A Mathematical Model Of Dengue-Chikungunya Co-Infection
In A Closed Population

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Abstract. Dengue disease has been a major health problem in many tropical and sub-tropical countries since the early 1900s. On the other hand, according to a 2017 WHO fact sheet, Chikungunya was detected in the first outbreak in 1952 in Tanzania and has continued increasing until now in many tropical and sub-tropical countries. Both these diseases are vector-borne diseases which are spread by the same mosquito, i.e. the female Aedes aegypti. According to the WHO report, there is a great possibility that humans and mosquitoes might be infected by dengue and chikungunya at the same time. Here in this article, a mathematical model approach will be used to understand the spread of dengue and chikungunya in a closed population. A model is developed as a nine-dimensional deterministic ordinary differential equation. Equilibrium points and their local stability are analyzed analytically and numerically. We find that the basic reproduction number, the endemic indicator, is given by the maximum of three different basic reproduction numbers of a complete system, i.e. basic reproduction numbers for dengue, chikungunya and for co-infection between dengue and chikungunya. We find that the basic reproduction number for the co-infection sub-system dominates other basic reproduction numbers whenever it is larger than one. Some numerical simulations are provided to confirm these analytical results.

1. Introduction

Dengue disease is one of the most infectious diseases in the world, where more than two over three population in the world are at risk every year [1]. This disease is spread by Aedes mosquitoes and is caused by one or more of four serotypes of the DEN virus. Although dengue vaccine has been introduced in several tropical and sub-tropical countries, a medicine to cure infected humans has not been found yet.

Like dengue, chikungunya is also a mosquito-borne disease. Chikungunya is also spread by female Aedes mosquitoes, as with dengue disease. Chikungunya was first detected in 1952 in Africa, on the Makonde Plateau [2]. Between 1960 and 1980, chikungunya has been reached its outbreak which was reported in many countries in Asia and Africa. Unlike dengue which is life-threatening, not many reported cases of chikungunya have ended with death.

Since these diseases are spread by the same mosquito, there is a possibility that humans and mosquitoes might be infected by these diseases at the same time. For an example, reported in California [3], Central
Africa [4], and Colombian [5]. Therefore, it is very important to understand how these diseases spread among the human and mosquito populations and understand the best prevention or control programs for both of these diseases.

Many mathematical models have been developed to understand dengue [6-10] and chikungunya [11,12], and also some models of co-infection between dengue and chikungunya [13,14]. In contrast to the articles in [13,14], in this article, the effect of co-infection is not only analyzed in the human population, but also in the mosquito population. The mosquito population may also get infected by dengue and chikungunya at the same time.

The paper is organized as follows. In chapter 2, the mathematical model construction will be discussed and followed with mathematical model analysis about the equilibrium points and the basic reproduction number in chapter 3. Numerical experiments to give a better interpretation of the analytical results in chapter 3 are reported in chapter 4. Some conclusions are given in chapter 5.

2. The construction of the mathematical model
In this section, the mathematical models will be described. Firstly, some basic assumptions are given which form the basis of the model construction process, namely:

1. The total human and mosquito populations are constant.
2. There is no increase in the death rate of human and mosquito except from natural death rate.
3. The health status of humans can be seen physically.
4. Humans can be infected by dengue and chikungunya at the same time.
5. The first virus that come into the mosquito's body dominates the other virus, except the mosquito bites the co-infected human.
6. Infection only occurs from direct contact between mosquito and human. Infection cannot occur from human to human or mosquito to mosquito contact.
7. All newborn are susceptible for human and mosquito.

With these assumptions, the construction of the model is given as follows. Let the human population be divided into five compartments, i.e. susceptible humans \(x_1\), humans infected with dengue \(x_2\), humans infected with chikungunya \(x_3\), co-infected humans, or humans infected with both dengue and chikungunya \(x_4\), and recovered humans \(x_5\). On the other hand, the mosquito population is divided into four compartments, i.e. susceptible mosquitoes \(y_1\), mosquitos infected with dengue \(y_2\), mosquitos infected with chikungunya \(y_3\) and mosquitos co-infected with dengue and chikungunya \(y_4\). To construct the model, the transmission and transition between each compartment can be seen in Figure 1. More detail about the model construction is given below.
Susceptible humans increase from the newborn stage at a constant rate of $A_x$ and decreases by infection and natural death rate with constant rate of $\mu_x$. Susceptible humans might be infected by mosquitos that carry the DEN virus ($y_2$ and $y_4$) with a probability of success infection of $\beta_{xd}$, and mosquitos that carry the chikungunya virus ($y_3$ and $y_4$) with a probability of success infection of $\beta_{xc}$. Since we assume that co-infection between dengue and chikungunya might appear in human and mosquito populations, humans also might be infected by a mosquito carrying both the DEN and chikungunya viruses ($y_4$) with a probability of success infection of $\beta_{xe}$. Therefore, the dynamic of susceptible human respect to time is given by

$$
\frac{dx_1}{dt} = A_x - \beta_{xd}x_1(py_4 + y_2) - \beta_{xe}x_1(qy_4 + y_3) - \beta_{xe}x_1(1-p-q)y_4 - \mu_x x_1 + \delta x_5 ,
$$

where $p$ and $q$ are the proportion of humans who have contact with $y_4$ who will be infected by dengue and chikungunya, respectively, and $N_x = x_1 + x_2 + x_3 + x_4 + x_5$ is the total of the human population.

Infected humans with dengue ($x_2$), chikungunya ($x_3$) and both dengue and chikungunya ($x_4$) increase caused by infection process from susceptible human ($x_1$). Multiple infections might appear in the $x_2$ and $x_3$ compartments which allows a possible transition from these compartments into the $x_4$ compartment. We also assume that infected humans might recover from infection, depending on their natural immune system, with the per capita recovery rate given by constant $\gamma$. Therefore, the dynamic of all infected compartments in respect to time is given by

$$
\frac{dx_2}{dt} = \frac{\beta_{xd}x_1(py_4 + y_2)}{N_x} - \frac{\beta_{xe}x_1(qy_4 + y_3)}{N_x} - \frac{\beta_{xe}x_1(1-p-q)y_4}{N_x} - \mu_x x_2 - \gamma x_2
$$

$$
\frac{dx_3}{dt} = \frac{\beta_{xe}x_1(qy_4 + y_3)}{N_x} - \frac{\beta_{xd}x_3(y_2 + y_4)}{N_x} - \mu_x x_3 - \gamma x_3
$$

$$
\frac{dx_4}{dt} = \frac{\beta_{xe}x_1(1-p-q)y_4}{N_x} + \frac{\beta_{xe}x_2(y_3+y_4)}{N_x} + \frac{\beta_{xd}x_3(y_2+y_4)}{N_x} - \mu_x x_4 - \gamma x_4 .
$$

Recovered human increased by transition from infected compartment as a recovery process and decreased caused by natural death rate and as an effect of disappearance of temporary immunity with constant rate $\delta$. Therefore, the dynamic of recovered human compartments with respect to time is given by
\[
\frac{dx_5}{dt} = \gamma (x_2 + x_3 + x_4) - \mu_x x_5 - \delta x_5 .
\]

In the mosquito population, the susceptible mosquitos compartment is increased by constant newborns at the rate of \( A_y \) and decreased according to the natural death rate \( \mu_y \). This compartment also decreases due to the effect of infection from direct contact with humans infected with dengue \( y_2 \), chikungunya \( y_3 \) and both \( y_4 \) with the probability of successful infection given by \( \beta_{yd}, \beta_{yc}, \) and \( \beta_{ye} \), respectively. Therefore, the dynamic of the susceptible mosquitos compartment in respect to time is given by

\[
\frac{dy_1}{dt} = A_y - \frac{\beta_{yd} y_1 x_2}{N_x} - \frac{\beta_{yc} y_1 x_3}{N_x} - \frac{\beta_{ye} y_1 x_4}{N_x} - \mu_y y_1 .
\]

On the other hand, all infected mosquitos \( (y_2, y_3, y_4) \) increased by infection term from susceptible mosquitos compartment and decreased by natural death rate \( \mu_y \) which gave us the dynamic of infected mosquitos is given by

\[
\begin{align*}
\frac{dy_2}{dt} &= \frac{\beta_{yd} y_1 x_2}{N_x} - \mu_y y_2 \\
\frac{dy_3}{dt} &= \frac{\beta_{yc} y_1 x_3}{N_x} - \mu_y y_3 \\
\frac{dy_4}{dt} &= \frac{\beta_{ye} y_1 x_4}{N_x} - \mu_y y_4 .
\end{align*}
\]

Therefore, the mathematical model of co-infection between dengue and chikungunya is given by 9-dimensional system of ordinary differential equation which given by system (1) below:

\[
\begin{align*}
\frac{dx_1}{dt} &= A_x - \frac{\beta_{xd} x_1 (py_4 + y_2)}{N_x} - \frac{\beta_{xc} x_1 (q y_4 + y_3)}{N_x} - \frac{\beta_{xe} x_1 (1 - p - q) y_4}{N_x} - \mu_x x_1 + \delta x_5 \\
\frac{dx_2}{dt} &= \frac{\beta_{xd} x_1 (py_4 + y_2)}{N_x} - \frac{\beta_{xc} x_2 (y_3 + y_4)}{N_x} - \mu_x x_2 - \gamma x_2 \\
\frac{dx_3}{dt} &= \frac{\beta_{xc} x_1 (q y_4 + y_3)}{N_x} - \frac{\beta_{xd} x_3 (y_2 + y_4)}{N_x} - \mu_x x_3 - \gamma x_3 \\
\frac{dx_4}{dt} &= \frac{\beta_{xe} x_1 (1 - p - q) y_4}{N_x} + \frac{\beta_{xc} x_2 (y_3 + y_4)}{N_x} + \frac{\beta_{xd} x_3 (y_2 + y_4)}{N_x} - \mu_x x_4 - \gamma x_4 \\
\frac{dx_5}{dt} &= \gamma (x_2 + x_3 + x_4) - \mu_x x_5 - \delta x_5 \\
\frac{dy_1}{dt} &= A_y - \frac{\beta_{yd} y_1 x_2}{N_x} - \frac{\beta_{yc} y_1 x_3}{N_x} - \frac{\beta_{ye} y_1 x_4}{N_x} - \mu_y y_1 \\
\frac{dy_2}{dt} &= \frac{\beta_{yd} y_1 x_2}{N_x} - \mu_y y_2 \\
\frac{dy_3}{dt} &= \frac{\beta_{yc} y_1 x_3}{N_x} - \mu_y y_3 \\
\frac{dy_4}{dt} &= \frac{\beta_{ye} y_1 x_4}{N_x} - \mu_y y_4 .
\end{align*}
\]
\[ \frac{d y_3}{d t} = \frac{\beta_{yx} y_1 x_3}{N_x} - \mu_y y_3 \quad (1h) \]

\[ \frac{d y_4}{d t} = \frac{\beta_{yx} y_1 x_4}{N_x} - \mu_y y_4 . \quad (1i) \]

with initial condition of humans and mosquitoes are given by \( x_i(t = 0) = x_{i0} \geq 0 \) for \( i = 1, 2 \ldots 5 \) and \( y_i(t = 0) = y_{i0} \geq 0 \) for \( i = 1, 2 \ldots 4 \), respectively. Choosing \( A_x = \mu_x N_x \) and \( A_y = \mu_y N_y \), we have that total of humans and mosquitoes population will remain constant all the time, since

\[ \frac{d N_x}{d t} = A_x - \mu_x N_x \quad \text{and} \quad \frac{d N_y}{d t} = A_y - \mu_y N_y . \]

### 3. Mathematical model analysis

In this section, a mathematical model analysis of system (1) will be performed with analyzing the existence and local stability of the equilibrium points, and also their relationship with the basic reproduction number.

#### 3.1. Equilibrium points

System (1) have 4 different equilibrium points which represent the situation that might appear in the field related to the coexistence between dengue and chikungunya. The first equilibrium point is the disease-free equilibrium point (\( \Omega_1 \)) where all infected population equal to 0 in both human and mosquitoes population, which given by

\[ \Omega_1 = \left( x_1 = \frac{A_x}{\mu_x}, x_2 = 0, x_3 = 0, x_4 = 0, x_5 = 0, y_1 = \frac{A_y}{\mu_y}, y_2 = 0, y_3 = 0, y_4 = 0 \right). \]

The second and the third equilibrium point is the equilibrium when only dengue infection occur (\( \Omega_2 \)) and only chikungunya infection occur (\( \Omega_3 \)), respectively, which are given by

\[ \Omega_2 = \left( x_1 = \frac{N_s + \beta_{yx} y_1 (\mu_x + \gamma) (N_s + \beta_{yx} y_1) + \gamma N_s, x_2 = 0, x_3 = 0, x_4 = 0, x_5 = 0, y_1 = \frac{A_y}{\mu_y}, y_2 = 0, y_3 = 0, y_4 = 0 \right). \]
It can be seen that all compartments in $\Omega_2$ and $\Omega_3$ will remain non-negative if and only if $R_{0d} > 1$ and $R_{0c} > 1$, respectively, where $R_{0d} = \sqrt{\mu_x(\mu_x+\mu_y)\mu_y\beta_{yd}\beta_{ecd}^2}/\mu_x(\mu_x+\mu_y)\mu_yN_x$ and $R_{0c} = \sqrt{\mu_x(\mu_x+\mu_y)\mu_y\beta_{yd}\beta_{ecd}^2}/\mu_x(\mu_x+\mu_y)\mu_yN_x$. The last equilibrium point is the endemic equilibrium point, when all compartment is non-negative ($\Omega_4$) which is not in simple form to be shown in this article. However, the existence of this equilibrium point still could be shown numerically with substituting parameters value in to system (1). Choosing parameters value:

\[\begin{align*}
\delta &= 1 - \frac{1}{30}, \quad \gamma = \frac{1}{14}, \quad p = 0.45, q = 0.45, \quad A_x = \frac{40}{949}, \quad A_y = \frac{100}{3}, \quad N_x = 1000, \quad \beta_{xc} = 0.01, \quad \beta_{xd} = 0.02, \quad \beta_{xe} = 0.2, \quad \beta_{yc} = 0.01, \quad \beta_{yd} = 0.02, \quad \beta_{ye} = 0.2, \quad \mu_x = \frac{1}{23725}, \quad \mu_y = \frac{1}{30},
\end{align*}\]

which gave us $R_{0e} = \sqrt{\mu_x(\mu_x+\mu_y)\mu_y\beta_{yd}\beta_{ecd}^2(-1+p+q)}/\mu_x(\mu_x+\mu_y)\mu_yN_x > 1$, we find that the $\Omega_4$ is given by

\[\begin{align*}
x_1 &= 751.8887214, \quad x_2 = 22.05258485, \quad x_3 = 9.903206336, \quad x_4 = 47.05674131, \quad x_5 = 169.0987461,
\end{align*}\]

\[\begin{align*}
y_1 &= 770.0938901, \quad y_2 = 10.18953651, \quad y_3 = 2.287919607, \quad y_4 = 217.4286538.
\end{align*}\]

To analyze the local stability of the equilibrium point, system (1) will be linearized with Jacobian matrix approach. Evaluate the $\Omega_1$ in the Jacobian matrix of system (1), we find that this equilibrium point will locally stable if and only if $R_{0d} < 1, R_{0c} < 1$ and $R_{0e} < 1$. With numerical approach, local stability of each equilibrium points is summarized in Figure 2 below.
Basic Reproduction Number

Basic reproduction number is defined as an expected number of secondary cases caused by one primary case in a virgin population during one infection period [15,16]. Basic reproduction number could be taken from the spectral radius of the next-generation matrix. More detail about the construction of the next-generation matrix could be seen in [15].

The next-generation matrix of system (1) is given by

\[
\begin{pmatrix}
0 & 0 & 0 & \frac{\beta_{xd}A_x}{\mu_x N_x \mu_y} & 0 & -\frac{\beta_{xd}A_x p}{\mu_x N_x \mu_y} \\
0 & 0 & 0 & 0 & -\frac{\beta_{xe}A_x}{\mu_x N_x \mu_y} & -\frac{\beta_{xe}A_x q}{\mu_x N_x \mu_y} \\
0 & 0 & 0 & 0 & 0 & -\frac{\beta_{ye}A_y}{\mu_y N_y (y + \mu_x)} \\
0 & 0 & \frac{\beta_{ye}A_y}{\mu_y N_y (y + \mu_x)} & 0 & 0 & 0 \\
0 & -\frac{\beta_{ye}A_y}{\mu_y N_y (y + \mu_x)} & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0
\end{pmatrix}
\]

The element of the next generation read as number of new infection from in column-i caused by one infected person/mosquito in row-j. For example, \(NGM_{1,4}\) represent that one infected human by dengue \((x_2)\) produce \(\frac{\beta_{xd}A_x}{\mu_x N_x \mu_y}\) new infection in infected mosquito by dengue \((y_2)\). With this NGM in hand, the basic reproduction number of system (1) is given by

\[
R_0 = \max\{R_{0d}, R_{0c}, R_{0e}\},
\]

where \(R_{0d}, R_{0c}, R_{0e}\) is given in the previous subsection. Therefore, it can be seen that the existence and local stability of each equilibrium point fully depends on magnitude of the \(R_0 = \max\{R_{0d}, R_{0c}, R_{0e}\}\), where \(R_{0d}\) is the basic reproduction number for dengue infection, \(R_{0c}\) is the basic reproduction number for chikungunya infection, and \(R_{0e}\) is the basic reproduction number for the co-infection between dengue and
chikungunya. In Figure 3 below, we present the dependency of the infection rate respect to the basic reproduction number. It can be seen that smaller the infection rate will reduce basic reproduction number.

Figure 3. Dependency of infection probability rate for dengue, chikungunya and co-infection (dengue and chikungunya) respect to basic reproduction number from left to right, respectively. Others parameter (except $\beta_{xy}, \beta_{y}, \beta_{yc}, \beta_{yd}, \beta_{ye}$) are $\delta = \frac{1}{30}, \gamma = \frac{1}{14}, p = 0.45, q = 0.45, A_x = \frac{40}{949}, A_y = \frac{100}{3}, N_x = 1000, \mu_x = \frac{1}{23725}, \mu_y = \frac{1}{30}$.

In the next section, some numerical simulation will be given to give an interpretation of the analytical results.

4. Numerical experiments
Except it is stated, parameters value to run the simulations in this section is given in Table 1 and the initial condition for system (1) is $x_i(0) = (980, 10, 10, 0, 0, 990, 5, 5, 0)$ for $i = 1, 2, ..., 9$.

| Parameters | $A_x$ | $A_y$ | $\mu_x$ | $\mu_y$ | $\gamma$ | $p$ | $q$ | $N_x$ |
|------------|-------|-------|---------|---------|---------|-----|-----|------|
| Value      | 1000  | 1000  | 1       | 1       | 1       | 0.45| 0.45| 1000 |
|            | $65 \times 365$ | $30$  | $65 \times 365$ | $30$ | $14$    |

First simulation in this section will be performed in two different scenarios to give a better interpretation of analytical result from the previous section. First case is given when $R_{oe} < 1$ while $R_{od}$ and $R_{oc}$ are varied. In the other hand, the second case is given when $R_{oe} > 1$ while $R_{od}$ and $R_{oc}$ are varied. Parameters value and the magnitude of the basic reproduction number is given in Table 2 for each case.

| Case | Color in Figure | $R_0$ condition | $\beta_{xy}$ | $\beta_{xd}$ | $\beta_{xe}$ | $\beta_{yc}$ | $\beta_{yd}$ | $\beta_{ye}$ | $R_0$ |
|------|-----------------|-----------------|-------------|-------------|-------------|-------------|-------------|-------------|------|
| 1    | Red             | $R_{od} > R_{ac} > 1$ | 0.1         | 0.2         | 0.05        | 0.1         | 0.2         | 0.05        | $R_{ac} = 2.04$ |
|      |                 |                 |             |             |             |             |             |             | $R_{od} = 4.09$ |
|      |                 |                 |             |             |             |             |             |             | $R_{oe} = 0.32$ |
| 1    | Green           | $R_{ac} > R_{od} > 1$ | 0.2         | 0.1         | 0.05        | 0.2         | 0.1         | 0.05        | $R_{ac} = 4.09$ |
|      |                 |                 |             |             |             |             |             |             | $R_{od} = 2.04$ |
|      |                 |                 |             |             |             |             |             |             | $R_{oe} = 0.32$ |
In Figure 4, it can be seen that when $R_{oe} < 1$, no matter magnitude of $R_{oc}$ and $R_{od}$ taken, the co-infection subpopulation both in human and mosquitoes population tend to zero for $t \rightarrow \infty$. However, in a beginning time period of simulation, the co-infected subpopulation $(x_4, x_9)$ are increasing and then tends to zero afterward. On the other hand, dengue-infected subpopulation $(x_2, x_7)$ and chikungunya infected subpopulation $(x_3, x_8)$ tend to equilibrium $\Omega_2$ and $\Omega_3$, respectively.

In Figure 5, the other condition of $R_{oe}$ is performed, i.e when $R_{oe} > 1$ while $R_{oc}$ and $R_{od}$ are varied. It can be seen that when $R_{oe} > 1$, then system (1) will tend to endemic equilibrium of co-infection situation between dengue and chikungunya ($\Omega_4$) no matter the condition of $R_{oc}$ and $R_{od}$. It can be seen also that when basic reproduction number for dengue and chikungunya, $R_{oc}$ and $R_{od}$, respectively less than 1, number of co-infection subpopulation are much larger in the equilibrium point rather than when one or both of $R_{oc}$ and $R_{od}$ are worth less than 1.

Second simulation is given in Figure 6 to show how the various value of infection rate for co-infection in human and mosquito population affect the dynamic of all subpopulation in system (1). It can be seen that when $\beta_{xe}$ and $\beta_{ye}$ are given for various value from 0.01 to 0.2, susceptible and recovered subpopulation in human and mosquitoes population only slightly different. In the other hand, number of infected human and mosquito (co-infection subpopulation) change significantly. This situation confirms the analytical result that $\beta_{xe}$ and $\beta_{ye}$ will dominate the dynamic of system (1) whenever these value increase in to larger than 1 (see Figure (3)).
**Figure 4.** Simulation results for 1\textsuperscript{st} case showing that when $R_{0e} < 1$, then the co infection subpopulation will tend to zero when time is increasing.

**Figure 5.** Simulation results for 2\textsuperscript{nd} case showing that when $R_{0e} > 1$, then the co infection subpopulation will tend to the equilibrium point $\Omega_4$ when time is increasing.
Figure 6. Simulation results for 3rd scenario when $R_{0e}$ is varying while $R_{0c}$ and $R_{0d}$ are remaining the same.

5. Conclusions
In this paper, a comprehensive mathematical model for the co-infection between dengue and chikungunya has been discussed. The mathematical model is developed using a deterministic approach with a nine-dimensional system of ordinary differential equation. Mathematical analysis of the existence and local stability criteria of the equilibrium is given and connected with the basic reproduction number for the related model. We find that the basic reproduction number of the complete system is given by the maximum of three different basic reproduction numbers of three subsystems, i.e. for dengue, for chikungunya, and for co-infection between dengue and chikungunya. From numerical experiments for the local stability criteria, we find that the basic reproduction number for the co-infection sub-system dominates other basic reproduction numbers whenever this value is larger than one. The numerical simulation allowed us to observe this situation, as shown in the last figure in the numerical experiment section.

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