A Two-dimensional Model for the Transmission of Dengue Fever Disease*

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A transmission model for dengue fever is discussed here. Restricting the dynamics for the constant host and vector populations, the model is reduced to a two-dimensional planar equation. In this model the endemic state is stable if the basic reproductive number of the disease is greater than one. A trapping region containing the heteroclinic orbit connecting the origin (as a saddle point) and the endemic fixed point occurs. By the use of the heteroclinic orbit, we estimate the time needed for an initial condition to reach a certain number of infectives. This estimate is shown to agree with the numerical results computed directly from the dynamics of the populations.

1. Introduction

Dengue fever is regarded as a serious infectious disease that risks about 2.5 billion people all over the world, especially in the tropical countries [2]. Mortality rate of this infectious disease may reach 40 % if the infected person is left untreated [3]. Although almost all of the occurrences of the dengue are in the tropical countries, a recent study shows that the dengue may occur in cooler countries due to the global warming effects [4]. The climate change may convert a region from an unsuitable habitat for *Aedes aegypti* mosquitoes to live to a new suitable habitat; the *Aedes* are the responsible vector in transmitting the disease.

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To control the dengue effectively, we should understand the dynamics of the disease transmission and take into account all of the relevant details, such as the dynamics of the vector. Recently Esteva and Vargas [1] developed a model for the dengue disease transmission and included the dynamics of the *Aedes aegypti* mosquitoes into a standard SIR (susceptible-infective-recover) epidemic model of a single population. Their model shows that there is a threshold value *R* which is a function of *Aedes* equilibrium population size and of the *Aedes* recruitment rate, above which the disease will be endemic and below which the disease will vanish.

In developing their model, Esteva and Vargas assume that once a person recover from the disease he or she will not re-infected by the disease. We show in this paper that, in their model, if the *Aedes* recruitment rate is very large then only a small proportion of the population becomes infected. This situation is not alarming and may not have a good psychological effect on the management of the disease, that is, it may not persuade a health manager to take a quick response in controlling the disease. In this paper we remove the immunity assumption and predict the time needed by an initial number of infected population to multiply. The result can alert us because for a large *Aedes* recruitment rate, the time to multiply (e.g. ten times) is very short. In the next section we review the model of Esteva and Vargas in more detail.

2. Host-Vector Model for a Dengue Transmission

We review the Host-Vector model of Esteva-Vargas [1] for the transmission of dengue fever as follows. The model is based on the assumption that the host population N_H is constant, i.e. the death rate and birth rate are equal to μ_H. The vector population N_V, which is in general very difficult to estimate, is governed by a monotonic model

$$N_V^{'} = A - \mu_V N_V. \tag{1}$$

Here μ_N is the mortality rate of the vector, and *A* is the recruitment rate. This mosquito model can be explained from the fact that only a small portion of a large supply of eggs survive to the adult stage [6]. Hence, *A* is independent from the adult population. The dynamics of the vector approaches to the equilibria A/μ_V as $t \to \infty$.

In the Esteva-Vargas model [1] the majority of the host population eventually becomes immune. The host population is subdivided into the susceptible S_H, the infective I_H and the recovered, assumed immune, R_H. The vector population, due to a short life period, is subdivided into the susceptible S_V and the infective I_V.

The interaction model for the dengue transmission [1] is given as follows

$$\begin{aligned}
\frac{d}{dt}S_H &= \mu_H N_H - \frac{\beta_H b}{N_H} S_H I_V - \mu_H S_H \\
\frac{d}{dt}I_H &= \frac{\beta_H b}{N_H} S_H I_V - (\mu_H + \gamma_H) I_H \\
\frac{d}{dt}R_H &= \gamma_H I_H - \mu_H R_H \\
\frac{d}{dt}S_V &= A - \frac{\beta_V b}{N_H} S_V I_H - \mu_V S_V \\
\frac{d}{dt}I_V &= \frac{\beta_V b}{N_H} S_V I_H - \mu_V I_V
\end{aligned} \tag{2}$$

where

N_H = *the host population*
S_H = *the number of suspectibles in the host population*
I_H = *the number of infectives in the host population*
R_H = *the number of immunes in the host population*
N_V = *the vector population*
S_V = *the number of suspectibles in the vector population*
I_V = *the number of infectives in the vector population*
μ_H = *the birth/death rate in the host population*
μ_V = *the death rate in the vector population*
β_H = *the transmission probability from vector to host*
β_V = *the transmission probability from host to vector*
γ_H = *the recovery rate in the host population*
b = *the biting rate of vector.*

Note that we remove the alternative blood resource from [1] due to the fact that practically there is no other blood resource other than human in urban areas.

Further reduction of (2) to a three-dimensional dynamics is obtained from a restriction to an invariant subset defined by

$$S_H + I_H + R_H = N_H \text{ and } S_V + I_V = \frac{A}{\mu_V}. \tag{3}$$

The resulting dynamics, expressed in proportions $x = \frac{S_H}{N_H}, y = \frac{I_H}{N_H}, z = \frac{I_V}{A/\mu_V}$, is given by

$$\begin{aligned} \frac{d}{dt}x &= \mu_H(1-x) - \alpha\, x\, z \\ \frac{d}{dt}y &= \alpha\, x\, z - \beta\, y \\ \frac{d}{dt}z &= \gamma(1-z)y - \delta\, z \end{aligned} \tag{4}$$

where $\alpha = \frac{b\beta_H A}{\mu_V N_H}$, $\beta = \gamma_H + \mu_H, \gamma = b\beta_V, \delta = \mu_V$. Two possible fixed points of the system are

$$F_1 = (1,0,0) \text{ and } F_2 = (x_0, y_0, z_0), \tag{5}$$

where $x_0 = \frac{\mu_H\gamma + \beta\delta}{\gamma(\mu_H + \alpha)}, y_0 = \frac{\mu_H(\alpha\gamma - \beta\delta)}{\beta\gamma(\mu_H + \alpha)}$ and $z_0 = \frac{\mu_H(\alpha\gamma - \beta\delta)}{\alpha(\mu_H\gamma + \beta\delta)}$.

Note that the second fixed point exists in the region of biological interest, i.e. $0 < x, y, z < 1$, only if the threshold parameter $R = \frac{\alpha\gamma}{\delta\beta} > 1$. The number $R_0 = \sqrt{R}$ represents the *basic reproductive number*. The following theorem has been proven in [1].

Theorem 1 *If* $R \le 1$, *the fixed point* F_1 *is globally asymptotically stable in the region of interest* $\Omega = \{(x, y, z) : 0 < x, y, z < 1\}$ *and if* $R > 1$, F_1 *is unstable and the endemic fixed point* F_2 *is globally asymptotically stable in the interior of* Ω.

Global stability of F_1 for $R<1$ is shown in [1] using Lyapunov-like function $\frac{\alpha}{\delta}z+y$ satisfying

$$\frac{d}{dt}\left(\frac{\alpha}{\delta}z+y\right)=\left(\frac{\alpha\gamma}{\delta\beta}-1\right)\beta y-\frac{\alpha\gamma}{\delta}yz-\alpha z(1-x)<0$$

if $R<1$. On the other hand, if $R>1$ the fixed point F_1 becomes locally unstable and F_2 becomes locally asymptotically stable. The global stability is shown in [1] by use of the property of stability of periodic orbits.

Note that α is the only parameter in (4) containing *A*. Study [4] has indicated that the mosquito population (and therefore the recruitment number *A*) may change from time to time due to climate change. Although there is a report indicated that the biting behavior of the mosquito has gradually changed and *b* is thought to vary with climate, we assume that during a long period of observation, the biting rate *b* and the rest of the parameters remain constant.

Regarding the control strategy for the epidemic, it is always the interest of everyone to lower the basic reproductive number R_0 as small as possible (or equivalently to lower the recruitment number *A* as small as possible). Various applications of insecticides such as ULV have been used. Simulation of the application of ULV is shown in [1]. It shows that the delay of the abrupt change of μ_V due to ULV will give effect to the delay of the endemic stage but will only slightly reduce the severity. The strategy to lower R_0 seems unrealistic as indicated by the reappearance of the outbreak almost every year in the last 10 years. On the other hand, what is going to happen if *A* is so large? This can be seen by taking the limit as $A\to\infty$. In this case, the endemic state approaches the limit

$$F2\to\left(0,\frac{\mu_H}{\gamma_H+\mu_H},1\right). \qquad (6)$$

It shows that although all mosquitoes are infected, only a small proportion of the human population becomes infected, that is, $I_H\approx\frac{\mu_{\mathrm{H}}}{\gamma_H+\mu_{\mathrm{H}}}$, where $\mu_{\mathrm{H}}<<\gamma_H$. This may be true

since in this model the majority of the population eventually become immune (we will remove the immunity condition in Section 3).

We are interested to investigate what happens if few infectives $(I_H$ or $I_V)$ are introduced to the population. This illustrates, more or less, how the outbreak started. The following pictures show the dynamics of the S_H, I_H and I_V in 100 *days* after one infected human entered the population (all parameter values are taken from [1]).

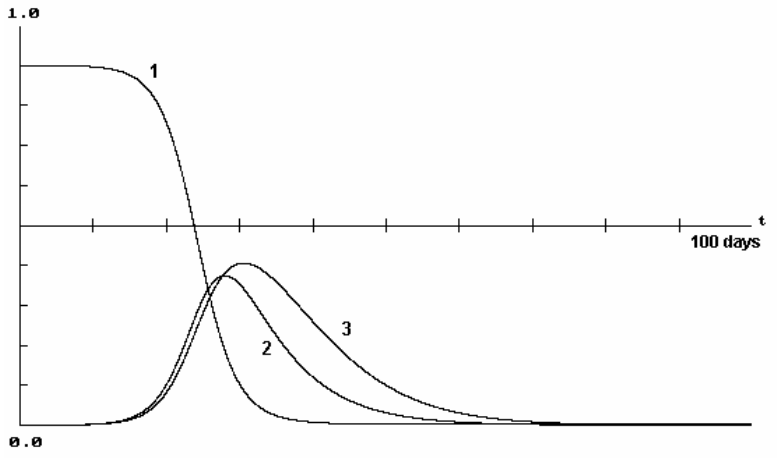

Figure 1: Dynamics of $S_H(1), I_H(2)$ and $I_V(3)$ in 100 days with the initial condition (0.9,0.0001,0) for $\mu_H = .0000457/day,\ \ \mu_V = .25/day,\ b = .5, \beta_H = .75,\ \beta_V = 1,$ $\gamma_H = .1428/day,\ N_H = 10{,}000$ and $A = 5{,}000$. With these parameters, $R = 3.24$.

Figure 1 shows that S_H drops significantly in a relatively small period of time. Both I_H and I_V increases significantly during the period of 30 days, and then eventually oscillate around the endemic state (0.09529,0.0.00029,0.00058). This seems unrealistic in the nature. With constant population of mosquitoes, this fluctuation (in a short period of time) can not be shown to happen in the nature. The sharp decrease of S_H and increase of R_H in the model (2) are due to the fact that $\mu_H R_H$ is relatively smaller than both $I_H I_V$ and $S_H I_V$ at least in the domain of observation where I_H in reality is relatively very small. The following simplified model gives a more realistic result.

3. Host-Vector Model without Immunity

Not enough information is known about the immunity after recovery. Reports indicate that recovery from a certain serotype virus is not immune from other serotype viruses (Dr. R. Agoes, MPH. Personal. Comm.). Assuming that immune subpopulation is negligible, then we have the dynamics

$$\begin{aligned}
\frac{d}{dt}S_H &= \mu_H N_H - \frac{\beta_H b}{N_H} S_H I_V - \mu_H S_H + \gamma_H I_H \\
\frac{d}{dt}I_H &= \frac{\beta_H b}{N_H} S_H I_V - (\mu_H \gamma_H) I_H \\
\frac{d}{dt}S_V &= A - \frac{\beta_V b}{N_H} S_V I_H - \mu_V S_V \\
\frac{d}{dt}I_V &= \frac{\beta_V b}{N_H} S_V I_H - \mu_V I_V .
\end{aligned} \tag{7}$$

Reducing the dynamics along invariant subsets $N_H = S_H + I_H$ and $\mathrm{S_V} + \mathrm{I_V} = \frac{\mathrm{A}}{\mu_V}$, and using the same notation for the proportion variables *x* and *y* as before, we have

$$\begin{aligned}
\frac{d}{dt}y &= \alpha(1-y)z - \beta y \\
\frac{d}{dt}\mathrm{z} &= \gamma(1-\mathrm{z})\mathrm{y} - \delta\,\mathrm{z} .
\end{aligned} \tag{8}$$

3.1 Stability of the endemic state

The corresponding characteristic equation of the fixed point (0,0) is

$$\lambda^2 + (\beta + \delta)\lambda - \alpha\gamma + \beta\delta = 0. \tag{9}$$

The origin remains locally stable if $\alpha\gamma - \beta\delta \le 0$. The same Lyapunov-like function $L = \frac{\alpha}{\delta} z + y$ can be used to show that the origin is globally stable. When $\alpha\gamma - \beta\delta > 0$ (this is equivalent to $R > 1$), the origin becomes unstable and the second fixed point (y_0, z_0), where $y_0 = \frac{\alpha\gamma - \beta\delta}{\gamma(\alpha+\beta)}$ and $z_0 = \frac{\alpha\gamma - \beta\delta}{\alpha(\gamma+\delta)}$, appears. The characteristic equation for the second fixed point is

$$\lambda^2 + a_0\lambda + \alpha\gamma - \beta\delta = 0 \tag{10}$$

where $a_0 = \frac{\alpha(\delta+\gamma)^2+\gamma(\alpha+\beta)^2}{(\gamma+\delta)(\alpha+\beta)}$. Both eigenvalues of (10) have negative real parts if R>1. Hence the second fixed point is locally stable. Global stability can be easily shown by simple phase plane analysis with the direction of the vector fields of the system, as indicated by the following theorem.

Theorem 2 *Let* $\Omega = \left\{(y,z) \mid \frac{\beta y}{\alpha(1-y)} \le z \le \frac{\gamma y}{\gamma y+\delta}, 0 \le y \le y_0\right\}$. *If* $\alpha\gamma - \beta\delta > 0$, *then* Ω *is a trapping region and contains the heteroclinic orbit connecting* $(0,0)$ *and* (x_0, y_0).

Proof:

We write $\partial\Omega = \Gamma_1 \cup \Gamma_2$, where $\Gamma_1 = \left\{(y,z) \mid G_1(y,z) \equiv \alpha(1-y)z - \beta y = 0, 0 < y < y_0\right\}$ and $\Gamma_2 = \left\{(x,y) \mid G_2(x,y) \equiv \gamma(1-z)y - \delta z = 0,\ 0 < y < y_0\right\}$. Then along Γ_1 and Γ_2 we have $\frac{d}{dt}G_j > 0$, j = 1,2. This shows that any orbit crossing $\partial\Omega$ is trapped inside Ω since the gradient of G_j along $\partial\Omega$ is pointing inward. With the vector field inside Ω pointing away from the origin we have the unstable manifold of the fixed point (0,0) connecting the origin with the second fixed point. By rewriting Γ_1 and Γ_2 in the form

$$\Gamma_1 : z = \frac{z_0}{y_0} y + \frac{y(y-y_0)}{\alpha\gamma(1-y)(\gamma+\delta)(\alpha+\beta)}$$

and

$$\Gamma_2 : z = \frac{z_0}{y_0} y - \frac{\gamma y(y-y_0)}{\alpha\gamma(\gamma+\delta)(\gamma y+\delta)(\alpha+\beta)},$$

it can be seen that both Γ_1 and Γ_2 approach the line $z = \frac{z_0}{y_0} y$ as $y \to y_0$ (see Figure 2).

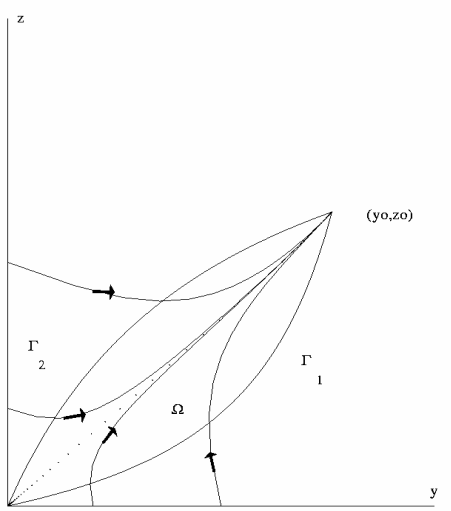

Figure 2: Trapping region Ω. The dotted curve is the heteroclinic orbit

Further we will answer the question *"how long it takes from a given initial condition (one infective) to reach a certain stage ?"*. In the neighborhood of (0,0), the orbits quickly enter Ω and then follow close to the unstable manifold (the heteroclinic orbit). Since the heteroclinic orbit is monotonic then it is reasonable to approximate this orbit by a line connecting (0,0) and (x_0,y_0). Let the initial condition be $(y_0,0)$, the estimate time T to reach the infective y_1 can be done by integrating (8) along the line $z = \frac{z_0}{y_0} y$ as follow

$$T = \int_{y_0}^{y_1} \frac{dy}{\alpha(1-y)\frac{z_0}{y_0} y - \beta y}$$

$$= \frac{\gamma+\delta}{\alpha\gamma-\beta\delta}\left\{\ln\frac{y_1}{y_0} - \ln\frac{\gamma y_1(\alpha+\beta)-(\alpha\gamma-\beta\delta)}{\gamma y_0(\alpha+\beta)-(\alpha\gamma-\beta\delta)}\right\}. \qquad (11)$$

Note that $T \to \infty$ as $y_1 \to y_0$ as expected. Figure 3 shows comparison between (11) and numerical calculation with PHASER [5]. It shows that it takes 186 days and 5 days for one infective human to become 10 for $A = 600$ and $A = 5000$ respectively.

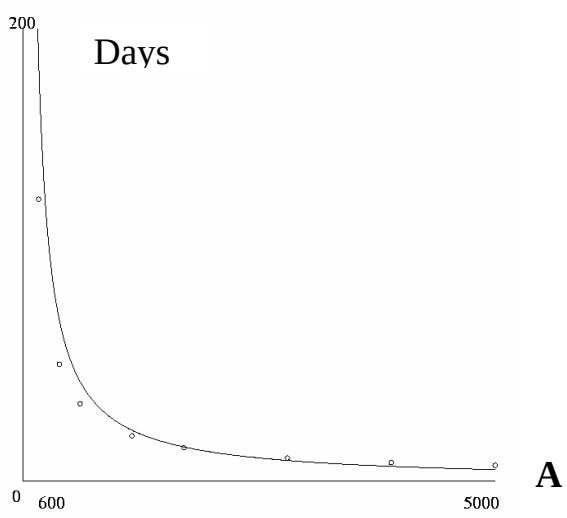

Figure 3: Estimate time (days) needed from one infected human to become ten (continuous graph) and the numerical calculation with PHASER directly from the dynamics in equation (8) (dotted graph).

4. Conclusion

We have shown the analysis of a two-dimensional dynamics of human-mosquito interaction based on the host-vector model of Esteva-Vargas [1]. In the case of large recruitment rate and when the number of infected human and infected vector are initially very small, the trajectory quickly enters the trapping region, monotonically increases and approaches the stable endemic state. Assuming that the fluctuation of the dynamics of I_H and I_V is due to the change of the vector population, this ‘’monotonic’’ model is a good representation for a short period simulation of the real situation. A study [7] has indicated that the mosquito population, and therefore the recruitment number *A*, may change from time to time due to climate changes. We discuss elsewhere the effects of a periodic mosquito recruitment rate on the dengue transmission [8]. Further development of the model can then be generated from the present model by adding relevant complexities, such as human migration and vector dispersal.

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