Quescence eggs and vertical transmission – Are they important in dengue transmission?

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Summary

- Introduction
- Quescence eggs
- Transovarial transmission
- Dengue and abiotic influences
- Conclusion
- References

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 quiescence eggs.
- Modelling transovarial transmission.
- Modelling influences of abiotic influences.

Mathematical modelling – Quescence eggs

Eggs

- Eggs of the mosquito *A. aegypti* – Embryonic development of the eggs is completed approximately within 3 days after oviposition, and a fully developed 1^{st} instar larva resides within the chorion of the egg in a dormant state referred to as quiescence.
- Life history traitpharate larvae – Withstand months of quiescence inside the egg where they depend on stored maternal reserves.
- Duration of quiescence and extent of nutritional depletion – Affect the physiology and survival of larvae that hatch in a suboptimal habitat.
- Quiescence – Desiccation resistant.

Laboratory

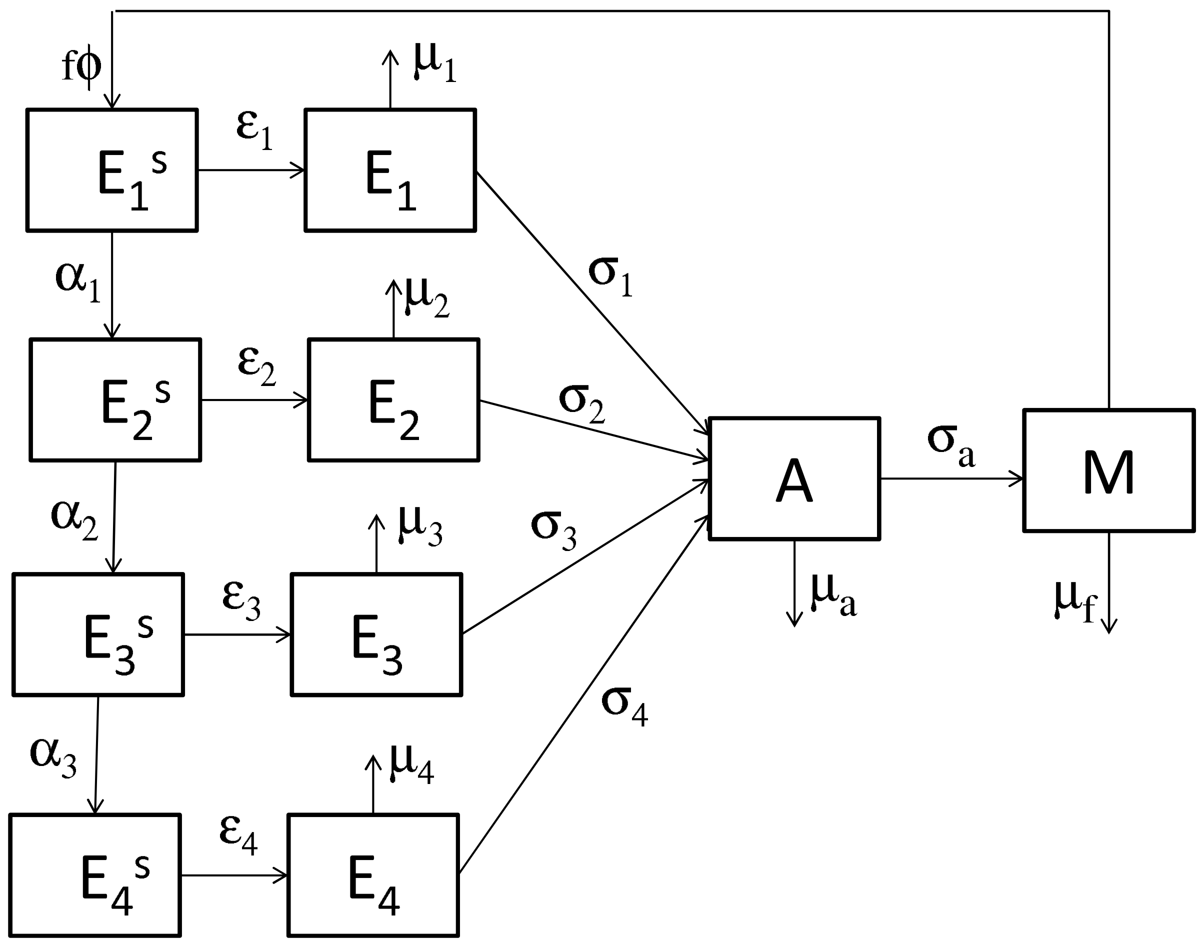
- Laboratorial experiments – Assessing the influence of the quiescence eggs on the life cycle of *A. aegypti*.
- Experiments – Classifying the quiescence eggs in roughly four categories according to their ability to hatch larvae.
- Quiescence eggs – Improvement of the fitness of mosquito population, or not ...

Life cycle

- Quiescence egg – E_i^s, for $i = 1, \cdots, 4$.
- Hatchable egg – E_i, for $i = 1, \cdots, 4$.
- Larva + Pupa – A.
- Female mosquito – F.

The passage from E_i^s to E_i is dictated by external stimuli (such as temperature, humidity, nutrients, etc.) and is irreversible.

Flow chart



The flow chart of mosquito's life cycle including quiescence eggs.

Parameters

- Oviposition rate – ϕ.
- Female fraction – f.
- Transition rate – α_i, for $i = 1, \cdots, 4$.
- Hatching rate – ε_i, for $i = 1, \cdots, 4$.
- Mortality rate (eggs) – μ_i, for $i = 1, \cdots, 4$.
- Transition rate (aquatic) – σ_a.
- Mortality rate (aquatic) – μ_a.
- Mortality rate (female mosquito) – μ_f.
- Carrying Capacity – k.

Equations:

$$
\left\{
\begin{array}{rcl}
\frac{d}{dt}E_1^s & = & f\phi M - (\alpha_1 + \varepsilon_1)\, E_1^s \\
\frac{d}{dt}E_1 & = & \varepsilon_1 E_1^s - (\mu_1 + \sigma_1)\, E_1 \\
\frac{d}{dt}E_2^s & = & \alpha_1 E_1^s - (\alpha_2 + \varepsilon_2)\, E_2^s \\
\frac{d}{dt}E_2 & = & \varepsilon_2 E_2^s - (\mu_2 + \sigma_2)\, E_2 \\
\frac{d}{dt}E_3^s & = & \alpha_2 E_2^s - (\alpha_3 + \varepsilon_3)\, E_3^s \\
\frac{d}{dt}E_3 & = & \varepsilon_3 E_3^s - (\mu_3 + \sigma_3)\, E_3 \\
\frac{d}{dt}E_4^s & = & \alpha_3 E_3^s - \varepsilon_4 E_4^s \\
\frac{d}{dt}E_4 & = & \varepsilon_4 E_4^s - (\mu_4 + \sigma_4)\, E_4 \\
\frac{d}{dt}A & = & (\sigma_1 E_1 + \sigma_2 E_2 + \sigma_3 E_3 + \sigma_4 E_4)\left(1 - \frac{A}{k}\right) \\
 & & - (\mu_a + \sigma_a)\, A \\
\frac{d}{dt}M & = & \sigma_a A - \mu_f M
\end{array}
\right.
$$

Steady state

Auxiliary parameters, for $i = 1, \cdots, 4$:

- probabilities of transition from quiescence stage i to stage $i+1$ (a_i) and to hatchable stage i (b_i):

$$\begin{cases} a_i = \frac{\alpha_i}{\alpha_i + \varepsilon_i} \\ b_i = \frac{\varepsilon_i}{\alpha_i + \varepsilon_i} \end{cases}$$

- The average periods of time that eggs stay at quiescence (d_i) and hatchable (g_i) stages i:

$$\begin{cases} d_i = \frac{1}{\alpha_i + \varepsilon_i} \\ g_i = \frac{1}{\mu_i + \sigma_i} \end{cases}$$

- ...

Steady state

Auxiliary parameters, for $i = 1, \cdots, 4$:

- ...
- Probability of eggs surviving the hatchable stage i and hatch as larvae (c_i), and the probability of aquatic forms (larvae and pupae) surviving the aquatic phase and emerging as adult mosquitoes (c_a):

$$\begin{cases} c_i = \frac{\sigma_i}{\mu_i+\sigma_i} \equiv \sigma_i g_i \\ c_a = \frac{\sigma_a}{\mu_a+\sigma_a} \end{cases}$$

Steady state

Trivial equilibrium P^0:

$$P^0 = \left(\left[\left(\bar{E}_i^s = 0, \bar{E}_i = 0\right), i = 1, \cdots, 4\right], \bar{A} = 0, \bar{M} = 0\right),$$

- Basic offspring number Q_0:

$$Q_0 = q_0 c_a \frac{f\phi}{\mu_f}$$

- Average number of eggs that survive four compartments and hatch as larvae q_0:

$$q_0 = b_1 c_1 + b_2 a_1 c_2 + b_3 a_2 a_1 c_3 + a_3 a_2 a_1 c_4$$

Trivial equilibrium is LAS if $Q_0 < 1$.

Non-trivial equilibrium P^*:

$$P^* = \left(\left[\bar{E}_i^s = E_i^{s*}, \bar{E}_i = E_i^*, i = 1, \cdots, 4\right], \bar{A} = A^*, \bar{M} = M^*\right)$$

- Auxiliary parameters:

$$\begin{cases} E_1^{s*} & = & d_1 f \phi M^* \\ E_1^* & = & b_1 g_1 f \phi M^* \\ E_2^{s*} & = & d_2 a_1 f \phi M^* \\ E_2^* & = & b_2 a_1 g_2 f \phi M^* \\ E_3^{s*} & = & d_3 a_2 a_1 f \phi M^* \\ E_3^* & = & b_3 a_2 a_1 g_3 f \phi M^* \\ E_4^{s*} & = & d_4 a_3 a_2 a_1 f \phi M^* \\ E_4^* & = & a_3 a_2 a_1 f \phi M^* \\ A^* & = & \frac{\mu_f}{\sigma_a} M^* \end{cases}$$

- ...

Steady state

Non-trivial equilibrium P^*:

$$P^* = \left(\left[\bar{E}_i^s = E_i^{s*}, \bar{E}_i = E_i^*, i = 1, \cdots, 4\right], \bar{A} = A^*, \bar{M} = M^*\right)$$

- ...
- Number of adult mosquitoes M^*:

$$M^* = \frac{\sigma_a}{\mu_f} k \left(1 - \frac{1}{Q_0}\right)$$

- Q_0 is the basic offspring number

Non-trivial equilibrium is LAS if $Q_0 > 1$.

Table 1

Experiment number	Quiescence ($days$)	Number of eggs	Eclosion ($eggs \times days^{-1}$)	Eclosion (%)
1	3	807	86.1	85.4
2	32	698	5.3	41.1
3	63	586	6.4	36.0
4	91	738	12.1	47.7
5	121	749	13.2	97.2
6	154	800	1.6	1.3
7	273	612	8.6	4.3
8	337	611	1.0	0.3
9	427	842	5.6	10.9
10	462	800	1.0	0.5
11	492	1708	1.0	0.2

From H.H.G. Silva, I.G. Silva, "Influence of eggs quiescence period on the *Aedes aegypti* (Linnaeus, 1762) (Diptera, Culicidae) life cycle at laboratory conditions", *Rev. Soc. Bras. Med. Trop.*, 32(4), 1999, pp. 349-355.

Table 2

Experiment number	Per-capita eclosion rate $(days^{-1})$	Per-capita mortality rate $(days^{-1})$
1	0.1067	0.0182
2	0.007593	0.0109
3	0.01092	0.0194
4	0.01640	0.0180
5	0.01762	0.00051
6	0.002	0.1518
7	0.01405	0.3127
8	0.00164	0.5439
9	0.00665	0.05437
10	0.00125	0.2488
11	0.000585	0.2922

Calculation of the per-capita eclosion and mortality rates.

Table 3

Stage – i	σ_i $(days^{-1})$	μ_i $(days^{-1})$	p_i	α_i $(days^{-1})$	ε_i $(days^{-1})$
1	0.10669	0.01824	5.85	0.2	0.1249
2	0.01164	0.01609	0.72	0.0091	0.02773
3	0.01762	0.0005077	34.7	0.0333	0.01813
4	0.00436	0.26730	0.016	0	0.27166

Estimation of the parameters σ_i, μ_i, calculation of the productivity indexes $p_i = \sigma_i/\mu_i$, α_i and ε_i, for $i = 1, \cdots, 4$.

Table 4

Temperature	σ_a $(days^{-1})$	μ_a $(days^{-1})$	μ_f $(days^{-1})$	ϕ $(eggs \times days^{-1})$
16^oC	0.02615	0.01397	0.03642	0.69714
28^oC	0.11612	0.06001	0.02877	8.29500

The estimated values of the parameters σ_a, μ_a, μ_f and ϕ for 16 and 28 degree Celsius (^oC).

Table 5

Seasons	Stage 1	Stage 2	Stage 3	Stage 4	Q_0
Summer (high)	78.04	1.531	6.4×10^{-3}	7.1×10^{-7}	79.57
Summer (low)	0.404	3.933	2.412	1.328	8.076
Winter (high)	5.122	0.101	4.2×10^{-4}	4.6×10^{-8}	5.223
Winter (low)	0.027	0.258	0.153	0.087	0.530

The basic offspring number Q_0 calculated using the values given in Tables 3 and 4, varying only the transition rates ε_i for two seasons: Summer (28^oC) and winter (16^oC). Two values are used for $i = 1, \cdots, 4$ $(days^{-1})$: $\varepsilon_i = 5.0$ (high) and $\varepsilon_i = 0.001$ (low). The basic offspring number corresponding to a unique eggs compartment is $Q_0^1 = 5.327$ for winter season.

Quiescence eggs in mosquito population

- The capacity of the *A. aegypti* eggs being stored during hostile abiotic factors and, then, hatch to larvae in favorable season with increased fitness – Essential to sustain *A. aegypti* population to face seasonality.
- Quiescence eggs having approximately 120 days – When allowed to hatch, these eggs presented the most producible capacity to originate larvae.
- Period of 4 months – Approximately the worst abiotic conditions to *A. aegypti* to survive.
- Quiescence of eggs of 4 months joined to the higher capacity of hatching – An important strategy to *A. aegypti* population to persist in seasonally varying environment.

Mathematical modelling – Transovarial transmission

Variables

- Human population is divided into four 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.
- l is the number of larvae (female) at time t, and the number of pupae in time t is p.
- The female mosquito population is divided into three 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 μ_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. Larva death is μ_l. Uninfected and infected larvae are denoted by l_1 and l_2. Larvae are transformed in adult mosquitoes at rate σ_a. The female mosquitoes mortality rate is μ_f.
- Among humans the transmission coefficient (or rate) is β_h, depending on ϕ. The infected persons are removed to recovered (immune) class by σ_h, the recovery rate. With respect to the vector, the susceptible mosquitoes are infected at a rate β_m.
- The transmission coefficients β_h and β_m are divided by N.

Model

- Modelling transovarian transmission

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

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

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

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

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

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

The gross reproduction number R_e, which encompasses transovarian transmission, is

$$R_e = R_0 + j,$$

where the basic reproduction number for horizontal transmission is

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

R_0 can be split in two partial contributions R_0^h and R_0^m defined by

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

Equilibrium points

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

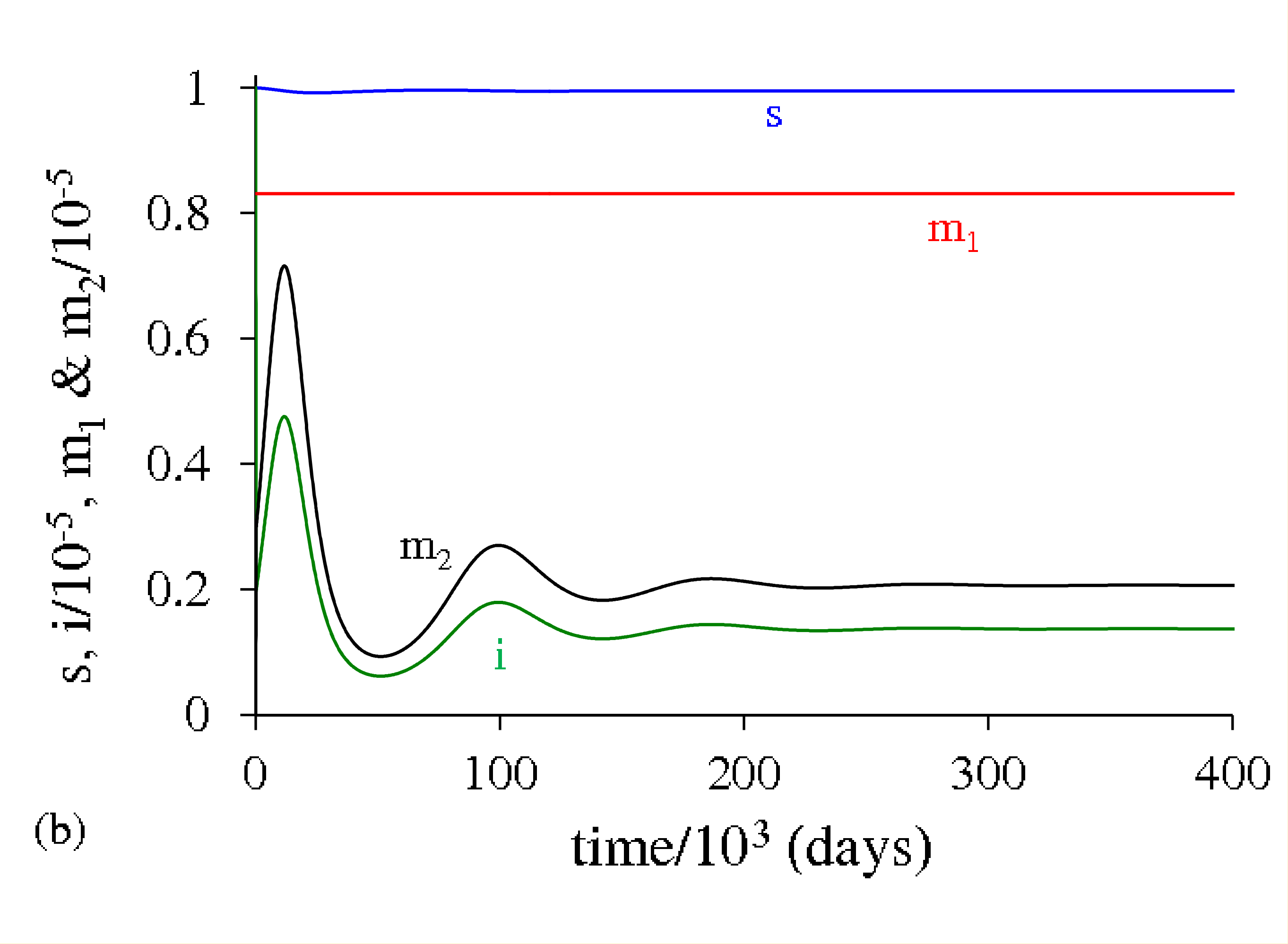
$$s^* \frac{m_1^*}{m^*} = \chi_e = \frac{1-j}{R_0}$$

and the threshold of product of fractions χ_e^{-1}, which encompasses transovarian transmission, can be written as

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

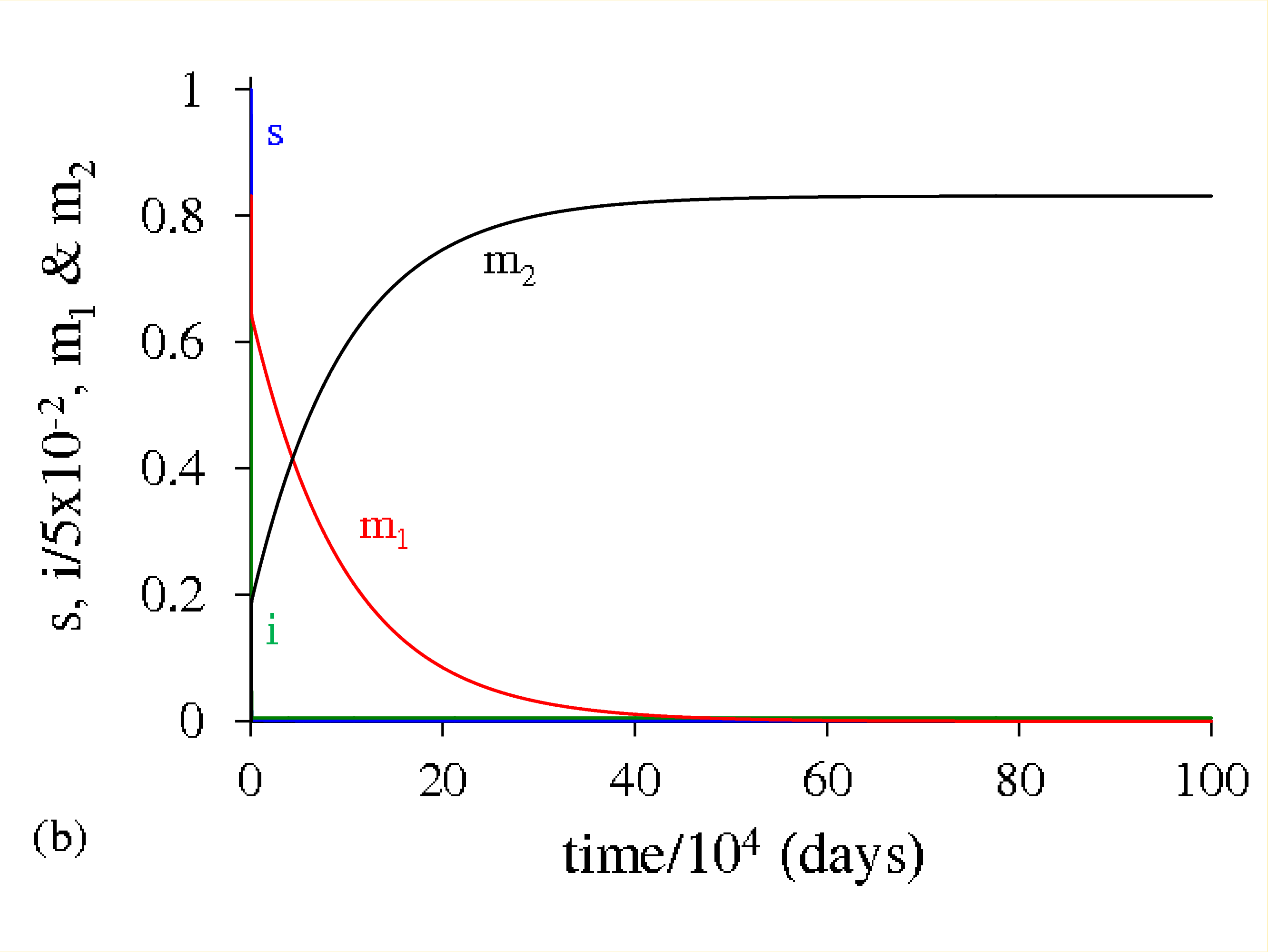
thus $\chi_e^{-1} = R_0^h[R_0^m/\,(1-j)]$.

Case $j = 0.02$ and $R_0 = 0.98495$



The case $R_e = R_0 + j = 1.00495 > 1$: non-trivial equilibrium.

Case $j = 1$ and $R_0 = 0.0099$



The case $R_e = R_0 + j = 1.0099 > 1$: non-trivial equilibrium. Displacement of susceptible mosquitoes.

Transovarial transmission in dengue epidemics

- Gross reproduction number $R_e = R_0 + j$.
- Basic reproduction number R_0 – Short term dynamics.
- Transovarial contribution j – Long term dynamics.
- Important role when R_0 near one.

Mathematical modelling – Abiotic effects

Variables

- Human population is divided into four compartments: s, e, i and r, which are the fractions at time t of, respectively, susceptible, exposed, infectious and recovered persons, with $s + e + i + r = 1$. The total number of the human population is N, which varies with time.
- l is the number of larvae (female) at time t, and the number of pupae in time t is p.
- The female mosquito population is divided into three compartments: m_1, m_2 and m_3, which are the numbers at time t of, respectively, susceptible, exposed and infectious mosquitoes. The size of mosquito population is $m = m_1 + m_2 + m_3$.

Parameters

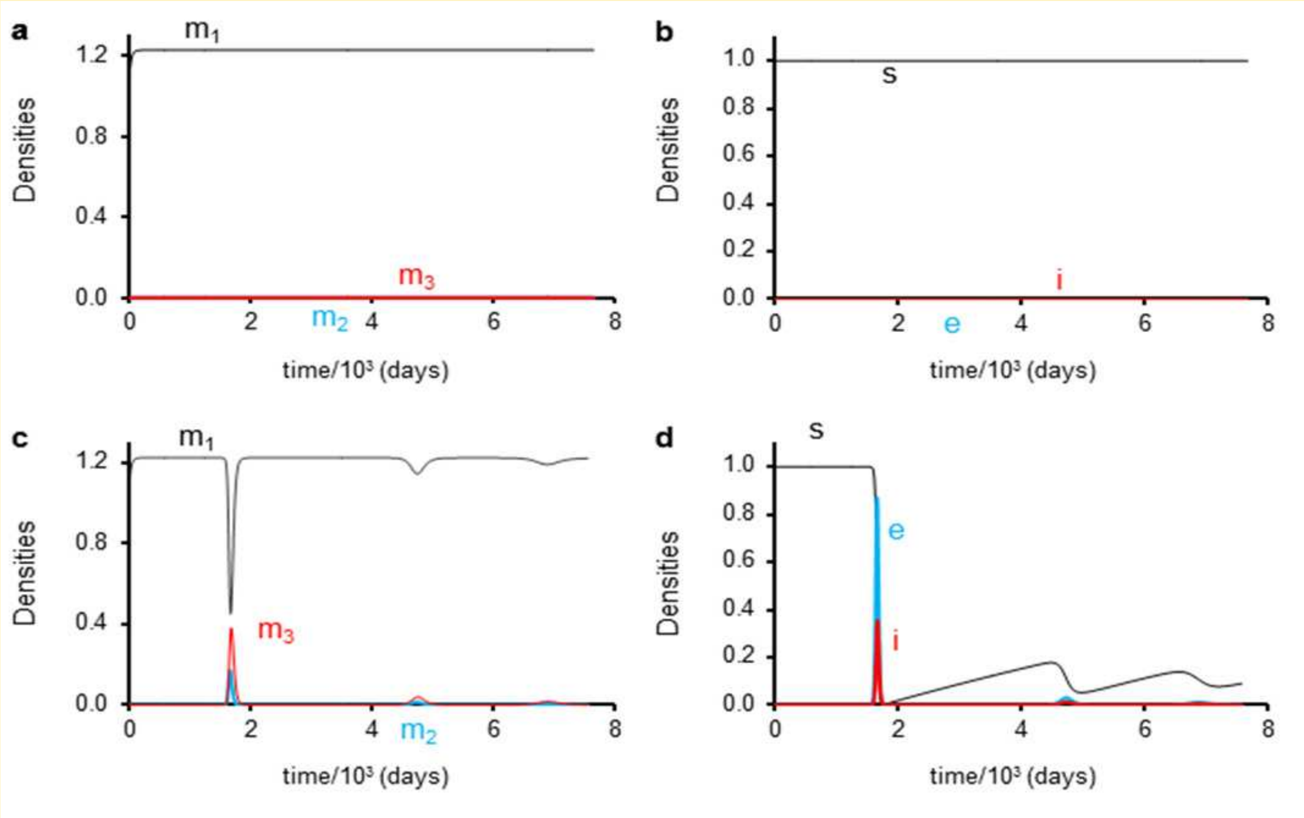
- The human natality rate is ϕ_h.
- The effective larvae production rate is given by $qf\left(1-l/C\right)\phi m$, where q and f are the fractions of eggs that are hatching to larva and that will originate female mosquitoes, respectively, and C is the total (carrying) capacity of the breeding sites. Change rate of larvae to pupae and larva death are σ_l and μ_l. The transformation rate of pupae to adult mosquitoes and death are σ_p and μ_p. The female mosquitoes mortality rate is μ_f.
- Among humans the transmission coefficient (or rate) is β_h, depending on ϕ. The exposed persons are transferred to infectious class by rate γ_h, and are removed to recovered (immune) class by σ_h, the recovery rate. With respect to the vector, the susceptible mosquitoes are infected at a rate β_m. These exposed mosquitoes are transferred to infectious class at a rate γ_m.
- The transmission coefficients β_h and β_m are divided by N.
- All mosquito related parameters depend om time (temperature and precipitation).

Abiotic: temnperature and precipitation

- Dengue transmission modelling

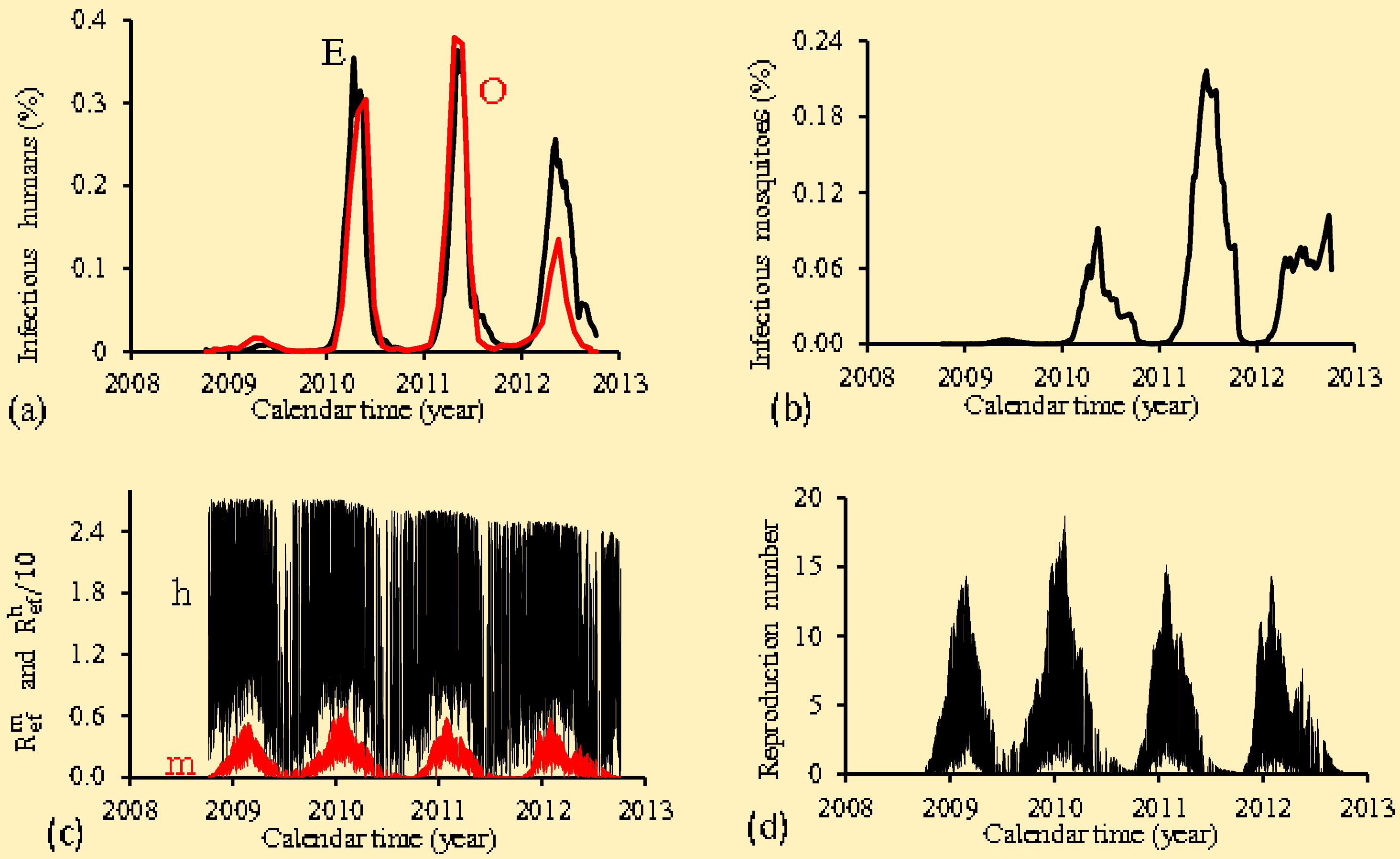
$$
\begin{cases}
\frac{d}{dt}l & = & qf\phi m\left(1-\frac{l}{C}\right)-\left(\sigma_l+\mu_l\right)l \\
\frac{d}{dt}p & = & \sigma_l l-\left(\sigma_p+\mu_p\right)p \\
\frac{d}{dt}m_1 & = & \sigma_p p-\left(\beta_m\phi i+\mu_f\right)m_1 \\
\frac{d}{dt}m_2 & = & \beta_m\phi i m_1-\left(\gamma_m+\mu_f\right)m_2 \\
\frac{d}{dt}m_3 & = & \gamma_m m_2-\mu_f m_3 \\
\frac{d}{dt}s & = & \phi_h-\left(\frac{\beta_h\phi}{N}m_3+\phi_h\right)s \\
\frac{d}{dt}e & = & \frac{\beta_h\phi}{N}m_3 s-\left(\gamma_h+\phi_h\right)e \\
\frac{d}{dt}i & = & \gamma_h e-\left(\sigma_h+\phi_h\right)i.
\end{cases}
$$

Constant parameters



No abiotic effects.

Varying parameters



Effects of abiotic factors: temperature and precipitation.

Abiotic conditions in dengue epidemics

- No abiotic factors – epidemics period of 2 years.
- Abiotic factors – annual epidemics.
- High incidence in summer and very low incidence in winter.

Conclusion

Conclusion

- Eggs surviving winter season.
- More fitted than fresh eggs.
- Transovarial transmission – infected eggs.

- Infected eggs – can dengue virus survive?
- Temperature and precipitation lead to annual cycle.
- Quescence egggs, infected eggs and abiotic variation – joint effects are ...

Thank You

Bibiography

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