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QUALITATIVE ANALYSIS OF A MATHEMATICAL MODEL FOR MALARIA TRANSMISSION AND ITS VARIATION

ZHENBU ZHANG, TOR A. KWEMBE

Abstract. In this article we consider a mathematical model of malaria transmission. We investigate both a reduced model which corresponds to the situation when the infected mosquito population equilibrates much faster than the human population and the full model. We prove that when the basic reproduction number is less than one, the disease-free equilibrium is the only equilibrium and it is locally asymptotically stable and if the reproduction number is greater than one, the disease-free equilibrium becomes unstable and an endemic equilibrium emerges and it is asymptotically stable. We also prove that, when the reproduction number is greater than one, there is a minimum wave speed c^* such that a traveling wave solution exists only if the wave speed c satisfies $c \geq c^*$. Finally, we investigate the relationship between spreading speed and diffusion coefficients. Our results show that the movements of mosquito population and human population will speed up the spread of the disease.

1. Introduction

Malaria is one of the most devastating diseases and a leading cause of death in the tropical regions of the world [10]. Half of the world's population is at risk for malaria, which is endemic in more than 100 countries. Although preventable and treatable, malaria causes significant morbidity and mortality, especially in resource-poor regions [30].

Malaria is an infectious disease caused by the Plasmodium parasite and transmitted to humans through the bite of infected anopheles mosquitoes [7]. The incidence of malaria has been growing recently due to increasing parasite drug-resistance on one hand and mosquito insecticide-resistance on the other hand.

Malaria is spread in three ways. The most common way is by the bite of an infected anopheles mosquito. Although malaria could also be spread through a transfusion of infected blood and by sharing needle with an infected person, they can, in this case, be effectively prevented. Therefore, as long as we can find an effective preventive measure to prevent the spread of malaria by mosquitoes, malaria could be reduced or eradicated. Although, in some tropical regions, malaria has decreased recently, in some areas, the transmission of the disease is still a severe

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threat and the factors that maintain the transmission continues to be of great challenge. As reported in ([30]) intervention mechanisms have increased but other factors including poor sanitation, weak health systems, limited disease surveillance capabilities, drug and insecticide resistance, natural disasters, armed conflicts, migration, and climate change continue to complicate malaria control efforts in the most affected regions of the world. Therefore, it is very important to investigate these factors thoroughly by developing and analyzing appropriate mathematical models to establish the essential tools and identifiable targets needed to eliminate the transmission of malaria.

Mathematical models are among the most important useful tools that are often applied in identifying control measures that are most important, as well as in quantifying the effectiveness of different control strategies in controlling or eliminating malaria in endemic regions ([25]). Mathematical modeling as a tool for gaining deeper insights in the control of the spread of malaria began in 1911 with the Ross's model ([26]) and extended by MacDonald in his 1957 landmark book [19]. The resulting two-dimensional prey-predator model describing the interactions between the human and mosquito populations and malaria transmission is commonly known as the Ross-MacDonald model [19]. Since then, mathematical models of various levels of complexity have been developed to explore the possibilities of controlling and eliminating malaria infection. Notable contributions include dynamics models incorporating acquired immunity proposed by Dietz, Molineaux and Thomas [8]. Aron expanded on the ideas of Dietz, Molineaux and Thomas in [4]. A thorough review of existing mathematical models of malaria and control can be found in Anderson and May [3], Aron and May [5], Koella [11] and Nedelman [21]. There have also been some recent elegant models that included environmental factors in [17, 34, 35]. The spread of anti-malaria resistance models is treated in [12] and the mathematical models incorporating the evolution of immunity is covered in [13]. Very recently, Ngwa and Shu [23] and Ngwa[22] proposed a dynamical system of compartmental model for the spread of malaria with a susceptible - exposed - infectious - recovered - susceptible (SEIRS) pattern for humans and a susceptible - exposed - infectious (SEI) pattern for mosquitoes. In his Ph.D. dissertation, Chitnis in [6] and Chitnis et al in [7] analyzed a similar model for malaria transmission. Although some of these models are quite sophisticated, they are non-spatial. The common trend for these models is in the investigation of the dynamic characteristics of the Ross mosquitoes and human reproductive number R_0. The Ross reproductive number R_0 is generally defined as the number of secondary infections that one infectious person would produce in a fully susceptible population through the entire duration of the infectious period. As a concept, it is derived from the idea of a reproductive number in population dynamics which is defined as the expected number of offspring that one organism will produce over its lifespan. In the dynamic malaria models that have evolved over time, the reproductive number in each case defers only by the number of equations in the systems and the parameters characterizing the evolution of the population variables. The analysis of the models in each case shows the existence of two equilibriums, the endemic and disease-free equilibriums. In particular, they proved the Ross assertion that when $R_0 > 1$, there exist a unique endemic equilibrium and when $R_0 \leq 1$, there is a disease-free equilibrium. Other variations included bifurcation and stability analysis of the ensuing systems of the first order ordinary differential equations [1, 6, 7, 10, 23].

However, the fact that human and mosquito populations move randomly suggests the development of the malaria mathematical models that incorporate the diffusive movements of human and mosquitoes. In particular, with the development of transportation and globalization, human movement becomes more and more popular. It turns out that, for many diseases including malaria, human population movement contributes greatly to the spread and persistence of the disease [9], and is therefore an important consideration when implementing intervention strategies [32]. Despite this, little is known about human movement patterns and their epidemiological consequences [29]. In fact, the failure of the Global Malaria Eradication Programme in the 1950s and 1960s may be due, in part, to the failure to take into account human movement [9]. In this project we will assume that both human hosts and mosquitoes are in random motion drifting from areas of high densities to low densities. In fact, Weinberger, et al. incorporated this principle in the development of theories for the linear determinacy for spread in cooperative models [31]. In this development they constructed a discrete-time recursion system with a vector of population distributions of species and an operator that models the growth, interaction, and migration of the species. They developed results that incorporated the local invasion of equilibrium of cooperating species by a new species or mutant. They established that the change in equilibrium density of each species spreads at its own asymptotic speed with the speed of the invader the slowest of the speeds. The growth, interaction, and migration operator is chosen to insure that all species spread at the same asymptotic speed and the speed agreed with that of the invader for a linearized problem in which case the recursion has a single linearly determinate speed. They suggested that these conditions could be verified for the case of age dependent reaction-diffusion models. Following their work, Lou and Zhao [18] studied an age-dependent reaction-diffusion malaria model with incubation period in the vector population and established the existence of spread speed for malaria in endemic and disease-free regions. Inspired by this work, Wu and Xiao [33] derived a non-age dependent time-delayed reaction-diffusion malaria model. In this work, they analyzed the positivity and invariance of traveling wave solutions of the resulting Cauchy problem in an unbounded domain. They then related the Ross reproduction ratio R_0 to the threshold that predicts the spread of malaria and showed the existence of traveling wave solutions connecting the two steady states known as the disease-free steady state and the endemic steady state that exist if $R_0 > 1$ and traveling wave solutions connecting the disease-free steady state itself do not exist if $R_0 < 1$. There is no conclusion in the case when $R_0 = 1$.

In this paper, we have modified the Ross-MacDonald model to a reaction-diffusion system that is not a time-delayed system having the Weinberger et al. growth, interaction, and migration operator type to investigate the existence and stability of steady states. We will also investigate the existence of traveling wave solutions and establish the endemic and disease-free steady states in terms of the asymptotic spread speeds of mosquitoes and human. It is well-known that, for an epidemic disease model, the existence of traveling wave solutions implies the spatial spread of the epidemic wave of infectiousness into the population. We will investigate the existence of traveling wave solutions under different assumptions and derive some sufficient and (or) necessary conditions on the parameters for the existence of traveling wave solutions that provide for a deeper insights into how malaria invade the human population. These results will provide the decision maker some

useful references to take appropriate control or preventive measures. We will also investigate the effect of human movement on the spreading speed of the disease.

This paper is organized as follows: In Section 2, we describe the model and the meaning of the parameters in the model. In Section 3, we consider a simplified model and investigate the existence of traveling waves. In Section 4, we consider the full model and investigate the existence of steady states and their stability, the existence of travelling waves, and the effect of diffusion on the spreading speed of the disease. In section 5, we present some numerical simulations to verify some of our theoretical results derived in previous sections, and finally we make a short conclusion based on our mathematical analysis.

2. Description of the model

We will consider a simple modification of Ross-Macdonald model. We consider one spatial dimension case. Since malaria transmission is restricted to only a few kilometers from specific mosquito breeding sites [1], we take the region to be the whole space $\mathbb{R}$. Because the life expectancy of a human is much longer than that of a mosquito we assume that the population of humans is closed with no births and no deaths except from malaria. We also assume that humans and mosquitoes are either infected or uninfected and the total numbers of humans and mosquitoes are constants. Thus we need only investigate the dynamics of the infected humans and mosquitoes. Let $u(t,\ x)$ and $v(t,\ x)$ be the spatial densities of infected humans and infected mosquitoes at time t in x, respectively. Let a be the human-biting rate; that is, the rate at which mosquitoes bite humans, b be the mosquito-to-human transmission efficiency, that is, the probability, given an infectious mosquito has bitten a susceptible human, that the human becomes infected, and r be the human-to-mosquito transmission efficiency, that is, the probability, given a susceptible mosquito has bitten an infectious human, that the mosquito becomes infected. Assume that both humans and mosquitoes are allowed to diffuse with diffusive coefficients D and d, respectively. We let m denote the ratio of the number of mosquitoes to humans, η denote the human recovery rate due to treatment, and δ denote the per capita death rate of infected human hosts due to the disease. We let μ denote the mosquito death rate. Then one version of the modified Ross-MacDonald mathematical model for malaria transmission with diffusion in one spatial dimension case is

$$\begin{aligned}
\frac{\partial u}{\partial t} &= Du_{xx} + mabv(1-u) - (\eta+\delta)u, \quad x \in \mathbb{R},\ t > 0,\\
\frac{\partial v}{\partial t} &= dv_{xx} + aru(1-v) - \mu v, \quad x \in \mathbb{R},\ t > 0,\\
u(0,x) &= u_0(x), \quad v(0,x) = v_0(x), \quad x \in \mathbb{R},
\end{aligned} \tag{2.1}$$

where $u_0(x) \geq 0 \not\equiv 0$ and $v_0(x) \geq 0 \not\equiv 0$ are the initial densities of infected human population and infected mosquito population, respectively.

3. A reduced model

As the first step, same as in [25], we assume that the infected mosquito population equilibrates much faster than the infected human population. Thus, by assuming that the mosquito population dynamics is at equilibrium, the equations in (2.1) can be reduced to the single equation:

$$\frac{\partial u}{\partial t} = Du_{xx} + \frac{ma^2 bru}{aru + \mu}(1-u) - (\eta+\delta)u, \quad x \in \mathbb{R},\ t > 0.$$

Simplifying this equation as in [25], we obtain

$$\frac{\partial u}{\partial t} = Du_{xx} + f(u), \quad x \in \mathbb{R},\ t > 0, \tag{3.1}$$

where

$$f(u) = \frac{[\alpha\beta - \mu(\eta+\delta) - \beta(\alpha+\eta+\delta)u]u}{\beta u + \mu},$$

$\alpha = mab$, $\beta = ar$. This is the equation we are going to analyze in this Section.

First, we investigate constant steady states and their stability. By setting $f(u) = 0$ we obtain the following two equilibria: one disease-free equilibrium $u_0 = 0$ and the other one is the endemic equilibrium,

$$u_e = \frac{\alpha\beta - \mu(\eta+\delta)}{\beta(\alpha+\eta+\delta)},$$

which exists when

$$\alpha\beta - \mu(\eta+\delta) > 0. \tag{3.2}$$

In terms of the original parameters, (3.2) is equivalent to the basic reproduction number $R_0 > 1$:

$$R_0 = \frac{ma^2 br}{\mu(\eta+\delta)} > 1.$$

By direct computations, we have

$$f'(u) = \frac{\mu[\alpha\beta - \mu(\eta+\delta)] - 2\beta\mu(\alpha+\eta+\delta)u - \beta^2(\alpha+\eta+\delta)u^2}{(\beta u+\mu)^2}.$$

Thus, we have

$$f'(0) = \frac{\alpha\beta - \mu(\eta+\delta)}{\mu}.$$

Therefore, if $\alpha\beta - \mu(\eta+\delta) < 0$, that is, in the case that there exists only one equilibrium u_0, then $f'(0) < 0$ and $u_0 = 0$ is locally asymptotically stable. If $\alpha\beta - \mu(\eta+\delta) > 0$, that is, when the endemic equilibrium u_e exists, then $f'(0) > 0$ and $u_0 = 0$ is unstable. In this case,

$$f'(u_e) = -\frac{(\alpha+\eta+\delta)[\alpha\beta - \mu(\eta+\delta)]}{\alpha(\beta+\mu)} < 0.$$

Therefore, u_e is asymptotically stable. Specifically, we have the following stability theorem from [36, Theorem 4.3.12].

Theorem 3.1. *If $\alpha\beta - \mu(\eta+\delta) > 0$, $0 \le \phi(x) \le u_e$ and $\phi(x) \not\equiv 0$, then the initial value problem*

$$\frac{\partial u}{\partial t} = Du_{xx} + f(u), \quad x \in \mathbb{R},\ t > 0,$$
$$u(0,x) = \phi(x), \quad x \in \mathbb{R},$$

has a unique global solution $u_\phi(t,x)$ which satisfies

$$\lim_{t\to\infty} u_\phi(t,x) = u_e.$$

Let $w = u/u_e$, then (3.1) can be written as

$$\frac{\partial w}{\partial t} = Dw_{xx} + g(w), \quad x \in \mathbb{R},\ t > 0, \tag{3.3}$$

where

$$g(w) = \frac{(\alpha+\eta+\delta)[\alpha\beta - \mu(\eta+\delta)]w(1-w)}{[\alpha\beta - \mu(\eta+\delta)]w + \mu(\alpha+\eta+\delta)}.$$

Obviously, we have $g(0) = g(1) = 0$ and for $0 < w < 1$, $g(w) > 0$. By direct computations we have

$$g'(0) = f'(0) = \frac{\alpha\beta - \mu(\eta+\delta)}{\mu}.$$

It is easily seen that, when $\alpha\beta - \mu(\eta+\delta) > 0$ and $0 < w < 1$,

$$g(w) < \frac{(\alpha+\eta+\delta)[\alpha\beta - \mu(\eta+\delta)]w}{\mu(\alpha+\eta+\delta)} = \frac{\alpha\beta - \mu(\eta+\delta)}{\mu} w = g'(0)w.$$

Therefore, by a well-known result from [14] (see also[24, 31]), we know that

$$c^* = 2\sqrt{g'(0)D} = 2\sqrt{D[\alpha\beta - \mu(\eta+\delta)]/\mu}$$

is the spreading speed of (3.3). It is also the spreading speed of (3.1). This means that if an observer travels in the direction of propagation at a speed that is above c^*, he would observe that there is no infected population. Specifically, this means that any solution $u(t,x)$ with initial value $u(0,x) \equiv 0$ outside a finite ball $|x| \le R$ satisfies

$$\lim_{t\to\infty, |x|\ge(c^*+\epsilon)t} u(t,x) = 0,$$

where $\epsilon > 0$ is an arbitrarily small number.

Now we investigate the existence of traveling wave solutions of (3.3). Let's assume that (3.3) has a traveling wave solution $w(t,x) = q(x - ct)$, then $q(\xi)$ satisfies

$$Dq'' + cq' + g(q) = 0, \tag{3.4}$$

where

$$q' = \frac{dq}{d\xi}.$$

We investigate the existence of two types of traveling wave solutions. That is, the existence of pulse wave solutions and the existence of wave fronts. To study the existence of pulse wave solutions, we require that $q(-\infty) = q(\infty) = 0$ and $q(\xi) > 0$. This implies there is a pulse wave of infections which propagates into the uninfected population. By linearizing (3.4) near $q = 0$, we have

$$Dq'' + cq' + \frac{\alpha\beta - \mu(\eta+\delta)}{\mu} q \approx 0, \tag{3.5}$$

Thus,

$$q(\xi) \approx e^{\frac{-c \pm \sqrt{c^2 - 4D[\alpha\beta - \mu(\eta+\delta)]/\mu}}{2D}}.$$

Since we require $q(\xi) \to 0$ as $\xi \to \pm\infty$ with $q(\xi) > 0$, this solution cannot oscillate about $q = 0$. Otherwise, $q(\xi) < 0$ for some ξ. So, if a pulse wave solution exists, the wave speed c must satisfy

$$c \ge c^* = 2\sqrt{D[\alpha\beta - \mu(\eta+\delta)]/\mu}.$$

Thus, if $\alpha\beta - \mu(\eta+\delta) < 0$, there is no pulse wave solution. A pulse wave solution can exist only if $\alpha\beta - \mu(\eta+\delta) > 0$. But we know that this is the condition for the endemic equilibrium to exist. Thus, we know that a pulse wave solution can exist only when u_e exists. We also see that the minimum wave speed is the spreading speed and it depends on D. The bigger D is , the bigger the wave speed. This implies that the movement of human will speed up the spread of the infection.

Now we investigate the existence of wave fronts. To do this we require that $q(-\infty) = 1$ and $q(+\infty) = 0$ and $q(\xi)$ is monotonic decreasing. Due to the specific form of $g(w)$ which satisfies the conditions of [36, Theorem 2.2.13], we have the following theorem.

Theorem 3.2. *There exists a minimal wave speed c^*:*

$$c^* = 2\sqrt{\frac{D[\alpha\beta - \mu(\eta+\delta)]}{\mu}}$$

such that the sufficient and necessary condition for (3.3) *to have a wave front $w = q(x-ct)$ satisfying*

$$q(-\infty) = 1,\ q(+\infty) = 0$$

is $c \geq c^*$.

Again we see that if $\alpha\beta - \mu(\eta+\delta) < 0$, there is no wave front. Same as before, we know that only when the endemic equilibrium u_e exists that a wave front solution can exist. We also see that the minimum wave speed is the spreading speed and depends on D. The bigger D is, the bigger the wave speed is. This implies that the movement of human will speed up the spread of the infection.

4. The full model

In this section, we will investigate the full model described by the system (2.1). In terms of α and β, (2.1) can be written as

$$\begin{aligned} \frac{\partial u}{\partial t} &= Du_{xx} + f_1(u,v), \quad x \in \mathbb{R},\ t > 0, \\ \frac{\partial v}{\partial t} &= dv_{xx} + f_2(u,v) \quad x \in \mathbb{R},\ t > 0, \\ u(x,0) = u_0(x), &\quad v(x,0) = v_0(x), \quad x \in \mathbb{R}, \end{aligned} \tag{4.1}$$

where

$$f_1(u,v) = \alpha v(1-u) - (\eta+\delta)u,\ f_2(u,v) = \beta u(1-v) - \mu v.$$

We first study the spatial-independent steady states of the system. By solving

$$\begin{aligned} \alpha v(1-u) - (\eta+\delta)u = 0, \\ \beta u(1-v) - \mu v = 0, \end{aligned} \tag{4.2}$$

we found two equilibria: disease-free equilibrium: $E_0 = (u_0, v_0) = (0,0)$ and endemic equilibrium $E_e = (u_e, v_e)$, where

$$u_e = \frac{\alpha\beta - \mu(\eta+\delta)}{\beta(\alpha+\eta+\delta)}, \quad v_e = \frac{\alpha\beta - \mu(\eta+\delta)}{\alpha(\beta+\mu)},$$

which exists when $\alpha\beta - \mu(\eta+\delta) > 0$, i.e. $R_0 > 1$.

4.1. **Stability as the steady states of corresponding spatially-independent model.** To investigate the stability of E_0 and E_e as the steady states of corresponding spatially-independent model, we let $\mathbf{F}(u,v) = (f_1(u,v), f_2(u,v))^T$. Then by direct computations we found that the Jacobian matrix of (4.1) at E_0 is

$$J_0 = \mathbf{DF}(E_0) = \begin{bmatrix} -(\eta+\delta) & \alpha \\ \beta & -\mu \end{bmatrix}.$$

Its trace, $\mathrm{Tr}(J_0)$, and determinant, $\det(J_0)$, are

$$\mathrm{Tr}(J_0) = -(\mu+\eta+\delta) < 0,$$
$$\det(J_0) = \mu(\eta+\delta) - \alpha\beta.$$

Thus, $\det(J_0) < 0$ if $R_0 > 1$ and $\det(J_0) > 0$ if $R_0 < 1$. Therefore, if $R_0 < 1$, there is no endemic equilibrium and the disease-free equilibrium is locally asymptotically stable. If $R_0 > 1$, the endemic equilibrium E_e exists and the disease-free equilibrium is unstable (see [2]). The Jacobian matrix of (4.1) at E_e is

$$J_e = \mathbf{DF}(E_e) = \begin{bmatrix} -\frac{\beta(\alpha+\eta+\delta)}{\beta+\mu} & \frac{\alpha(\eta+\delta)(\beta+\mu)}{\beta(\alpha+\eta+\delta)} \\ \frac{\beta\mu(\alpha+\eta+\delta)}{\alpha(\beta+\mu)} & -\frac{\alpha(\beta+\mu)}{\alpha+\eta+\delta} \end{bmatrix}.$$

Its trace, $\mathrm{Tr}(J_e)$, and determinant, $\det(J_e)$, are

$$\mathrm{Tr}(J_e) = -\frac{\alpha(\beta+\mu)^2 + \beta(\alpha+\eta+\delta)^2}{(\alpha+\eta+\delta)(\beta+\mu)} < 0,$$
$$\det(J_e) = \alpha\beta - \mu(\eta+\delta) > 0.$$

Therefore, E_e is locally asymptotically stable. In fact, we claim that

> If $R_0 > 1$, the distributions of human and mosquito populations are spatially uniform (hence, (2.1) is reduced to a spatially-independent model), and $u(0) + v(0) > 0$, then the endemic equilibrium E_e, as a steady state of the corresponding spatially-independent model, is globally stable in the first quadrant.

Indeed, it is easily seen that

$$\frac{\partial f_1}{\partial u} + \frac{\partial f_2}{\partial v} = -\alpha v - \beta u - (\mu+\eta+\delta) < 0,$$

for $u, v > 0$. Thus, by Bendixson's Criterion, there is no periodic solutions in the first quadrant. We also know that $0 \le u \le 1$ and $0 \le v \le 1$. Therefore, the Poincaré-Bendixson theorem implies the global stability of E_e in the first quadrant.

4.2. **Stability as the steady states of** (4.1)**.** Next we will prove that the endemic equilibrium E_e is a global attractor of (4.1) in the first quadrant by constructing a family of contracting rectangles in the first quadrant. For the convenience of explanations, we write the first equation in (4.2) as

$$u = \frac{\alpha v}{\alpha v + \eta + \delta}$$

and denote the curve in the $u - v$ plane as C_1 and write the second equation in (4.2) as

$$v = \frac{\beta u}{\beta u + \mu}$$

and denote the curve in the $u-v$ plane as C_2. Then $E_e=(u_e,v_e)$ is the unique intersection point of C_1 and C_2 in the first quadrant. Now we use [28, Definition 14.18] to construct a family of contracting rectangles

$$\Sigma_k=\{(u,v)|\ 0<a_k\le u\le b_k, 0<c_k\le v\le d_k\}$$

as follows: the line segment $u=a_k, c_k\le v\le d_k$ is always to the left of C_1; the line segment $u=b_k, c_k\le v\le d_k$ is always to the right of C_1; the line segment $v=c_k, a_k\le u\le b_k$ is always below C_2; the line segment $v=d_k, a_k\le u\le b_k$ is always above C_2, and as $k\to\infty$, the rectangles contract to E_e. Then we claim that

> For any point $p=(u,v)\in\partial\Sigma_k$, $\mathbf{F}(p)\cdot\mathbf{n}(p)<0$, where $\partial\Sigma_k$ is the boundary of Σ_k, $\mathbf{n}(p)$ is the outward pointing normal at p and $\mathbf{F}(p)=(f_1(p),f_2(p))^T$.

Indeed, on $u=a_k, c_k\le v\le d_k$, $\mathbf{n}(p)=(-1,0)^T$, $u<\frac{\alpha v}{\alpha v+\eta+\delta}$. Therefore,

$$mathbfF(p)\cdot\mathbf{n}(p)=(\alpha v+\eta+\delta)u-\alpha v<(\alpha v+\eta+\delta)\cdot\frac{\alpha v}{\alpha v+\eta+\delta}-\alpha v=0.$$

On $u=b_k, c_k\le v\le d_k$, $\mathbf{n}(p)=(1,0)^T$, $u>\frac{\alpha v}{\alpha v+\eta+\delta}$. Therefore,

$$\mathbf{F}(p)\cdot\mathbf{n}(p)=\alpha v-(\alpha v+\eta+\delta)u<\alpha v-(\alpha v+\eta+\delta)\cdot\frac{\alpha v}{\alpha v+\eta+\delta}=0.$$

On $v=c_k, a_k\le u\le b_k$, $\mathbf{n}(p)=(0,-1)^T$, $v<\frac{\beta u}{\beta u+\mu}$. Therefore,

$$\mathbf{F}(p)\cdot\mathbf{n}(p)=(\beta u+\mu)v-\beta u<(\beta u+\mu)\cdot\frac{\beta u}{\beta u+\mu}-\beta u=0.$$

On $v=d_k, a_k\le u\le b_k$, $\mathbf{n}(p)=(0,1)^T$, $v>\frac{\beta u}{\beta u+\mu}$. Therefore,

$$\mathbf{F}(p)\cdot\mathbf{n}(p)=\beta u-(\beta u+\mu)v<\beta u-(\beta u+\mu)\cdot\frac{\beta u}{\beta u+\mu}=0.$$

Thus we know that Σ_k is a family of contracting rectangles contracting to E_e and E_e is a global attractor of (4.1) in the first quadrant.

4.3. **Existence of travelling wave solutions.** Next we will investigate the existence of traveling wave solutions. As usual, a traveling wave solution of (4.1) is a solution of the form $(u(t,x),v(t,x))=(u(\xi),v(\xi))$ with $\xi=x-ct$. c is called the wave speed. We are looking for a traveling wave solution connecting the endemic equilibrium and the disease-free equilibrium. That is, $(u(\xi),v(\xi))$ satisfies

$$\lim_{\xi\to-\infty}(u(\xi),v(\xi))=(u_e,v_e),\quad \lim_{\xi\to\infty}(u(\xi),v(\xi))=(0,0).$$

By substituting $(u(\xi),v(\xi))$ in (4.1), we have

$$Du''+cu'+\alpha v(1-u)-(\eta+\delta)u=0,$$
$$dv''+cv'+\beta u(1-v)-\mu v=0.$$

To prove the existence of traveling wave solutions, as in [15], we use [16, Theorem 4.2]. To do so, we need to verify the five conditions in this theorem. First we have

$$\mathbf{F}(E_0)=0,\quad \text{and}\quad \mathbf{F}(E_e)=0.$$

It is easily seen that system given by (4.1) is cooperative in the sense that $f_1(u,v)$ is non-decreasing with respect to v and $f_2(u,v)$ is non-decreasing with respect to u.

It is also true that $\mathbf{F}$ does not depend explicitly on x and t and the diffusion coefficient matrix is a constant diagonal matrix.

$\mathbf{F}(p)$ is continuous and has uniformly bounded piecewise continuous first partial derivatives for $p = (u, v)$ satisfying $0 \le u \le u_e, 0 \le v \le v_e$, and it is differentiable at E_0. The off-diagonal entries of J_0 are nonnegative. When $\alpha\beta - \mu(\eta + \delta) > 0$, J_0 has a positive eigenvalue given by

$$\lambda_1 = \frac{-(\mu + \eta + \delta) + \sqrt{(\mu + \eta + \delta)^2 + 4[\alpha\beta - \mu(\eta + \delta)]}}{2}.$$

The eigenvector corresponding to λ_1 is

$$\mathbf{V}_1 = \begin{bmatrix} \mu - (\eta + \delta) + \sqrt{[\mu - (\eta + \delta)]^2 + 4\alpha\beta} \\ 2\beta \end{bmatrix},$$

which has positive components.

Finally, all the diagonal entries of the diffusion coefficient matrix are positive. Therefore, when $\alpha\beta - \mu(\eta + \delta) > 0$, by [16, Theorem 4.2], there is a minimum wave speed c^* such that for every $c \ge c^*$, system (4.1) has a traveling wave solution $(u(x - ct), v(x - ct))$ which is non-increasing in x and for which $(u(-\infty), v(-\infty)) = E_e$ and $(u(+\infty), v(+\infty)) = E_0$. Thus, as before, we know that only when the endemic equilibrium E_e exists that a travelling wave solution can exist.

4.4. **Analysis of spreading speed.** Next we will investigate the relationship between the minimum wave speed and the spreading speed. It turns out this is much more complicated than the single equation case. To do so, we first need to define spreading speed in the case of a system of equations.

As in [15], we give the following reaction-diffusion system version of the definition of spreading speed introduced in [31].

Definition 4.1. The spreading speed of (4.1) is defined as the positive number c^* with the properties that for any initial functions $(u_0(x), v_0(x))$ which lies between E_0 and E_e and which coincides with E_0 outside a bounded set, the corresponding solution $(u(t, x), v(t, x))$ of (4.1) has the properties that for each positive $\epsilon > 0$

$$\lim_{t\to\infty} \{ \sup_{|x|\ge(c^*+\epsilon)t} \|(u(t, x), v(t, x))\| \} = 0$$

and for any strictly positive constant vector $\mathbf{w} = (\omega_1, \omega_2)$ there is a positive $R_{\mathbf{w}}$ with the property that if $u_0(x) \ge \omega_1 > 0, v_0(x) \ge \omega_2 > 0$ on an interval of length $2R_{\mathbf{w}}$, then the corresponding solution $(u(t, x), v(t, x))$ of (4.1) satisfies

$$\lim_{t\to\infty} \big\{ \sup_{|x|\le(c^*-\epsilon)t} \|(u(t, x) - u_e, v(t, x) - v_e)\| \big\} = 0.$$

From [16, Theorem 4.2] we know that the aforementioned minimum wave speed c^* is the unique spreading speed of (4.1). To analyze the spreading speed c^*, we need to introduce the concept of *linearly determinacy* (see [31, 15])

Definition 4.2. The spreading speed $\bar{c}$ of the linearized system of (4.1) at E_0

$$\begin{aligned} \frac{\partial u}{\partial t} &= Du_{xx} - (\eta + \delta)u + \alpha v, \quad x \in \mathbb{R},\ t > 0, \\ \frac{\partial v}{\partial t} &= dv_{xx} + \beta u - \mu v \quad x \in \mathbb{R},\ t > 0, \\ u(x, 0) &= u_0(x), \quad v(x, 0) = v_0(x), \quad x \in \mathbb{R}, \end{aligned}$$

is defined as the positive number $\bar{c}$ with the properties that for any $\epsilon > 0$,

$$\lim_{t\to\infty} \Big\{ \sup_{|x|\geq(\bar{c}+\epsilon)t} \|(u(t,x), v(t,x))\| \Big\} = 0,$$
$$\lim_{t\to\infty} \Big\{ \sup_{|x|\leq(\bar{c}-\epsilon)t} \|(u(t,x), v(t,x))\| \Big\} > 0.$$

When $c^* = \bar{c}$, the spreading speed of (4.1) is said to be linearly determined.

We claim that the spreading speed of (4.1) is linearly determined. To prove this, we need to verify the conditions in [31, Theorem 4.2]. Indeed, since the five conditions [16, Theorem 4.2] imply the [31, Hypotheses 4.1] and we have verified these conditions, all we need to verify now is the following subtangential condition

$$\mathbf{F}\left(\rho \begin{bmatrix} u \\ v \end{bmatrix}\right) \leq \rho \mathbf{DF}(E_0) \begin{bmatrix} u \\ v \end{bmatrix}. \tag{4.3}$$

holds for all positive ρ. An easy calculation shows that (4.3) is true. Thus, $c^* = \bar{c}$. Therefore, to calculate c^*, we only need to find $\bar{c}$. $\bar{c}$ is given by (see [31], [15])

$$\bar{c} = \inf_{\xi>0} \lambda_1(\xi)$$

where $\lambda_1(\xi)$ is the largest eigenvalue of

$$\mathbf{A}(\xi) = \begin{bmatrix} \xi D - \frac{\eta+\delta}{\xi} & \frac{\alpha}{\xi} \\ \frac{\beta}{\xi} & \xi d - \frac{\mu}{\xi} \end{bmatrix}.$$

The two eigenvalues of $\mathbf{A}(\xi)$ are the solutions of quadratic equation

$$\lambda^2 + p\lambda + k = 0, \tag{4.4}$$

where

$$p = \frac{\mu+\eta+\delta}{\xi} - \xi(d+D),$$
$$k = \frac{\mu(\eta+\delta)-\alpha\beta}{\xi^2} + \xi^2 Dd - \mu D - d(\eta+\delta).$$

A direct computations gives

$$\lambda_1(\xi) = \frac{-p+\sqrt{Q}}{2},$$

where

$$Q = \frac{4\alpha\beta}{\xi^2} + (\frac{\mu-\eta-\delta}{\xi} + \xi(D-d))^2.$$

It turns out that it is very difficult to find the infimum of $\lambda_1(\xi)$. Our main interest is to investigate the dependence of the spreading speed on the diffusion rates using some specific values of other parameters. To determine the values of the related parameters, a lot of clinic research has been done. Due to the variety of populations, regions, treatments, it seems many different specific values are possible as long as they stay in a reasonable range. Here we take the parameter values from different sources as cited. We take $d = 8.838 \times 10^{-3}$ (km^2/day, [1]), $a = 0.2$ (day^{-1}, [20]), $b = 0.5$ ([1]), $r = 0.5$ ([27]), $m = 2$ ([27]), $\eta = 0.05$ (day^{-1}, [27]), $\delta = 0.05$ (day^{-1}, [1]), $\mu = 0.1$ (day^{-1}, [27]). Thus $\alpha = 0.2$, $\beta = 0.1$. We assume that $D = Kd$ with K a positive number. Then

$$p = \frac{0.2}{\xi} - (1+K)d\xi,$$

TABLE 1. K, Critical Point, and Spreading Speed

K	1	5	10	20	50	100
ξ_0	2.16489	1.15804	0.831208	0.59164	0.375562	0.265875
$\bar{c}$	0.0382665	0.0681764	0.0934187	0.130022	0.203613	0.287027

$$Q = \frac{0.08}{\xi^2} + 7.811 \times 10^{-5}(K-1)^2\xi^2,$$

$$\lambda_1(\xi) = 4.419 \times 10^{-3}(1+K)\xi - \frac{0.1}{\xi} + \frac{0.5}{\xi}\sqrt{0.08 + 7.811 \times 10^{-5}(K-1)^2\xi^4}.$$

It is easily seen that

$$\lim_{\xi\to 0} \lambda_1(\xi) = \lim_{\xi\to\infty} \lambda_1(\xi) = \infty.$$

With the help of Mathematica, we can see that for any positive K, $\lambda_1(\xi)$ has a unique positive critical point ξ_0. We take $K = 1, 5, 10, 20, 50, 100$ and list the corresponding positive critical points and the minimum values of $\lambda_1(\xi)$. That is, $\bar{c}$, in Table 1.

From Table 1 we can see that, the critical point is a decreasing function of K and the spreading speed is an increasing function of K. Therefore, we know that the larger the diffusive coefficient of human is, the faster the disease spread. That is, the movement of human will speed up the spread of the disease.

5. Numerical simulations

In this section, we will perform some numerical simulations to support some of our theoretical results. To do so, first, we take the parameters as we did in the last section. That is, we take $d = 8.838 \times 10^{-3}$ (km^2/day, [1]), $a = 0.2$ (day^{-1}, [20]), $b = 0.5$ ([1]), $r = 0.5$ ([27]), $m = 2$ ([27]), $\eta = 0.05$ (day^{-1}, [27]), $\delta = 0.05$ (day^{-1}, [1]), $\mu = 0.1$ (day^{-1}, [27]). Thus $\alpha = 0.2$, $\beta = 0.1$(day^{-1}, [27]). For these values,

$$\alpha\beta - \mu(\eta + \delta) = 0.01 > 0.$$

Therefore, the endemic equilibrium $E_e = (u_e, v_e)$ exists with

$$u_e = \frac{1}{3},\ v_e = \frac{1}{4}.$$

Our results imply that, as a steady state of the corresponding spatially-independent model, E_e is globally stable in the first quadrant. Figure 1 below is the graph of the numerical solution with $u(0) = 0.35$ and $v(0) = 0.05$. From the graph we can see that as $t \to \infty$, $(u(t), v(t)) \to (\frac{1}{3}, \frac{1}{4}) = (u_e, v_e)$. In fact, when we choose different initial values, we have the same scenario. That is, $E_e = (u_e, v_e)$ is globally stable.

Next we adjust the parameters. Recall that the meaning of b and r are mosquito-to-human and human-to-mosquito transmission efficiency, respectively. Small values of b or r leads to small values of α or β. Without loss of generality, we assume that α is decreased from 0.2 to 0.05 so that

$$\alpha\beta - \mu(\eta + \delta) = -0.05 < 0.$$

Thus the disease-free equilibrium $E_0 = (u_0, v_0) = (0, 0)$ is the only steady state and our result shows that it is locally stable. Now we choose $u(0) = 0.15$ and $v(0) = 0.05$ to find the numerical solution. Figure 2(a) below is the graph of the solution. We can see that, as $t \to \infty$, $(u(t), v(t)) \to (0, 0) = (u_0, v_0)$.

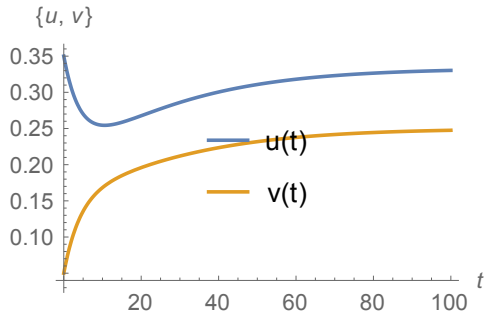
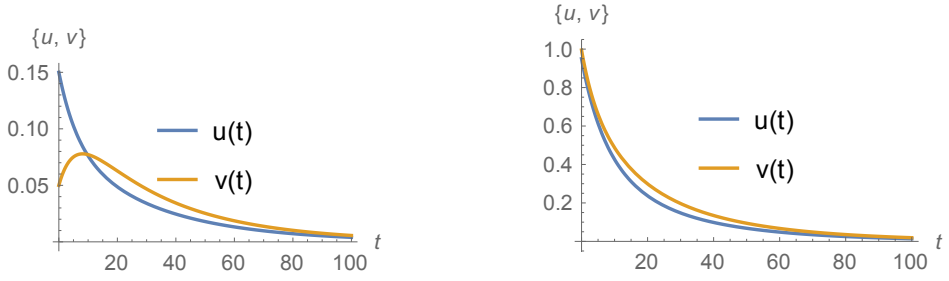


FIGURE 1. The graphs of of $u(t)$ and $v(t)$ with $\alpha = 0.2$.



(a) $u(0) = 0.15$, $v(0) = 0.05$ (b) $u(0) = 0.95$, $v(0) = 0.995$

FIGURE 2. The graphs of of $u(t)$ and $v(t)$ with $\alpha = 0.05$

In fact, our numerical results show that E_0 is globally stable since the choice of $u(0) = 0.95$ and $v(0) = 0.995$, as seen in Figure 2(b), tells us that, as $t \to \infty$, $(u(t), v(t)) \to (0, 0) = (u_0, v_0)$.

Next we consider the full model (4.1). We will use the same parameter values as in the previous section, then we have that

$$f_1(u, v) = 0.2v(1 - u) - 0.1u, \ f_2(u, v) = 0.1u(1 - v) - 0.1v.$$

For these values of parameters, since $\alpha\beta - \mu(\eta + \delta) = 0.01 > 0$, our results showed that E_e is a global attractor. As an example, we take $D = 100d = 0.8838$. Although we are considering the initial value problem, to do simulations, we need to restrict ourselves to a finite but large interval, say, $x \in [-100, 100]$. It is reasonable to assume that, at the end points of this interval, u and v satisfy

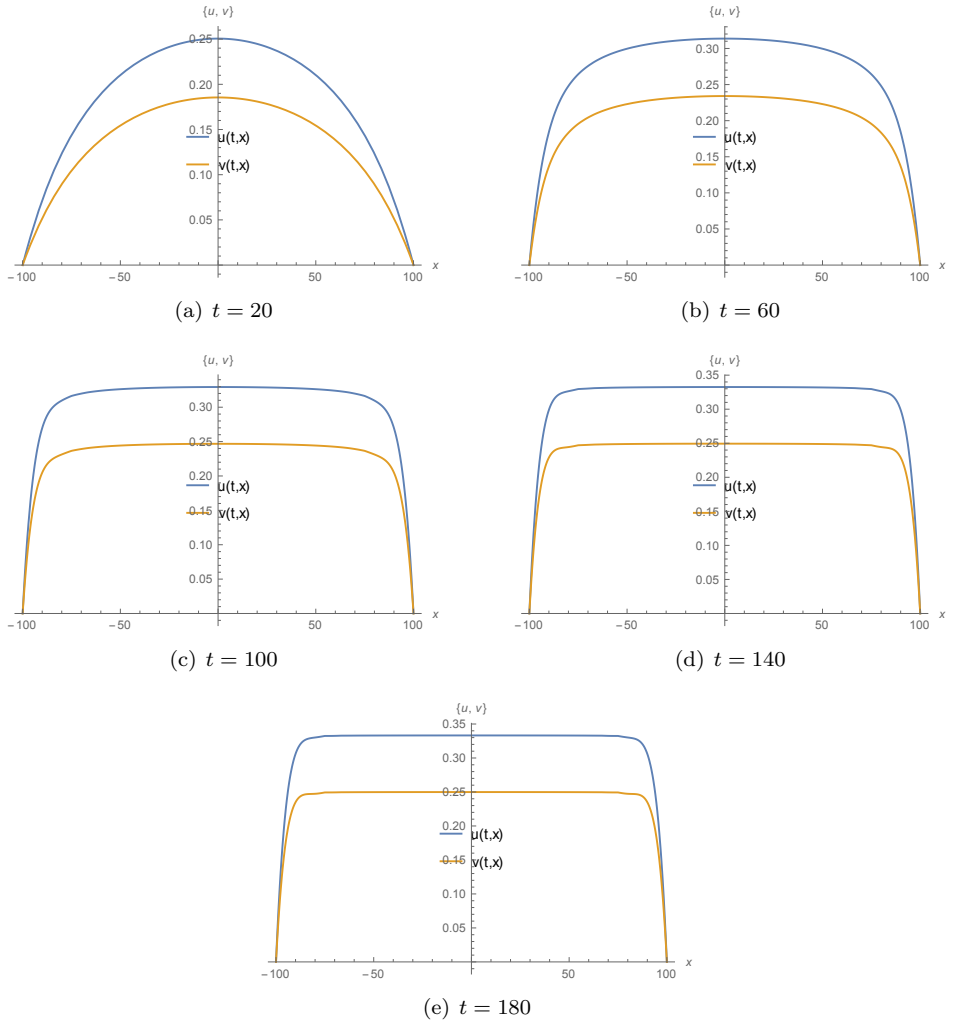
$$u(t, -100) = u(t, 100) = v(t, -100) = v(t, 100) = 0.$$

For initial conditions, in order to be consistent with the homogeneous boundary conditions, we take

$$u(0, x) = -0.00001x^2 + 0.1, \ v(0, x) = -0.00002x^2 + 0.2.$$

To see what happens as $t \to \infty$, we will take snapshots of $u(t, x)$ and $v(t, x)$ with $t = 20, 60, 100, 140, 180$ as shown in Figure 3. From the graphs we see that, as t

becomes larger and larger, $(u(t,x), v(t,x))$ tends closer and closer to $E_e = (\frac{1}{3}, \frac{1}{4})$. This implies that E_e is a global attractor.



(a) $t = 20$ (b) $t = 60$

(c) $t = 100$ (d) $t = 140$

(e) $t = 180$

FIGURE 3. The graphs of of $u(t,x)$ and $v(t,x)$ with $\alpha = 0.2$

Conclusion. From our mathematical analysis of a model of malaria transmission, we see that when the basic reproduction number is less than one, the disease-free equilibrium is the only equilibrium and it is locally asymptotically stable and if the reproduction number is greater than one, the disease-free equilibrium becomes unstable and an endemic equilibrium emerges and it is asymptotically stable. We also proved that, when the reproduction number is greater than one, there is a minimum wave speed c^* such that for every $c \geq c^*$, there exists a travelling wave solution with wave speed c and the minimum wave speed is also the spreading speed of the disease. We also investigated the relationship between spreading speed and

diffusion coefficients. Our results show that when the infected mosquito population equilibrates much faster than the human population, the spreading speed of the disease is proportional to the square root of the human diffusive coefficient. In general situation, we only know that the movements of mosquito population and human population will speed up the spread of the disease. Therefore, when malaria breaks out in some regions, it is necessary to limit the movement of human being to keep the spread of the disease under control. The exact relationship between the spreading speed and the diffusion coefficients need to be further investigated.

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Zhenbu Zhang
Department of Mathematics and Statistical Sciences, Jackson State University, Jackson, MS 39217, USA
E-mail address: zhenbu.zhang@jsums.edu

Tor A. Kwembe
Department of Mathematics and Statistical Sciences, Jackson State University, Jackson, MS 39217, USA
E-mail address: tor.a.kwembe@jsums.edu