] I_h^{i+1}, \\
 \frac{R_h^{i+1} - R_h^i}{l} &= \gamma_h I_h^{i+1} - (\mu_1 + \mu_2 (S_h^{i+1} + I_h^{i+1} \\
 & + R_h^{i+1})) R_h^{i+1}, \\
 \frac{S_v^{i+1} - S_v^i}{l} &= b_2 (S_v^{i+1} + I_v^i) (1 - u_3^i) - \beta_3 S_v^{i+1} I_h^{i+1} (1 - u_2^i) \\
 & - (\mu_3 + \mu_4 (S_v^{i+1} + I_v^i)) S_v^{i+1} - r_0 u_3^i S_v^{i+1}, \\
 \frac{I_v^{i+1} - I_v^i}{l} &= \beta_3 S_v^{i+1} I_h^{i+1} (1 - u_2^i) - \delta_v I_v^{i+1} \\
 & - (\mu_3 + \mu_4 (S_v^{i+1} + I_v^{i+1})) I_v^{i+1} - r_0 u_3^i I_v^{i+1}.
 \end{aligned}$$

By using a similar technique, we approximate the time derivative of the adjoint variables by their first-order backward-difference and we use the appropriated scheme as follows

$$\begin{aligned}
 \frac{\lambda_1^{n-i} - \lambda_1^{n-i-1}}{l} &= -\alpha_h \lambda_1^{n-i-1} + (\lambda_1^{n-i-1} - \lambda_2^{n-i}) [\beta_1 \\
 & (1 - u_1^i) I_h^{i+1} + \beta_2 (1 - u_2^i) I_v^{i+1}] \\
 & + (\mu_1 + \mu_2 N_h^{i+1}) \lambda_1^{n-i-1} + \mu_2 \lambda_1^{n-i-1} S_h^{i+1} \\
 & + \mu_2 \lambda_2^{n-i} I_h^{i+1} + \lambda_3^{n-i} \mu_2 R_h^{i+1}, \\
 \frac{\lambda_2^{n-i} - \lambda_2^{n-i-1}}{l} &= -\alpha_h \lambda_1^{n-i-1} - A_1 + \beta_1 (\lambda_1^{n-i-1} \\
 & - \lambda_2^{n-i-1}) (1 - u_1^i) S_h^{i+1} + \mu_2 \lambda_1^{n-i-1} S_h^{i+1} \\
 & + (\gamma_h + \delta_h) \lambda_2^{n-i-1} + (\mu_1 + \mu_2 N_h^{i+1}) \lambda_2^{n-i-1} \\
 & + \mu_2 \lambda_2^{n-i-1} I_h^{i+1} - \gamma_h \lambda_3^{n-i} + \mu_2 \lambda_3^{n-i} R_h^{i+1} \\
 & + \beta_3 (\lambda_4^{n-i} - \lambda_5^{n-i}) (1 - u_2^i) S_v^{i+1}, \\
 \frac{\lambda_3^{n-i} - \lambda_3^{n-i-1}}{l} &= -\alpha_h \lambda_1^{n-i-1} + \mu_2 \lambda_1^{n-i-1} S_h^{i+1} \\
 & + \mu_2 \lambda_2^{n-i-1} I_h^{i+1} + (\mu_1 + \mu_2 N_h^{i+1}) \lambda_3^{n-i-1} \\
 & + \mu_2 \lambda_3^{n-i-1} R_h^{i+1}, \\
 \frac{\lambda_4^{n-i} - \lambda_4^{n-i-1}}{l} &= -A_2 - b_2 \lambda_4^{n-i-1} (1 - u_3^i) + \beta_3 (\lambda_4^{n-i-1} \\
 & - \lambda_5^{n-i}) (1 - u_2^i) I_h^{i+1} + (\mu_3 + \mu_4 N_v^{i+1}) \\
 & \lambda_4^{n-i-1} + \mu_4 \lambda_4^{n-i-1} S_v^{i+1} + r_0 \lambda_4^{n-i-1} u_3^i \\
 & + \mu_4 \lambda_5^{n-i} I_v^{i+1}, \\
 \frac{\lambda_5^{n-i} - \lambda_5^{n-i-1}}{l} &= -A_2 + \beta_2 (\lambda_1^{n-i-1} - \lambda_2^{n-i-1}) (1 - u_2^i) S_h^{i+1} \\
 & - b_2 \lambda_4^{n-i-1} (1 - u_3^i) + \mu_4 \lambda_4^{n-i-1} S_v^{i+1} \\
 & + \lambda_5^{n-i-1} \delta_v + (\mu_3 + \mu_4 N_v^{i+1}) \lambda_5^{n-i-1} \\
 & + \mu_4 \lambda_5^{n-i-1} I_v^{i+1} + r_0 \lambda_5^{n-i-1} u_3^i.
 \end{aligned}$$

The algorithm describing the approximation method for obtaining the optimal control is the following:

Algorithm

step 1 :

$$\begin{aligned}
 S_h(0) &= S_{h0}, I_h(0) = I_{h0}, R_h(0) = R_{h0}, S_v(0) = \\
 S_{v0}, I_v(0) &= I_{v0}, \lambda_i(t_f) = 0 \ (i=1, \dots, 5), u_1(0) = \\
 u_2(0) &= u_3(0) = 0.
 \end{aligned}$$

step 2 :

for i=1, ..., n-1, do :

$$\begin{aligned}
 S_h^{i+1} &= \frac{-1 - l[-\alpha_h + \beta_1 I_h^i (1 - u_1^i)]}{2l\mu_2} \\
 & - \frac{l[\beta_2 I_v^i (1 - u_2^i) + \mu_1 + \mu_2 (I_h^i + R_h^i)]}{2l\mu_2} \\
 & + \frac{1}{2l\mu_2} \{ [1 + l(-\alpha_h + \beta_1 I_h^i (1 - u_1^i) \\
 & + \beta_2 I_v^i (1 - u_2^i) + \mu_1 + \mu_2 (I_h^i + R_h^i))]^2 \\
 & + 4l\mu_2 [S_h^i + lb_1 + l\alpha_h (I_h^i + R_h^i)] \}^{\frac{1}{2}}, \\
 I_h^{i+1} &= \frac{-1 - l[-\beta_1 S_h^{i+1} (1 - u_1^i) + \gamma_h + \delta_h]}{2l\mu_2} \\
 & - \frac{l[\mu_1 + \mu_2 (S_h^{i+1} + R_h^i)]}{2l\mu_2} + \frac{1}{2l\mu_2} \{ [1 \\
 & + l(-\beta_1 S_h^{i+1} (1 - u_1^i) + \gamma_h + \delta_h + \mu_1 \\
 & + \mu_2 (S_h^{i+1} + R_h^i))]^2 + 4l\mu_2 [I_h^i \\
 & + l\beta_2 S_h^{i+1} I_v^i (1 - u_2^i)] \}^{\frac{1}{2}}, \\
 R_h^{i+1} &= \frac{-1 - l[\mu_1 + \mu_2 (S_h^{i+1} + I_h^{i+1})]}{2l\mu_2} \\
 & + \frac{1}{2l\mu_2} \{ [1 + l\mu_1 + l\mu_2 (S_h^{i+1} + I_h^{i+1})]^2 \\
 & + 4l\mu_2 [R_h^i + l\gamma_h I_h^{i+1}] \}^{\frac{1}{2}}, \\
 S_v^{i+1} &= \frac{-1 - l[-b_2 (1 - u_3^i) + \beta_3 I_h^{i+1} (1 - u_2^i)]}{2l\mu_4} \\
 & - \frac{l[\mu_3 + \mu_4 I_v^i + r_0 u_3^i]}{2l\mu_4} + \frac{1}{2l\mu_4} \{ [1 \\
 & + l(-b_2 (1 - u_3^i) + \beta_3 I_h^{i+1} (1 - u_2^i) + \mu_3 \\
 & + \mu_4 I_v^i + r_0 u_3^i)]^2 + 4l\mu_4 [S_v^i + lb_2 I_v^i (1 - u_3^i)] \}^{\frac{1}{2}}, \\
 I_v^{i+1} &= \frac{-1 - l(\delta_v + \mu_3 + \mu_4 S_v^{i+1} + r_0 u_3^i)}{2l\mu_4} \\
 & + \frac{1}{2l\mu_4} \{ [1 + l(\delta_v + \mu_3 + \mu_4 S_v^{i+1} + r_0 u_3^i)]^2 \\
 & + 4l\mu_4 (I_v^i + l\beta_3 S_v^{i+1} I_v^{i+1} (1 - u_2^i)) \}^{\frac{1}{2}}, \\
 \lambda_1^{n-i-1} &= \{ \lambda_1^{n-i} + l[\lambda_2^{n-i} \beta_1 (1 - u_1^i) I_h^{i+1} \\
 & + \lambda_2^{n-i} \beta_2 (1 - u_2^i) I_v^{i+1} \\
 & - \mu_2 I_h^{i+1} \lambda_2^{n-i} - \mu_2 R_h^{i+1} \lambda_3^{n-i}] \} \\
 & / \{ 1 + l[\beta_1 (1 - u_1^i) I_h^{i+1} \\
 & + \beta_2 (1 - u_2^i) I_v^{i+1} + \mu_2 S_h^{i+1} + \mu_1
 \end{aligned}$$

$$\begin{aligned}
 & +\mu_2 N_h^{i+1} - \alpha_h \}], \\
 \lambda_2^{n-i-1} &= \{ \lambda_2^{n-i} + l[\alpha_h \lambda_1^{n-i-1} + A_1 \\
 & - \beta_1 \lambda_1^{n-i-1} (1 - u_1^i) S_h^{i+1} - \mu_2 S_h^{i+1} \lambda_1^{n-i-1}] \} \\
 & / \{ 1 + l[\gamma_h + \delta_h + \mu_1 + \mu_2 N_h^{i+1} + \mu_2 I_h^{i+1} \\
 & - \beta_1 (1 - u_1^i) S_h^{i+1}] \}, \\
 \lambda_3^{n-i-1} &= \{ \lambda_3^{n-i} + l[\alpha_h \lambda_1^{n-i-1} - \mu_2 S_h^{i+1} \lambda_1^{n-i-1} \\
 & - \mu_2 I_h^{i+1} \lambda_2^{n-i-1}] \} / \{ 1 + l[\mu_1 \\
 & + \mu_2 N_h^{i+1} + \mu_2 R_h^{i+1}] \}, \\
 \lambda_4^{n-i-1} &= \{ \lambda_4^{n-i} + l[A_2 + \beta_3 (1 - u_2^i) \lambda_5^{n-i} I_h^{i+1} \\
 & - \mu_4 I_v^{i+1} \lambda_5^{n-i}] \} / \{ 1 + l[\beta_3 (1 - u_2^i) I_h^{i+1} + \mu_3 \\
 & + \mu_4 N_v^{i+1} + \mu_4 S_v^{i+1} + r_0 u_3^i - b_2 (1 - u_3^i)] \}, \\
 \lambda_5^{n-i-1} &= \{ \lambda_5^{n-i} + l[A_2 + b_2 \lambda_4^{n-i-1} (1 - u_3^i) \\
 & - \mu_4 \lambda_4^{n-i-1} + \beta_2 (\lambda_1^{n-i-1} \\
 & - \lambda_2^{n-i-1}) (1 - u_2^i) S_h^{i+1}] \} / \{ 1 + l[\delta_v + \mu_3 \\
 & + \mu_4 N_v^{i+1} + \mu_4 I_v^{i+1} + r_0 u_3^i] \}, \\
 R_1^{i+1} &= \frac{(\lambda_2^{n-i-1} - \lambda_1^{n-i-1}) \beta_1 S_h^{i+1} I_h^{i+1}}{B_1}, \\
 R_2^{i+1} &= \{ (\lambda_2^{n-i-1} - \lambda_1^{n-i-1}) \beta_2 S_h^{i+1} I_v^{i+1} \\
 & + (\lambda_5^{n-i-1} - \lambda_4^{n-i-1}) \beta_3 S_v^{i+1} I_h^{i+1} \} / B_2, \\
 R_3^{i+1} &= \{ b_2 \lambda_4^{n-i-1} N_v^{i+1} + r_0 (\lambda_4^{n-i-1} S_v^{i+1} \\
 & + \lambda_5^{n-i-1} I_v^{i+1}) \} / B_3, \\
 u_1^{i+1} &= \min(1, \max(R_1^{i+1}, 0)), \\
 u_2^{i+1} &= \min(1, \max(R_2^{i+1}, 0)), \\
 u_3^{i+1} &= \min(1, \max(R_3^{i+1}, 0)),
 \end{aligned}$$

end for

step 3 :

for $i=1, \dots, n-1$, write $S_h^*(t_i) = S_h^i, I_h^*(t_i) = I_h^i,$
 $R_h^*(t_i) = R_h^i, S_v^*(t_i) = S_v^i, I_v^*(t_i) = I_v^i, u_1^*(t_i) = u_1^i,$
 $u_2^*(t_i) = u_2^i, u_3^*(t_i) = u_3^i.$
 end for

To compare the disease progression before and after the controls, we simulate the model using the following parameters values: $b_1 = 2.5 \times 10^{-2} \text{ day}^{-1}, \alpha_h = 0.03 \text{ day}^{-1}, b_2 = 0.4 \text{ day}^{-1}, \mu_1 = 4 \times 10^{-5} \text{ day}^{-1}, \mu_2 = 2 \times 10^{-7} \text{ day}^{-1}, \mu_3 = 0.15 \text{ day}^{-1}, \mu_4 = 2.8 \times 10^{-4} \text{ day}^{-1}, \delta_h = 0.03 \text{ day}^{-1}, \delta_v = 0.04 \text{ day}^{-1}, \gamma_h = 3.7 \times 10^{-3} \text{ day}^{-1}, \beta_1 = 0.0004, \beta_2 = 0.0006, \beta_3 = 0.009, r_0 = 0.02.$

The graphs from simulation, given below, help to compare the infected host population, the total vector population before and after the controls. When viewing the graphs, remember that each of the individuals without control is marked by un-dashed lines. The control individuals are marked by dash-dotted lines. As it is shown in Fig. 2, application of control reduces the disease burden. The solid line denotes that there are more infected individuals when the control is not implemented for the infected individuals. The control vanishes in day 100 and there remains a

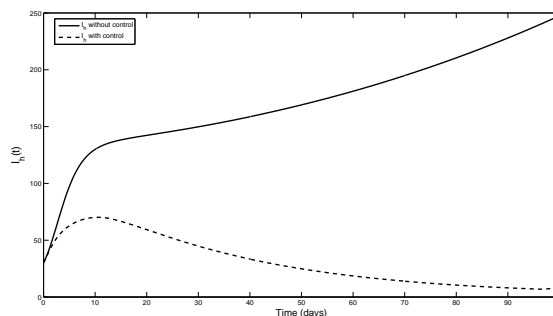


Figure 2 Simulations of the control problem, illustrating the populations of infected individuals I_h with both controls and without controls.

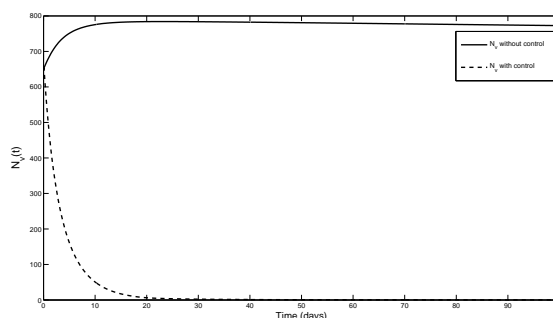


Figure 3 Simulations of the control problem, illustrating the total vectors population N_v with both controls and without controls.

very small number of infected hosts. Thus, the number of infected individuals after the control is smaller than that of infected individuals before the control. Fig. 3 represents the total vector population in the two systems (1) without controls and (11) with controls. The total host population with the controls is more sharply decreased than without controls and becomes very small. The techniques in [23,24] can be used for solving a wide range of problems whose mathematical models yield system of nonlinear differential equations.

7. Conclusion

In the present manuscript, we extended the model proposed above by taking into account the density-dependent demographic parameters and control functions to assess the impact of some control measures by using optimal control techniques which incorporate some important epidemiological features. The disease propagates from the infected to the susceptible in two different ways, through horizontal

transmission or direct contact and through indirect transmission. We have examined the model and have shown by elementary algebraic means how to analyze the existence of multiple endemic equilibria when the basic reproduction number is less than unity. As the model with standard incidence exhibits backward bifurcation, so $R_0 < 1$ is not sufficient to eliminate the disease from the population and we need another threshold less than one and R_0 should be reduced below this threshold to eliminate the disease from the population. This fact is demonstrated in the backward bifurcation diagram. We also determined the cost-effective strategies for combatting the spread of a vector borne infection in some community. By the application of Pontryagin's Maximum Principle, we performed the optimal analysis of the non-autonomous control model considering three controls, one for mosquito-reduction strategies and the other two for personal (human) protection and blood screening, respectively. Furthermore, we minimized the number of infected hosts and the total number of vector population by using three control variables. We have investigated the dynamics by an efficient numerical method based on optimal control to identify the best strategy of a vector-borne disease in order to reduce infection and prevent vector host as well as direct contacts by using three controls. The results support the hypothesis that preventive practices are very effective in reducing the incidence of infectious hosts and vectors.

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References

- [1] H. M. Wei, X. Z. Li, M. Martcheva, An epidemic model of a vector-borne disease with direct transmission and time delay, *J. Math. Anal. Appl.* **342**, (2008) 895-908.
- [2] M. W. Service, *Blood-Sucking Insects: Vector of Disease*, Edward Arnold (publishers) Ltd. (Victoriya, Australia, 1986).
- [3] A.A. Lashari, G. Zaman, Optimal control of a vector borne disease with horizontal transmission, *Nonlinear Anal. RWA.* **13**, (2012) 203-212.
- [4] V. Wiwanitkit, Unusual mode of transmission of dengue, *J. Infect Dev Ctries.* **30**, (2009) 51-54.
- [5] G.A. Ngwa, W.S. Shu, A mathematical model for endemic malaria with variable human and mosquito populations, *Math. Comput. Model.* **32**, (2000) 747-763.
- [6] K.W. Blayneh and S.R. Jang, A discrete SIS-model for a vector-transmitted disease, *Appl. Anal.* **85**, (2006) 1271-1284.
- [7] C. Bowman, A.B. Gumel, P.V.D. Driessche, J. Wu, H. Zhu, A mathematical model for assessing control strategies against West Nile virus, *Bull. Math. Biol.* **67**, (2005) 1107-1133.
- [8] A.A. Lashari, G. Zaman, Global dynamics of vector borne disease with horizontal transmission in host population, *Comput. Math. Appl.* **61**, (2011) 745-754.
- [9] P.V.D. Driessche, J. Watmough, Reproduction number and sub-threshold endemic equilibria for compartmental models of disease transmission, *Math. Biosci.* **180**, (2002) 29-48.
- [10] H. Wan, H. Zhu, The backward bifurcation in compartmental models for West Nile virus, *Math. Biosci.* **227**, (2010) 20-28.
- [11] J. Dushoff, W. Huang, C.C. Chavez, Backwards bifurcations and catastrophe in simple models of fatal diseases, *J. Math. Biol.* **36**, (1998) 227-248.
- [12] S. Bhattacharyya, S. Ghosh, Optimal control of vertically transmitted disease: an integrated approach, *Comput. Math. Met. Medic.* **11**, (2010) 369-387.
- [13] B. Beats, W.C. Marquardt, *The Biology of Disease Vectors*, the university press of colorado, (niwot colorado, US, 1996).
- [14] K.W. Blayneh, A.B. Gumel, S. Lenhart, T. Clayton, Backward bifurcation and optimal control in transmission dynamics of West Nile Virus, *Bull. Math. Biol.* **72**, (2010) 1006-1028.
- [15] J.M. Cushing, *An Introduction to Structured Population Dynamics*, CBMS-NSF Regional Conference Series in Applied Mathematics, **71**, (1998), SIAM, Philadelphia.
- [16] D.L. Lukes, *Differential Equations: Classical to Controlled*, Mathematics in Science and Engineering **162**, (Academic Press, New York, 1982).
- [17] L. S. Pontryagin, V. G. Boltyanskii, R. V. Gamkrelidze, E. F. Mishchenko, *The Mathematical Theory of Optimal Processes*, (Wiley, New York, 1962).
- [18] A.B. Gumel, P.N. Shivakumar, and B.M. Sahai, A mathematical model for the dynamics of HIV-1 during the typical course of infection, *Third world congress of nonlinear analysts*, **47**, (2001) 2073-2083.
- [19] K. Hattaf, M. Rachik, S. Saadi, Y. Tabit and N. Yousfi, Optimal control of tuberculosis with exogenous reinfection, *App. Math. Sci.* **3**, (2009) 231-240.
- [20] K. Hattaf, M. Rachik, S. Saadi, N. Yousfi, Optimal control of treatment in a basic virus infection model, *App. Math. Sci.* **3**, (2009) 949-958.
- [21] K. Hattaf, N. Yousfi, Two optimal treatments of HIV infection model, *World Journal of Modelling and Simulation*, **8**, (2012) 27-35.
- [22] J. Karrakchou, M. Rachik, and S. Gourari, Optimal control and infectiology: Application to an HIV/AIDS Model, *App. Math. Comput.* **177**, (2006) 807-818.
- [23] Y. Khan, Q. Wu, Homotopy perturbation transform method for nonlinear equations using He's polynomial, *Comp. Math. App.* **61**, (2011) 1963-1967.
- [24] Y. Khan, N. Faraz, A. Yildirim, Q. Wu, Fractional variational iteration method for fractional initial boundary value problems arising in the application of nonlinear science, *Comp. Math. App.* **62**, (2011) 2273-2278.



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