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Mathematical Model of Proportional Release on Population Suppression

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Abstract

To study the effects of the ratio of *Wolbachia* infected males to the wild males on population suppression strategy, we formulate a mathematical model based on systems of differential equations. Both mathematical analysis and numerical examples are provided to exhibit the complexity of the model dynamics.

Mathematics Subject Classification: 92B05, 37N25, 34D23, 92D30

Keywords: Dengue, *Wolbachia*, cytoplasmic incompatibility, population suppression, proportional release

1 Introduction

Dengue is a mosquito-borne disease caused by the dengue virus, which is spread by several species of mosquito of the *Aedes* type, principally *A. aegypti*. Over 2.5 billion people in 100 countries are at risk. Until now, there are no WHO pre-qualified vaccines for dengue. A novel strategy involves the maternally inherited endosymbiotic bacterium, *Wolbachia*, which can manipulate

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host reproduction through a mechanism known as cytoplasmic incompatibility (CI) [3, 7]. CI induces the death of embryos produced from fertilization of *Wolbachia*-uninfected ova by sperm from *Wolbachia*-infected males.

Back to 2005, Xi successfully introduced the *Wolbachia* infection into *A. aegypti* for the first time, and as expected, *Wolbachia* infection blocks the mosquito from transmitting dengue virus [19] . Since then, the research of dynamics of *Wolbachia* spread in mosquito populations has attracted more and more scholar's attention based on earlier studies [1, 2, 6]. Models of difference and differential equations have been built to explore the temporal and spatial dynamics of *Wolbachia* spread [4, 9, 11, 12, 13, 14, 15].

Population replacement and population suppression are the two proposed strategies to control the vector mosquitoes by using of *Wolbachia*. In population replacement, both infected females and infected males are released to replace the wild mosquitoes with infected ones which has a reduced capacity for disease transmission. In population suppression, only *Wolbachia* infected males are released to drive all the mated females with these males sterile and then suppress or eradicate the whole population. Compared to the models on the population replacement, there are only few papers focusing on the population suppression [8, 10]. The main purpose of this paper is to develop a model to assess the effect of proportional release policy on population suppress, which has not been emphasized in the existing literature.

2 Model Formulation

Let $I_M(t)$ denote the number of infected males at time t. We assume that the decay rate for $I_M(t)$ increases with its own size and the total population size $T(t)$ due to strong competition between adults [4, 14]. Let δ_I denote the decay rate constant. Then

$$\frac{dI_M}{dt} = -\delta_I I_M T + R_M(t), \tag{1}$$

where $R_M(t)$ is the number of released on time t. Let $U_F(t)$ and $U_M(t)$ denote the numbers of uninfected females and males, respectively. Then $T(t) = I_M(t) + U_F(t) + U_M(t)$. Like $I_M(t)$, we assume that U_F and U_M obey the same type of decay with the decay rate constant δ_U.

Based on the empirical data, we assume equal sex determination, perfect maternal transmission and complete CI [5, 17]. Let b_U be the natural birth rate of uninfected individuals. With random mating, the birth rate for uninfected offsprings is b_U if the father is uninfected, but only $b_U \cdot I_M/(I_M + U_M)$ if the father is infected. So, we have

$$\frac{dU_F}{dt} = \frac{1}{2} b_U \frac{U_M}{I_M + U_M} U_F - \delta_U U_F T, \tag{2}$$

$$\frac{dU_M}{dt} = \frac{1}{2} b_U \frac{U_M}{I_M + U_M} U_F - \delta_U U_M T. \tag{3}$$

It is easily seen that $U_F(t) = U_M(t)$ for $t > 0$, as long as $U_F(0) = U_M(0)$. Define $U(t) = U_F(t) + U_M(t)$. Adding (2) and (3), we obtain the equation for uninfected mosquitoes as

$$\frac{dU}{dt} = \frac{1}{2} b_U \frac{U}{2I_M + U} U - \delta_U U T. \tag{4}$$

For simplicity, let

$$x(t) = I_M(t), \quad y(t) = U(t), \quad \delta_1 = \delta_I, \quad \delta_2 = \delta_U, \quad \text{and} \quad b_2 = b_U/2.$$

Then the model for population suppression with proportional release is

$$x' = -\delta_1 x(x+y) + ky(t) := f(x,y), \tag{5}$$

$$y' = b_2 \frac{y^2}{2x+y} - \delta_2 y(x+y) := g(x,y). \tag{6}$$

where $R_M(t) \equiv ky(t)$ and k is the release ratio. As $g \to 0$ when $(x,y) \to (0,0)$, system (5)-(6) is then well-defined in $R_+^2 = \{(x,y) : x \geq 0, y \geq 0\}$ with the definition of $g(0,0) = 0$. For application purpose, we restrict our discussion on the first quadrant R_+^2 only.

3 Stability

3.1 Invariance and Boundedness

Let $\gamma(t) = (x(t), y(t))$ denote the orbit defined by (5)-(6) with $(x(0), y(0)) \in R_+^2$. Since $g(x,0) = 0$, $\gamma(t)$ remains on the x-axis if $y(0) = 0$, and so the x-axis is an invariant set. On the x-axis, the dynamics is fully determined by

$$dx/dt = -\delta_1 x^2,$$

for which $x = 0$ attracts all solutions $x(t)$ with $x(0) > 0$. Since $f(0,y) = ky > 0$, the y-axis is not invariant, but $x(0) = 0$ and $y(0) > 0$ imply $x(t) > 0$ for all $t > 0$. Hence

$$(x(0), y(0)) \in R_+^2 \Rightarrow \gamma(t) \in R_+^2, \quad \text{and} \quad (x(0), y(0)) \in R_+^2 \Rightarrow \gamma(t) \in R_{+0}^2$$

for all $t > 0$, where R_{+0}^2 is the interior of R_+^2. Both R_+^2 and R_{+0}^2 are positively invariant subjected to the dynamics defined by (5)-(6).

Furthermore, from (5), it is seen that

$$x > k/\delta_1 \Rightarrow x'(t) < -\delta_1 xy + ky = \delta_1 y(k/\delta_1 - x) < 0.$$

Hence $x(t) < \max\{k/\delta_1, x(0)\}$. Similarly, if $y > b_2/\delta_2$, then (6) gives

$$y'(t) < b_2 y - \delta_2 y^2 = \delta_2(b_2/\delta_2 - y) < 0,$$

and hence $y(t) < \max\{b_2/\delta_2, y(0)\}$, which justifies the boundedness of $\gamma(t)$.

3.2 Enumerating the Equilibrium Points

System (5)-(6) has no equilibrium point on axes except $E_0(0,0)$. A positive equilibrium of (5)-(6) satisfies

$$ky = \delta_1 x(x+y), \tag{7}$$

$$b_2 y = \delta_2(2x+y)(x+y). \tag{8}$$

Denote

$$\delta = \frac{\delta_1}{\delta_2}, \quad r = \frac{k}{b_2}.$$

We have

$$r = \frac{\delta x}{2x+y},$$

and hence $y = (\delta - 2r)x/r$, putting this back into (7) yields the unique interior equilibrium point as

$$x^* = \frac{k(\delta-2r)}{\delta_1(\delta-r)}, \qquad y^* = \frac{b_2(\delta-2r)^2}{\delta_1(\delta-r)},$$

where $\delta > 2r$, *i.e.*, $k < b_2\delta_1/(2\delta_2)$. Thus

Lemma 3.1. *System (5)-(6) has only one interior equilibrium point if and only if*

$$k < b_2\delta_1/(2\delta_2). \tag{9}$$

Otherwise, system (5)-(6) only has $E_0(0,0)$ as its equilibrium point.

3.3 Stability

The Jacobi matrix of (5)-(6) is

$$\mathbf{J} = \begin{pmatrix} -\delta_1(2x+y) & -\delta_1 x + k \\ -\dfrac{2b_2y^2}{(2x+y)^2} - \delta_2 y & b_2\dfrac{4xy+y^2}{(2x+y)^2} - \delta_2(x+2y) \end{pmatrix}. \tag{10}$$

Since

$$J_{21} = -\frac{2b_2y^2}{(2x+y)^2} - \delta_2 y = -2\cdot\frac{b_2y}{2x+y}\cdot\frac{y}{2x+y} - \delta_2 y = -2\delta_2\frac{y(x+y)}{2x+y} - \delta_2 y;$$

and

$$\begin{aligned} J_{22} &= b_2\frac{4xy+y^2}{(2x+y)^2} - \delta_2(x+2y) = \frac{b_2y}{2x+y}\cdot\frac{4x+y}{2x+y} - \delta_2(x+2y) \\ &= \delta_2(x+y)\cdot\left[1+\frac{2x}{2x+y}\right] - \delta_2(x+2y) = 2\delta_2\cdot\frac{x(x+y)}{2x+y} - \delta_2 y. \end{aligned}$$

We have

$$
\begin{aligned}
\delta_1\delta_2 \det J(x^*,y^*) &= -2x^*(x^*+y^*) + y^*(2x^*+y^*) - \frac{2x^*y^*(x^*+y^*)}{2x^*+y^*} - x^*y^* \\
&\quad + \frac{2k}{\delta_1}\cdot\frac{y^*(x^*+y^*)}{2x^*+y^*} + \frac{k}{\delta_1}y^* \\
&= -2x^*(x^*+y^*) + y^*(x^*+y^*) - \frac{2x^*y^*(x^*+y^*)}{2x^*+y^*} + \frac{2k}{\delta_1}\cdot\frac{y^*(x^*+y^*)}{2x^*+y^*} + \frac{k}{\delta_1}y^* \\
&= -\frac{2k}{\delta_1}y^* + \frac{b_2}{\delta_2}y^* - \frac{2k}{\delta_1}y^* - 2\cdot\frac{\delta_2(x^*+y^*)}{b_2}\cdot\frac{k}{\delta_1}y^* \\
&\quad + \frac{2k}{\delta_1}\cdot\frac{\delta_2(x^*+y^*)}{b_2}\cdot(x^*+y^*) + \frac{k}{\delta_1}y^* \\
&= \frac{b_2}{\delta_2}y^* - \frac{3k}{\delta_1}y^* - \frac{2r}{\delta}\cdot\frac{\delta-r}{\delta-2r}\cdot(y^*)^2 + \frac{2r}{\delta}\cdot\left(\frac{\delta-r}{\delta-2r}\right)^2\cdot(y^*)^2 \\
&= y^*\Big[\frac{b_2}{\delta_2} - \frac{3k}{\delta_1} + \frac{2r^2(\delta-r)}{\delta(\delta-2r)^2}\cdot y^*\Big] = y^*\Big[\frac{b_2}{\delta_2} - \frac{3k}{\delta_1} + \frac{2r^2(\delta-r)}{\delta(\delta-2r)^2}\cdot\frac{b_2(\delta-2r)^2}{\delta_1(\delta-r)}\Big] \\
&= y^*\cdot\frac{b_2^2\delta_1^2 - 3kb_2\delta_1\delta_2 + 2k^2\delta_2^2}{b_2\delta_1^2\delta_2} = y^*\cdot\frac{(b_2\delta_1-2k\delta_2)(b_2\delta_1-k\delta_2)}{b_2\delta_1^2\delta_2} \\
&= y^*\cdot\frac{b_2\delta_2}{\delta_1^2}\cdot(\delta-2r)(\delta-r) > 0.
\end{aligned}
$$

At the same time, we have

$$
\begin{aligned}
\mathrm{tr}J(x^*,y^*) &= -\delta_1(2x^*+y^*) + 2\delta_2\cdot\frac{x^*(x^*+y^*)}{2x^*+y^*} - \delta_2 y^* \\
&= -\delta_1\cdot\frac{b_2y^*}{\delta_2(x^*+y^*)} + 2\delta_2\cdot\frac{ky^*}{\delta_1}\cdot\frac{\delta_2(x^*+y^*)}{b_2y^*} - \delta_2y^* \\
&= -\frac{\delta b_2(\delta-2r)}{\delta-r} + 2\delta_2\cdot\frac{k\delta_2}{b_2\delta_1}\cdot(x^*+y^*) - \delta_2y^* \\
&= -\frac{\delta b_2(\delta-2r)}{\delta-r} + 2\delta_2\cdot\frac{r}{\delta}\cdot\frac{\delta-r}{\delta-2r}y^* - \delta_2y^* \\
&= -\frac{\delta b_2(\delta-2r)}{\delta-r} + \frac{b_2(4r\delta-2r^2-\delta^2)(\delta-2r)}{\delta^2(\delta-r)} \\
&= \frac{b_2(\delta-2r)}{\delta-r}\cdot\Big[-\delta + \frac{4r\delta-2r^2-\delta^2}{\delta^2}\Big] \\
&= \frac{b_2(\delta-2r)}{\delta-r}\cdot\frac{-\delta^3-\delta^2+4r\delta-2r^2}{\delta^2} \\
&= \frac{b_2(\delta-2r)}{\delta^2(\delta-r)}\cdot h(r,\delta),
\end{aligned}
$$

where

$$h(r,\delta) = -2r^2 + 4\delta r - \delta^2(1+\delta).$$

In terms of r, the discriminant of h is

$$\Delta = 16\delta^2 - 8\delta^2(1+\delta) = 8\delta^2(1-\delta). \tag{11}$$

So $h(\cdot,\delta)$ exists no, one or two positive roots if $\delta > 1$, $\delta = 1$ or $0 < \delta < 1$, respectively.

Case I: $\delta > 1$, which means $\Delta < 0$. It leads to $h(r) < 0$ for all $r > 0$. Hence,

$$\mathrm{tr}J(E^*) < 0,$$

which implies the existence of two negative eigenvalues for E^* which is local asymptotically stable.

Case II: $\delta = 1$, which means $\Delta = 0$. So, we have $h(r,\delta) = -2(r-1)^2 < 0$ due to $r < \delta/2 = 1/2$. It leads to $\mathrm{tr}J(E^*) < 0$. And again, E^* is local asymptotically stable.

Case III: $0 < \delta < 1$, and hence $\Delta > 0$. Two positive roots of $h(r) = 0$ are

$$r_1 = \frac{2\delta - \delta\sqrt{2-2\delta}}{2}, \qquad r_2 = \frac{2\delta + \delta\sqrt{2-2\delta}}{2}.$$

The sign of $h(r)$ depends on the relative position of r_1, r_2 and $\delta/2$. It is easy to know that $\frac{\delta}{2} < r_2$ always holds.

If $\delta/2 \le r_1$, *i.e.*, $1/2 \le \delta < 1$, then $h(r) < 0$ and hence $\mathrm{tr}J(E^*) < 0$.

If $r_1 < \delta/2 < r_2$, *i.e.*, $0 < \delta < 1/2$, then $\mathrm{tr}J(E^*) < 0$ when $r \in (0, r_1)$ and $\mathrm{tr}J(E^*) > 0$ when $r \in (r_1, \delta/2)$. In the latter case, E^* has two eigenvalues with positive real parts, and hence E^* is unstable.

Example 3.1. *Given the parameters*

$$b_2 = 160, \quad \delta_1 = 0.2, \quad \delta_2 = 0.8.$$

If $k < b_2\delta_1/(2\delta_2) = 20$, then E^* exists. If we take $k = 15$, then $E^* = (30, 20)$. In this case, tr$J(E^*) = -2 < 0$ and hence E^* is locally asymptotically stable. Solutions tends to E_0 or E^* as $t \to \infty$, depending on the initial conditions. For example, solutions started from $(35, 20)$ tends to E^* (the blue curve in the left panel in Figure 1). However, solutions initiated from $(36, 20)$ tends to $(0, 0)$ (the red curve). When we increase k from 15 to 18, the interior equilibrium are lowered to $(16.3636, 3.6364)$ and tr$J(E^*) = 4.2182 > 0$, which implies that E^* is unstable. And all solutions eventually approaches to $(0, 0)$, see the middle panel in Figure 1. Further, if we increase k from 18 to 21. There is no interior positive equilibrium and all solutions tends to $(0, 0)$, see the right panel in Figure 1.

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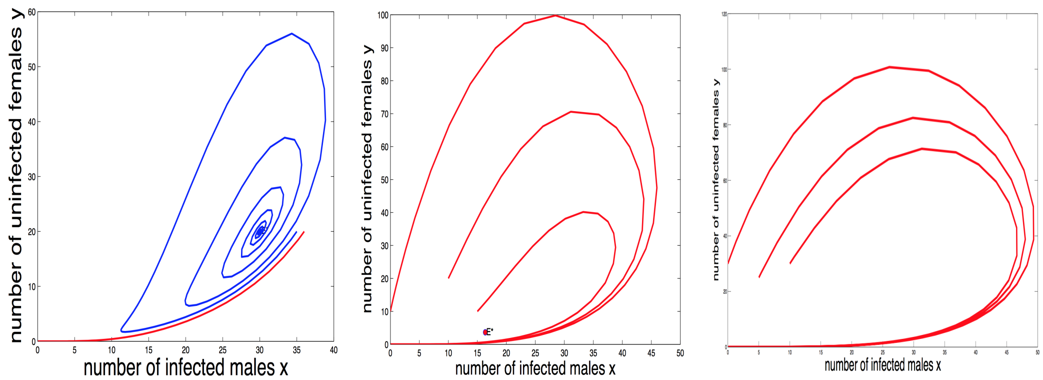

Figure 1: (Left): Solution started from $(0.028, 0.02)$ eventually goes to E^*, while solution started from $(0.029, 0.02)$ eventually goes to E_0 if $k = 0.04$. (Middle): When k is increased from 0.04 to 0.05, When the number of release $c > C$, then the wild population will be wiped out eventually in that every solution tends to the equilibrium E_1 on the x-axis, if only the initial values lies in R^2_{+0}. (Right): When $c < C$, for fixed wild population y_0, there is an unique $c_0 = c_0(C, y_0)$. To guarantee the successful population suppression, the number of released infected males c should be greater that c_0. Otherwise, the suppression will definitely fail.

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