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Optimal control of Human African Trypanosomiasis in a population with endemic malaria

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Abstract:

Optimal control theory is applied to a system of ordinary differential equations modelling a co-infection of malaria and sleeping sickness. The objective is to minimise chances of a malaria individual acquiring sleeping sickness. Two controls are used, one preventing infection and another preventing bites by the tsetse fly to the co-infected. The optimal controls are characterized in terms of the optimality system, which is solved numerically for three different scenarios. Results show that controlling co-infections of malaria and sleeping sickness can best be achieved if the bites from the tsetse fly are prevented.

Keywords: Human African Trypanosomiasis; Malaria; Co-Infection.

Mathematics Subject Classification: 34D20.

1 Introduction

Human African Trypanosomiasis (HAT), or sleeping sickness is a vector-borne disease caused by protozoan parasites. It is a major health threat to rural poor several African countries and kills over 60,000 people every year [21]. The disease is endemic in 36 countries in Sub-Saharan Africa [20], challenging to diagnose, and is regarded as fatal if left untreated [2]. Infection with HAT occurs when an individual is bitten by an infected tsetse fly. The parasites responsible for causing HAT belong to a group of closely related trypanosomes in the *Trypanosoma brucei* species complex, which enter the blood stream via the bite of blood feeding tsetse flies *Glossina species*. The disease exists in chronic form, caused by *Trypanosoma brucei gambiense* and acute form caused by *Trypanosoma brucei rhodesiense* [17]. The tsetse fly can acquire these parasites by feeding on infected animals or infected human individuals. The fly remains infective for life which makes human/fly contact a crucial component of the disease [4].

Over the last several years, with increasing parasite drug-resistance, and mosquito insecticide-resistance, malaria is still persistent in many parts of the world. The burden of malaria is not favored by the increasing number of malaria co-infections with many other killer diseases such as trypanosomiasis. Co-infections with malaria often lead to complications and severe cases for parasitic diseases [3]. These co-infections have long been recognized as major contributors to anemia in endemic countries, where severe anemia accounts for up to one half of the malaria-attributable deaths in children younger than 5 years of age. Trypanosomiasis, like malaria is a vector-borne protozoal disease which disproportionately affect the poor giving rise to immense human suffering. Malaria exerts its effect directly on human health, while trypanosomiasis causes damage largely through its effect on the health and productivity of the livestock on which so many poor people depend [8]. Both diseases are poorly understood combined with complex life cycles characterized by multiple stages in both the spreading vectors and human host with incubation periods ranging from weeks to months [4]. Trypanosomiasis parasites are very hard to treat especially when the parasites have reached the central nervous system [19]. A co-infection of such a disease with malaria would make a case so severe that the chances of recovery despite treatment may be minimal to none.

Mathematical models provide a rational basis for finding optimal control strategies for infectious diseases. Some models of sleeping sickness (or HAT) have been designed to study the disease at population level such as [11, 9, 15]. However, these models did not account for time dependent control strategies and their discussions are based on prevalence

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of the disease at equilibria. Time dependent control strategies have been studied for tuberculosis models [10] (and the references there in). Approaches of studying control strategies produce valuable theoretical results which can be used to suggest or design epidemic control programs. In this paper, a mathematical model for the dynamics of malaria and trypanosomiasis is developed. Since the major aim of the study is the co-infection of malaria and HAT, the model follows only those individuals with malaria that end up with an additional infection of sleeping sickness. Although there is reduced contact when an individual is ill with malaria [13], people in rural areas live in bushes, sleep with their cattle or near the kraals and are thus more likely to come in contact with tsetse flies from these animals. For this case, transmission of trypanosomiasis to a malaria infective is assumed via a sigmoid function. This is so since when infected with malaria, individuals may be hard to find by the tsetse fly and thus few may be infected, but as they recover, more can become infected. Since malaria in endemic in Uganda [5], it is assumed in the model that there is a constant malaria flow into the population. A single equation is used for the population of the tsetse fly. This is done since the major interest is on the dynamics of sleeping sickness in a human with malaria. A linear increase in the tsetse fly vector is considered. When the vector bites a human infected with both diseases, there is an increase in its population. The tsetse fly decreases due to many factors such as death, failure to transmit and migration. In the model is assumed that the increase due to infection is less than the decrease due to death or to other causes, or else sleeping sickness would be endemic in Uganda as well. Analysis of the model is done to determine stability and biological interpretation before optimal control is done.

2 Model formulation

The model developed in this paper is based on the assumption that malaria is endemic in the area of study. This assumption is made since the major objective is to study the dynamics of sleeping sickness (or HAT) co-infection with malaria. Therefore, the susceptible individuals to sleeping sickness (HAT) are infected with malaria. A parameter b is used to denote the constant flow of malaria infectives within the population. Let M denote the number of malaria infected individuals and V the number of tsetse flies ready to transmit HAT, at any time t. Let c denote the biting rate of the tsetse fly and e the probability of transmission of sleeping sickness to a malaria infected individual. Thus, if K is the half saturation constant, that is the point at which there is a 50% chance of an individual infected with malaria to become infected with trypanosomiasis, then rate at which co-infections are generated in the population is given by $\frac{ceVM^2}{K^2+M^2}$. The sigmoid functional response is used here based on the fact that individuals sick with malaria have limited movements, thereby making it hard for the tsetse flies to bite them. Therefore, at low densities, malaria infected humans are hard to find by the tsetse fly, but when the densities are high, bites by the tsetse fly increase rapidly. The removal rate of the malaria infected through death, recovery or hospitalization is modelled by parameter ζ. Once infection of M by V takes place, individuals move to the co-infected class T. These individuals recover, die, or are hospitalized at a rate ϑ.

Let the transmitting tsetse fly vector V multiply linearly as a function of itself at a constant rate g. A logistic growth could be considered as well but for simpler analysis, we shall use the linear growth here. As a result of bites to a co-infected human, it is assumed that the tsetse fly becomes infected leading to additional growth in the sub compartment at a rate cd, where d is the probability of acquiring infection on each bite of an infected human. The tsetse fly is removed at a rate μ, and this incorporates different mechanisms such as failure to locate an infected human, death, or emigration to a new location. Thus, $\mu > g$. The dynamics described above are given by the following equation:

$$\begin{cases} \dfrac{\mathrm{dM}}{\mathrm{dt}} = \mathrm{b} - \dfrac{\mathrm{ecVM^2}}{\mathrm{K^2+M^2}} - \zeta \mathrm{M}, \\ \dfrac{\mathrm{dT}}{\mathrm{dt}} = \dfrac{\mathrm{ecVM^2}}{\mathrm{K^2+M^2}} - \vartheta \mathrm{T}, \\ \dfrac{\mathrm{dV}}{\mathrm{dt}} = \mathrm{gV} + \mathrm{cdTV} - \mu \mathrm{V}. \end{cases} \tag{1}$$

The model is analysed for stability and an optimal control strategy for prevention of co-infections is determined.

2.1 Equilibrium points and their stability

Since malaria is endemic in this population, a disease-free equilibrium point is not possible. However, a sleeping sickness-free equilibrium point exists and is given by $\mathrm{E(M_*)} = \left(\frac{\mathrm{b}}{\zeta}, 0, 0\right)$. This is the point when malaria exists without

trypanosomiasis in the population. The linear stability of $E(M_*)$ is governed by the development potential of malaria in the population d_M given by $\frac{b}{\zeta}$. When $d_M < \frac{b}{\zeta}$, malaria does not develop and thus no co-infections are expected. In this case, individuals have more chances of recovery than acquiring sleeping sickness during the malaria episode. When $d_M > \frac{b}{\zeta}$, malaria develops and co-infections are probable. The word probable is used here since when individuals are very sick with malaria, there will be few contacts with the tsetse fly [14] and co-infections will be few. Stability of this point is analyzed using the following theorem:

Theorem 2.1 *The equilibrium point* $E(M_*)$ *is globally asymptotically stable if*

$$\frac{b-\zeta}{\vartheta} < \frac{\mu - g}{cd}. \tag{2}$$

Proof:

Consider a Lyapunov function

$$\mathcal{L} = \eta_1 T + \eta_2 V, \tag{3}$$

where $\eta_i, i = 1,2$ are positive constants. At $\left(\frac{b}{\zeta},0,0\right)$, $L = 0$ and when $T, V, \neq 0$, $\mathcal{L} > 0$. The derivative of the Lyapunov function is such that

$$\begin{aligned}\frac{d\mathcal{L}}{dt} &= \frac{d\mathcal{L}}{dT} \times \frac{dT}{dt} + \frac{d\mathcal{L}}{dV} \times \frac{dV}{dt}, \\ &= \eta_1 \left(\frac{ecVM^2}{K^2 + M^2} - \vartheta T\right) + \eta_2 (g + cdT - \mu) V.\end{aligned}$$

To have a negative derivative of $\mathcal{L}$,

$$\frac{ecVM^2}{K^2 + M^2} < \vartheta T \quad \text{and} \quad cdT < \mu - g. \tag{4}$$

This implies that

$$\frac{ecVM^2}{\vartheta(K^2 + M^2)} < \frac{\mu - g}{cd}. \tag{5}$$

Eliminating V using the first equation of model (1) implies that

$$\frac{b-\zeta}{\vartheta} < \frac{\mu - g}{cd}. \tag{6}$$

Therefore, $\mathcal{L}' < 0$ provided $b > \zeta$ and $\mu > g$. This implies that $E(M^*)$ is globally asymptotically stable when $d_M^* = \frac{b}{\zeta} > 1$ and $d_T^* = \frac{g}{\mu} < 1$. d_M^* and d_T^* are the thresholds for containment of sleeping sickness in a population with endemic malaria. A slight deviation from these points could lead to explosion of malaria and trypanosomiasis co-infection. □

When $d_M^* < 1$ and $d_T^* > 1$, then there is co-infection in the population. A co-infected endemic equilibrium point is when both malaria and sleeping sickness exist in the population. At this point, M, T, V are all greater than zero. This point is obtained by setting the left hand side of equation (1) to zero and solving the resulting system. This gives the equilibrium point E_* equal to:

$$\mathrm{E}_* = \begin{cases} \mathrm{M}_* = \dfrac{\mathrm{b}}{\zeta}\dfrac{1}{\mathcal{R}_\mathrm{C}}(\mathcal{R}_\mathrm{C}-1), \\ \mathrm{T}_* = \dfrac{\mathrm{b}}{\vartheta}\dfrac{1}{\mathcal{R}_\mathrm{C}}, \\ \mathrm{V}_* = \dfrac{\mathrm{K}^2\zeta}{\mathrm{ec}(\mathcal{R}_\mathrm{C}-1)} + \dfrac{\mathrm{b}^2}{\zeta \mathrm{e}}\dfrac{1}{\mathcal{R}_\mathrm{c}}(\mathcal{R}_\mathrm{C}-1), \end{cases} \tag{7}$$

where

$$\mathcal{R}_C = \frac{\mathrm{bcd}}{\mathcal{g}(\mu - \mathrm{g})}, \tag{8}$$

is the basic reproductive number for the co-infection. Therefore, the endemic equilibrium exits if $\mathcal{R}_C > 1$ otherwise the trypanosomiasis-free point $\mathrm{E}(\mathrm{M}_*)$ exists. This term is a product of two mechanisms. The first $\frac{b}{\mathcal{g}}$ gives the probability of a new malaria infective acquiring sleeping sickness during the removal process. The second term $\frac{cd}{\mu - g}$ is the probability of the tsetse fly becoming infected before emigration or death. Thus, $\mathcal{R}_C$ is the number of co-infections generated from a single sleeping sickness infective when introduced in a population where malaria is endemic. In the next subsection, we seek to find an optimal way to control these co-infections at minimum cost possible.

2.2 Analysis of optimal control

We introduce into model (1) time dependent preventive control $0 \le u_1(t) \le 1$ to reduce transmission of sleeping sickness among malaria infected individuals. This can be done through protection of the infected such as hospitalisation or providing insecticide treated nets. Therefore, $u_1(t)$ is the effort for effective prevention of infection of a malaria individual with sleeping sickness. An additional control $u_2(t)$ where $0 \le u_2(t) \le 1$ is used as the effort required to prevent infectious bites from sleeping sickness infected individuals to the tsetse fly. This can be done by providing protection of the infected individuals, and keeping them away from exposure. This control therefore models the effort required to reduce transmission of the disease from an infected human to the vector. Incorporating these controls in the model gives

$$\begin{cases} \dfrac{\mathrm{dM}}{\mathrm{dt}} &= \mathrm{b} - \dfrac{\mathrm{e}(1-\mathrm{u}_1(\mathrm{t}))\mathrm{cVM}^2}{\mathrm{K}^2+\mathrm{M}^2} - \zeta \mathrm{M}, \\ \dfrac{\mathrm{dT}}{\mathrm{dt}} &= \dfrac{\mathrm{e}(1-\mathrm{u}_1(\mathrm{t}))\mathrm{cVM}^2}{\mathrm{K}^2+\mathrm{M}^2} - \mathcal{g}\mathrm{T}, \\ \dfrac{\mathrm{dV}}{\mathrm{dt}} &= \mathrm{gV} + \mathrm{cd}(1-\mathrm{u}_2(\mathrm{t}))\mathrm{TV} - \mu \mathrm{V}. \end{cases} \tag{9}$$

The objective is then to minimize the number of infections with co-infection of malaria and sleeping sickness, and the subsequent transmission to the tsetse fly. Note that when $u_1(t), u_2(t) = 0,$ the model in equation (9) reduces to the previous model in equation (1). This would give a state without intervention. So the objective is to reduce the number of co-infections, while keeping costs as minimum as possible. To achieve this, relative costs associated with each control effort/policy are incorporated, directed towards limiting malaria and sleeping sickness co-infections. The objective function J to be used over a feasible set of controls $u_1(t)$ and $u_2(t),$ applied over the pre-defined finite time interval $[t_0, t_f]$ is given by

$$\mathrm{J}(\mathrm{u}_1, \mathrm{u}_2) = \int_{\mathrm{t}_0}^{\mathrm{t}_\mathrm{f}} \{\mathrm{A}_1\mathrm{T} + \mathrm{A}_2\mathrm{V} + \frac{1}{2}\mathrm{a}_1\mathrm{u}_1^2 + \frac{1}{2}\mathrm{a}_2\mathrm{u}_2^2\}\mathrm{dt}. \tag{10}$$

It is assumed, as in prior studies of [7, 12], that the costs of the prevention and treatments are non linear and take quadratic form. A_1T is the cost associated with controlling sleeping sickness in the human, while A_2V is the cost associated with prevention of transmission in the tsetse fly. The rest of the parameters a and b are relative cost weights for each control measure aimed at preventing co-infections by providing treated nets and treatment of the infected to avoid further transmission to the tsetse fly. The goal is to minimize the number of co-infected individuals $T(t)$, while minimising the

cost of controls $u_1(t), u_2(t)$. Therefore, an optimal control u_1^*, u_2^* is sought such that

$$J(u_1^*, u_2^*) = \min_{u_1,u_2}\{J(u_1, u_2 \mid u_1, u_2 \in U\}, \tag{11}$$

where the control set $U = \{(u_1, u_2 \mid u_i : [t_0, t_f] \to [0,1], \text{ for } i = 1,2\}$. The necessary conditions that an optimal control must satisfy are derived from the Pontryagin's Maximum Principle [18]. It converts equations (9)-(11) into a problem of minimizing a point-wise Hamiltonian H, with respect to (u_1, u_2) given by

$$H = A_1 T + A_2 V + \frac{1}{2} a_1 u_1^2 + \frac{1}{2} a_2 u_2^2 + \lambda_M \left\{ b - \frac{e(1-u_1(t))cVM^2}{K^2 + M^2} - \zeta M \right\}$$

$$+ \lambda_T \left\{ \frac{e(1-u_1(t))cVM^2}{K^2 + M^2} - \vartheta T \right\} + \lambda_V \{gV + cd(1-u_2(t))TV - \mu V\},$$

where $\lambda_M, \lambda_T, \lambda_V$ are the adjoint or co-state variables. By differentiating the Hamiltonian with respect to each state variable, the differential equation for the associated adjoint is determined. The corollary in [7] gives the existence of optimal control due to the convexity of the integrand of J with respect to u_1 and u_2, a *priori* boundedness of the state solutions, and the *Lipschitz* property of the state system with respect to the state variables. Applying Pontryagin's Maximum Principle [7] and the existence result for the optimal control from [18], the following proposition is made:

Proposition 2.1 *Consider an optimal control* u_1^*, u_2^* *and solutions* M_*, T_*, V_* *of the corresponding system (9) that minimizes* $J(u_1, u_2)$ *over* U. *Then, there exists adjoint functions* $\lambda_M, \lambda_T, \lambda_V$ *satisfying*

$$\begin{aligned}
\lambda_M' &= -\left[\left(-e(1-u_1(t))c\frac{2VM}{K^2 + M^2} - \zeta \right)\lambda_M + e(1-u_1(t))c\left(\frac{2VM}{K^2 + M^2} \right)\lambda_T \right], \\
\lambda_T' &= -[A_1 - \vartheta\lambda_T + cd(1-u_2(t))V\lambda_V], \\
-\lambda_V' &= -\left[A_2 - \frac{e(1-u_1(t))cM^2}{K^2 + M^2}\lambda_M + \frac{e(1-u_1(t))cM^2}{K^2 + M^2}\lambda_T + (g + cd(1-u_2(t))T - \mu)\lambda_V \right]
\end{aligned} \tag{12}$$

and with transversality conditions

$$\lambda_M(t_f) = \lambda_T(t_f) = \lambda_V(t_f) = 0. \tag{13}$$

On the interior of the control set, where $0 < u_i < 1$, for $i = 1,2$ we have $0 = \frac{\partial H}{\partial u_1} = \frac{\partial H}{\partial u_2}$ and thus obtain the controls u_1^* and u_2^* satisfying the optimality condition given as

$$\begin{cases}
u_1^* &= \min\left\{1, \max\left(0, \dfrac{ecV_*M_*^2(\lambda_T - \lambda_M)}{a_1(K^2 + M_*^2)} \right)\right\}, \\
u_2^* &= \min\left\{1, \max\left(0, \dfrac{cdT_*V_*\lambda_V}{a_2} \right)\right\}.
\end{cases} \tag{14}$$

Proof:

Proposition 2.1 is proved using Corollary 4.1 in Fleming and Rishel [7]. Applying Pontryagin's Maximum Principle gives

$$\frac{d\lambda_M}{dt} = -\frac{\partial \mathcal{H}}{\partial M}, \quad \lambda_S(t_f) = 0, \quad \frac{d\lambda_T}{dt} = -\frac{\partial \mathcal{H}}{\partial T}, \quad \lambda_T(t_f) = 0, \quad \frac{d\lambda_V}{dt} = -\frac{\partial \mathcal{H}}{\partial V}, \quad \lambda_V(t_f) = 0, \tag{15}$$

evaluated at the optimal control pair and corresponding states, which results in the stated adjoint system (12) and (13) [12]. On the interior of the control set, where $0 < u_i < 1$, for $i = 1,2$ we have

$$\frac{\partial \mathcal{H}}{\partial u_1} = 0, \quad = \frac{\partial \mathcal{H}}{\partial u_2} = 0,$$

and thus obtain the controls u_1^* and u_2^* satisfying the optimality condition. Solving for u_1^*, u_2^* on the interior of the control set gives

$$\begin{cases} u_1^* = \dfrac{ecV_*M_*^2(\lambda_T - \lambda_M)}{a_1(K^2 + M_*^2)}, \\ u_2^* = \dfrac{cdT_*V_*\lambda_V}{a_2}. \end{cases} \tag{16}$$

Taking the bounds into account gives the characterization of u_1^* and u_2^* in equation (14), and this completes the proof. □

3 Numerical results

In this section, the numerical results of the optimal control model are studied. These results are obtained by solving the optimality system of three ODE's from the state and adjoint equations. An iterative scheme is used to solve the optimality system. First, the state equations are solved with a guess for the controls over the simulated time using fourth order Runge-Kutta scheme. The controls are then updated by using a convex combination of the previous controls and the value from the characterizations in equation (14). This process is repeated and iterations are stopped if the values of the unknowns at the previous iterations are very close to the ones at the present iterations [18].

A simple model with prevention and treatment as control measures to study the effects of preventing co-infections of malaria and sleeping sickness is explored. Malaria is considered endemic in the area and a bite by a tsetse fly to an infected individual leads to co-infection with sleeping sickness. Therefore, providing protection from tsetse fly bites may be adopted as a control and prevention strategy. Using various combinations of the two controls, numerical results from the simulations are investigated and compared.

In the simulation it is assumed that the weight factor A_2 associated with preventing tsetse fly bites is less than A_1, which is for protecting malaria infected individuals from sleeping sickness during the malaria episode. This assumption is based on the fact that although protecting a person sick with malaria for the duration of the episode involves making sure treatment is provided and taken at the correct intervals and also involves use of bed nets, it is equally hard to protect sick people from tsetse bites since some of them are in hospitals and others stay at home. In addition, it is harder to prevent tsetse flies from biting humans. Therefore, this cost involves finding the sick, and providing treatment of both malaria and sleeping sickness, and may also need to provide protection against both such as bed nets. All these factors weigh heavily on the effectiveness of a control program. In all numerical simulations, the weight factors $A_1 = 4$ and $A_2 = 10$ are chosen to illustrate the optimal treatment strategy. Other epidemiological parameters are presented in Table 1. In all figures, the solid line represents the simulation of the infected malaria, co-infected and vector without control, and the dashed line with control.

Table 1: Parameter Description and Values

Parameters	Description	Nominal Value	Reference
g	Malaria recruitment rate	0.000992/day	Estimated
e	Transmission rate of trypanosomiasis in humans	0.62/day	[1]
c	Biting rate of tsetse fly	0.6/day	[6]
K	Malaria carrying capacity	5/day	Estimated
ζ	Malaria removal rate	0.0025854/day	Estimated
ϑ	Trypanosomiasis removal rate	0.087424/day	Estimated
g	Tsetse fly recruitment rate	0.1	[16]
d	Transmission rate of trypanosomiasis in tsetse fly	0.1/day	[1]

Figure 1 shows the simulation of the model without control, that is, both u_1 and u_2 equal to zero. In (a), the evolution of malaria infected individuals with time is given, in (b) the co-infected and in (c), the vector. In (d), the controls, u_1 (solid) and u_2 (dashed), are plotted as a function of time. The figure shows that malaria individuals steadily decrease to zero and the co-infected also first increase then decrease to a minimum. The vector increases steadily to a maximum.

Figure 2 shows the simulation of the infected humans and vector when transmission to the vector is controlled. It is observed that to minimize the total number of infections to the tsetse fly, optimal control u_2 is at the upper bound through about 100 days, then steadily declines. The proportion of tsetse flies at the final time t_f = 160 (days) is 0.6571 in the case with control and 1.0000 without control, and the proportion of tsetse flies prevented at the end of the control program is 0.3429 (= 1.0000- 0.6571). (See Table 2).

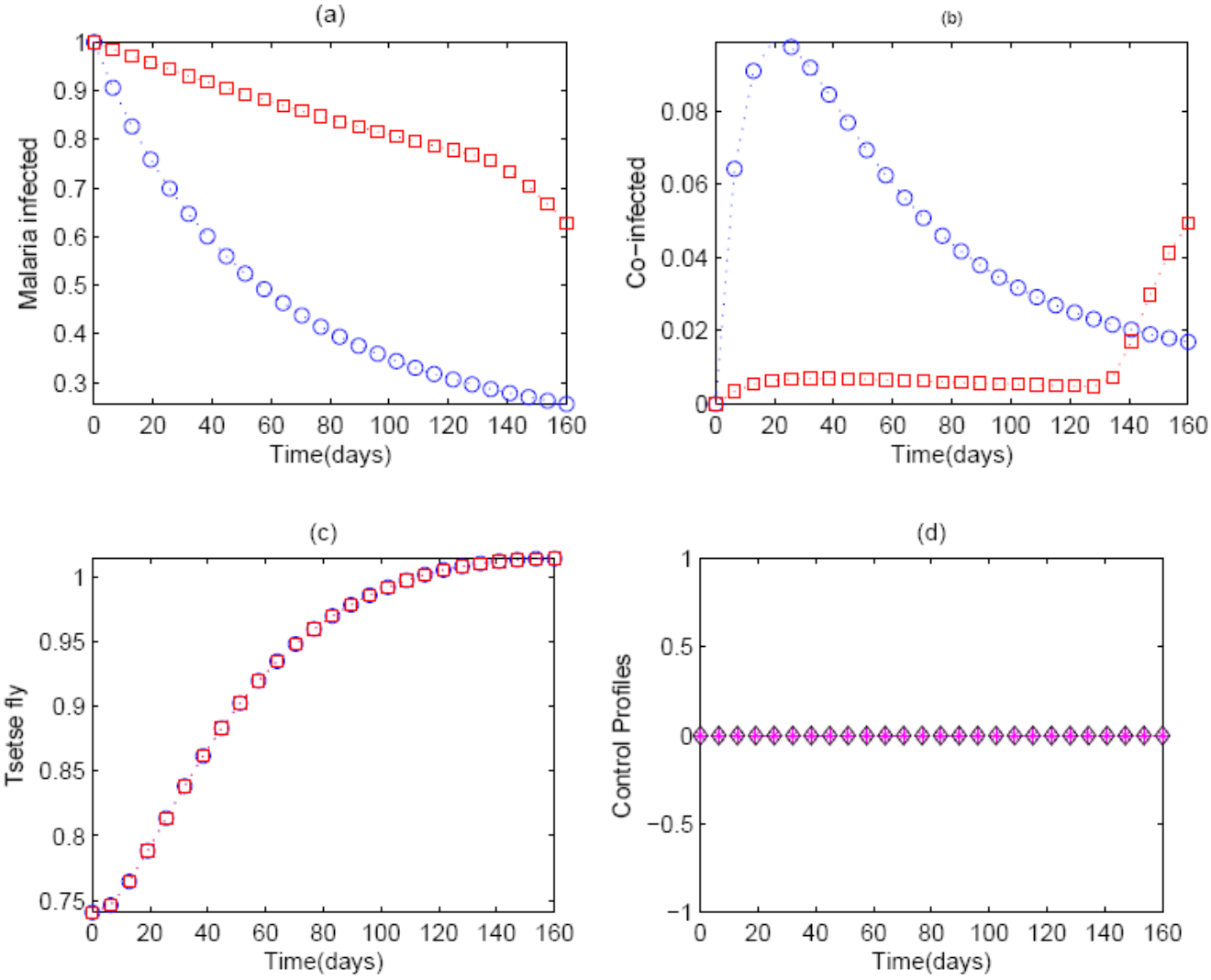

Figure 1: Simulation of malaria infected, co-infected, the vector without control, i.e. $u_1 = u_2 = 0$. The blue circled line is for the variables without control, while the red squared line are the variables with control. Control 1 (u_1) is represented by the magenta starred line, while control 2 (u_2) is the black diamond. Other parameter values are in Table 1.

Table 2: Computed parameters Controls

		M	T	V
$u_1 = 0,$	$u_2 = 0$	0.2561	0.0169	1.0000
$u_1 = 0,$	$u_2 \neq 0$	0.3039	0.0155	0.6571
$u_1 \neq 0,$	$u_2 = 0$	0.6283	0.0495	0.6913
$u_1 \neq 0,$	$u_2 \neq 0$	0.4489	0.0311	0.6753

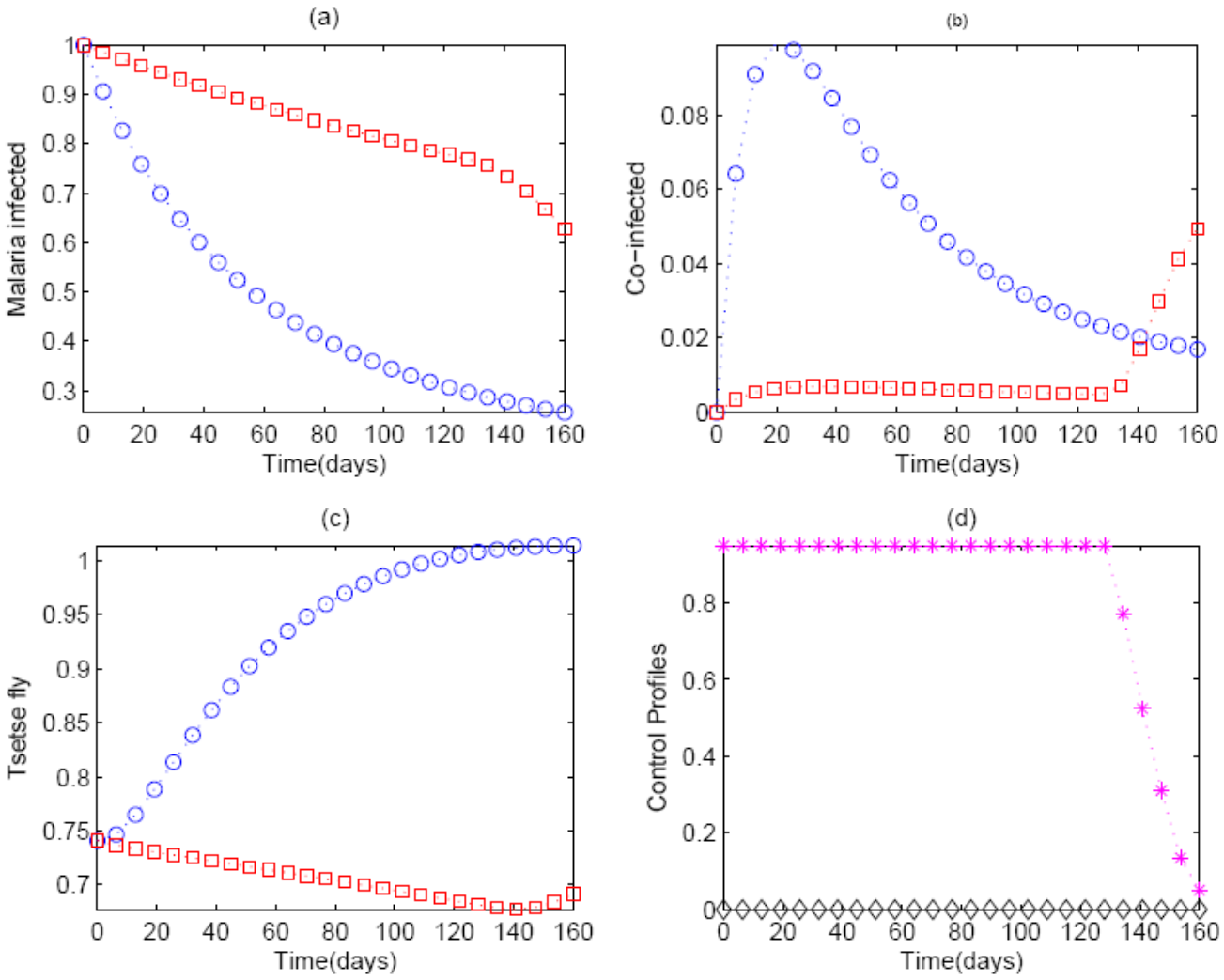

Figure 2: Simulation of malaria infected, co-infected, the vector with a control strategy when $u_1 = 0, u_2 \neq 0$. The blue circled line is for the variables without control, while the red squared line are the variables with control. Control 1 (u_1) is represented by the magenta starred line, while control 2 (u_2) is the black diamond. Other parameter values are in Table 1.

In Figure 3, there is no control of bites to the human by the vector $u_2 = 0$, but the transmission of trypanosomiasis in the malaria infected is controlled, $u_1 \neq 0$. To minimize the total number of co-infections, optimal control u_1 is at the upper bound for about 130 days, and then drops to the lower bound. The total number of co-infections at the final time t_f = 160 (days) is 0.6913 in the case with control. On the other hand, at the final time t_f, the fraction of malaria infected individual with control is 0.6283 compared to 0.2561 without control. It can be noted that protecting individuals against sleeping sickness without controlling the vector does not cut down on the number of infections within the community. When the malaria infected are protected from sleeping sickness, it only means that there will be more people who are healthy to be infected by the tsetse fly. Thus, it is imperative that vector control should be enforced as a priority before individual protection.

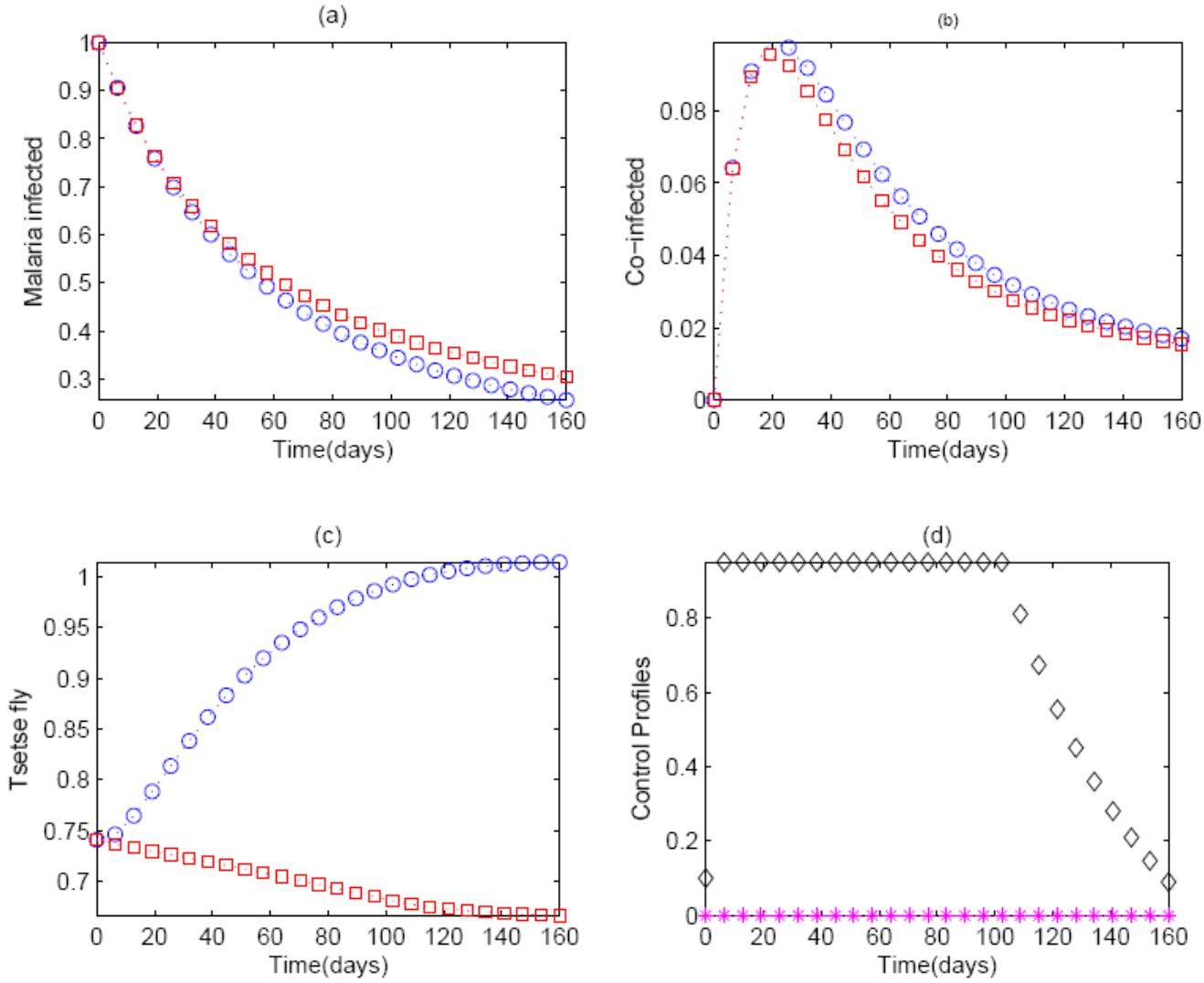

Figure 3: Simulation of malaria infected, co-infected, the vector with a control strategy when $u_1 \neq 0, u_2 = 0$. The blue circled line is for the variables without control, while the red squared line are the variables with control. Control 1 (u_1) is represented by the magenta starred line, while control 2 (u_2) is the black diamond. Other parameter values are in Table 1

. Figure 4 is when both controls are applied. It is observed that the only significant reduction is in the vector, from 1.0000 without control to 0.6753 with control. Therefore, the number of vectors averted are 0.3247, slightly less than when one control was used in Figure 2. Thus, it is more beneficial to apply all possible controls at the same time. We have to note here that the upper bound for the controls is 0.95 while the lower bound is 0.05. All these numerical results are shown in Table 2.

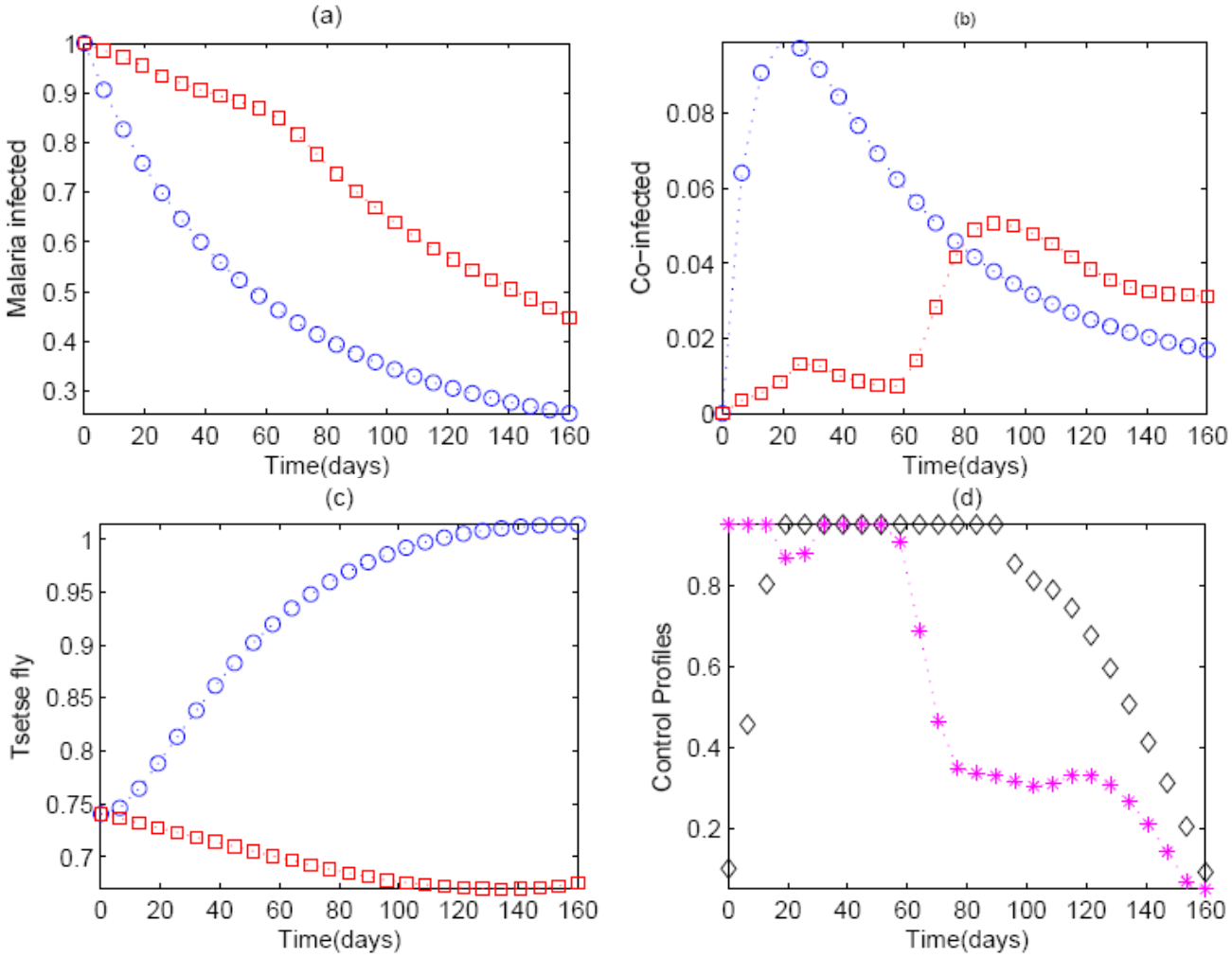

Figure 4: Simulation of malaria infected, co-infected, and the vector with a control strategy when $u_1, u_2 \neq 0$. The blue circled line is for the variables without control, while the red squared line are the variables with control. Control 1 (u_1) is represented by the magenta starred line, while control 2 (u_2) is the black diamond. Other parameter values are in Table 1.

In conclusion, results identify optimal control strategies for three scenarios. Although the results in this study may vary depending on the population size, cost of implementing treatment controls and parameter values of the model, a control program that follow our strategies may effectively reduce the number of co-infections of malaria and sleeping sickness, and could also be employed as a vector control strategy.

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