# Mathematical Modelling in Dengue Epidemics Encompassing Transovarial Transmission

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Summary

- Introduction
- Transovarial transmission
- Mathematical model
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# Introduction

# Dengue

- Dengue virus, a *flavivirus* transmitted by arthropod of the genus *Aedes*, is prevalent in different parts of the world
- The efforts of the eradication of dengue epidemics can be measured using mathematical models
- Modelling transovarial transmission
- Thresholds
- Epidemiological implications

# Transovarial transmission

# Characteristics

- There is evidence that transovarial (the transfer of pathogens to succeeding generations through invasion of the ovary and infection of the eggs) transmission can occur in some species of *Aedes* mosquitoes
- The role of transovarial transmission in the maintenance of dengue epidemics is not clearly understood
- The transovarial transmission of dengue virus in *A. aegypti* has been observed at a relatively low rate
- Mathematical modelling to evaluate the transovarial transmission

# Mathematical modelling

# Variables

Humans:

- Human population is divided into three compartments: $s$, $i$ and $r$, which are the fractions at time $t$ of, respectively, susceptible, infectious and recovered persons, with $s + i + r = 1$. The constant total number of the human population is $N$.

Mosquitoes:

- Aquatic (immature) forms – $l_1$ and $l_2$ are the numbers of aquatic forms (female) at time $t$ of, respectively, susceptible and infected, and $l = l_1 + l_2$ is the total number of aquatic forms
- The female mosquito (adult) population is divided into two compartments: $m_1$ and $m_2$, which are the numbers at time $t$ of, respectively, susceptible and infectious mosquitoes. The size of mosquito population is $m = m_1 + m_2$

# Parameters

- The human mortality rate is $\mu_h$.
- The effective larvae production rate is given by $qf\,(1 - l/C)\,\phi m$, where $q$ and $f$ are the fractions of eggs that are hatching to larva and that will originate female mosquitoes, respectively, and $C$ is the total (carrying) capacity of the breeding sites. Change rate of aquatic form to adult and death rate of acquatic form are $\sigma_a$ and $\mu_a$. The female mosquitoes mortality rate is $\mu_f$.
- Among humans the transmission coefficient (or rate) is $\beta_h$, depending on $\phi$. The infected persons are transferred to infectious class by rate $\gamma_h$, and are removed to recovered (immune) class by $\sigma_h$, the recovery rate. With respect to the vector, the susceptible mosquitoes are infected at a rate $\beta_m$. These infected mosquitoes are transferred to infectious class at a rate $\gamma_m$.
- The transmission coefficients $\beta_h$ and $\beta_m$ are divided by $N$.

- Modelling transovarian transmission

$$
\begin{cases}
\frac{d}{dt}m_2 &= \sigma_a l_2 + \beta_m \phi i m_1 - \mu_f m_2 \\
\frac{d}{dt}i &= \frac{\beta_h \phi}{N} m_2 s - (\sigma_h + \mu_h)\, i \\
\frac{d}{dt}l_2 &= q f \phi j m_2 \left[1 - \frac{(l_1+l_2)}{C}\right] - (\sigma_a + \mu_a)\, l_2 \\
\frac{d}{dt}l_1 &= q f \phi \left[m_1 + (1-j)\, m_2\right] \left[1 - \frac{(l_1+l_2)}{C}\right] - (\sigma_a + \mu_a)\, l_1 \\
\frac{d}{dt}m_1 &= \sigma_a l_1 - (\beta_m \phi i + \mu_f)\, m_1 \\
\frac{d}{dt}s &= \mu_h - \left(\frac{\beta_h \phi}{N} m_2 + \mu_h\right) s,
\end{cases}
$$

where $j$ is the fraction of eggs with dengue virus from all eggs laid by infected mosquitoes.

# Analysis

Trivial equilibrium $P^0$, or disease free equilibrium (DFE),

$$P^0 = \left(\bar{m}_2 = 0, \bar{\imath} = 0, \bar{l}_2 = 0, \bar{l}_1 = l^*, \bar{m}_1 = m^*, \bar{s} = 1\right),$$

where $l^*$, $p^*$ and $m^*$ are given by

$$\begin{cases} l^* & = & C\left(1 - \frac{1}{Q_0}\right) \\ m^* & = & \frac{\sigma_a}{\mu_f} C\left(1 - \frac{1}{Q_0}\right). \end{cases}$$

Clearly the mosquito population exists if $Q_0 > 1$, where

$$Q_0 = \frac{\sigma_a}{\sigma_a + \mu_a} \frac{q f \phi}{\mu_f}$$

is the basic offspring number.

Non-trivial equilibrium $P^*$, or endemic equilibrium,

$$P^* = \left(\bar{m}_2 = m_2^*, \bar{\imath} = i^*, \bar{l}_2 = l_2^*, \bar{l}_1 = l_1^*, \bar{m}_1 = m_1^*, \bar{s} = s^*\right),$$

where

$$\begin{cases} l_1^* & = & (1-j)\frac{\beta_m \phi i^* + \mu_f}{\beta_m \phi i^* + (1-j)\mu_f} C\left(1 - \frac{1}{Q_0}\right) \\ l_2^* & = & j\frac{\beta_m \phi i^*}{\beta_m \phi i^* + (1-j)\mu_f} C\left(1 - \frac{1}{Q_0}\right) \\ m_1^* & = & (1-j)\frac{\mu_f}{\beta_m \phi i^* + (1-j)\mu_f}\frac{\sigma_a}{\mu_f} C\left(1 - \frac{1}{Q_0}\right) \\ m_2^* & = & \frac{\beta_m \phi i^*}{\beta_m \phi i^* + (1-j)\mu_f}\frac{\sigma_a}{\mu_f} C\left(1 - \frac{1}{Q_0}\right) \\ s^* & = & 1 - \frac{\sigma_h + \mu_h}{\mu_h} i^* \\ i^* & = & \begin{cases} \frac{\mu_f (R_e - 1)}{\beta_m \phi + \frac{\mu_f(\sigma_h + \mu_h)}{\mu_h} R_0}, & for \quad j < 1 \\ \frac{\mu_f R_0}{\beta_m \phi + \frac{\sigma_h + \mu_h}{\mu_h} R_0}, & for \quad j = 1 \end{cases} \end{cases}$$

# Equilibrium points

The net reproduction number $R_e$, which encompasses transovarial transmission, is

$$R_e = R_0 + R_v,$$

where the reproduction number for horizontal transmission is

$$R_0 = \frac{\beta_h \phi}{\mu_f} \frac{\beta_m \phi}{\sigma_h + \mu_h} \frac{m^*}{N}.$$

and $R_v = j$ is the reproduction number for vertical (transovarial) transmission. $R_0$ can be split in two partial contributions $R_0^h$ and $R_0^m$ defined by

$$\begin{cases} R_0^h &= \frac{\beta_h \phi}{\mu_f} \\ R_0^m &= \frac{\beta_m \phi}{\sigma_h + \mu_h} \frac{m^*}{N} \end{cases}$$

thus $R_0 = R_0^h \times R_0^m$.

# Equilibrium points

The combination of $s^*$, $m_1^*$ and $m^*$ results in

$$s^* \frac{m_1^*}{m^*} = \chi_e = \frac{1-j}{R_0}$$

and the threshold of product of fractions $\chi_e^{-1}$, which encompasses transovarial transmission, can be written as

$$\frac{1}{\chi_e} = \frac{R_0}{1-j}$$

# Stability of DFE – $P^0$

Stability of DFE:

- Three methods – Next generation matrix, Routh-Hurwitz criteria and M-Matrix
- DFE is stable if $R_e < 1$, or, equivalently, $\chi_e > 1$

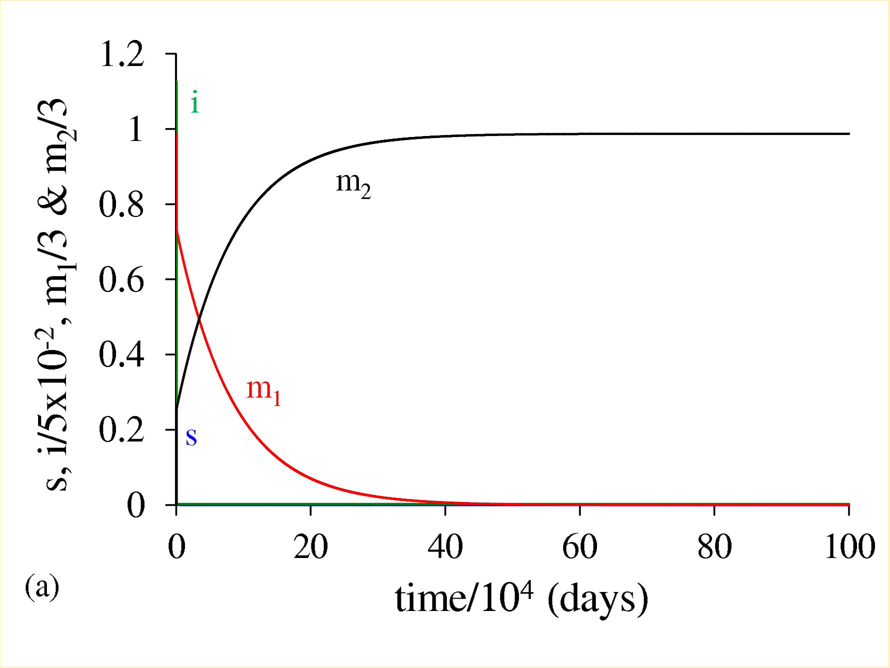
Reproduction numbers:

- $R_0$ – It is the basic reproduction number, that is, the average secondary cases in the beginning of epidemics
- $R_v = j$ – It accounts for long term infection
- $R_v = 1$ – Infectious (aquatic and adult) forms displace susceptible forms

# Results

- $R_v = 0$ and $R_g = R_0 = 1.0049448$
- $R_v = 0.2$, $R_0 = 1.0049448$ and $R_g = R_0 + R_v = 1.0049448$
- After initial $11.1 \times 10^3$ $days$, the infectious humans and mosquitoes are higher when transovarial transmission occurs
- The highest relative differences between infectious humans $\left(\left(i_{j=0.02} - i_{j=0}\right)/i_{j=0}\right)$ and mosquitoes $\left(\left(m_{2_{j=0.02}} - m_{2_{j=0}}\right)/m_{2_{j=0.02}}\right)$ with and without transovarial transmission are $12.95\%$ and $13.88\%$
- These highest differences occur at the peak of the first epidemics $(24.6 \times 10^3$ $days)$

# Dynamica simulations – Displacement




Displacement of susceptibles by infectious

# Conclusion

# Conclusion

- Jacobian and Next generation methods yielded same basic reproduction number (also, the product of the fractions of susceptible populations)

- Horizontal transmission modellings – One threshold ($R_0$)
- Spectral radius is the geometric mean of partial reproduction numbers
- The basic reproduction number is the product of the partial reproduction numbers
- Incorporating vertical transmission in modellings – Two thresholds ($R_e$ and $\chi_e$)
- Short ($R_0$) and long ($R_v$) terms in dynamics

# Thank You

Yang, H.M. (2017). Epidemiological implications of the transovarial transmission in the dynamics of dengue infection. Math. Biosc.: submitted.