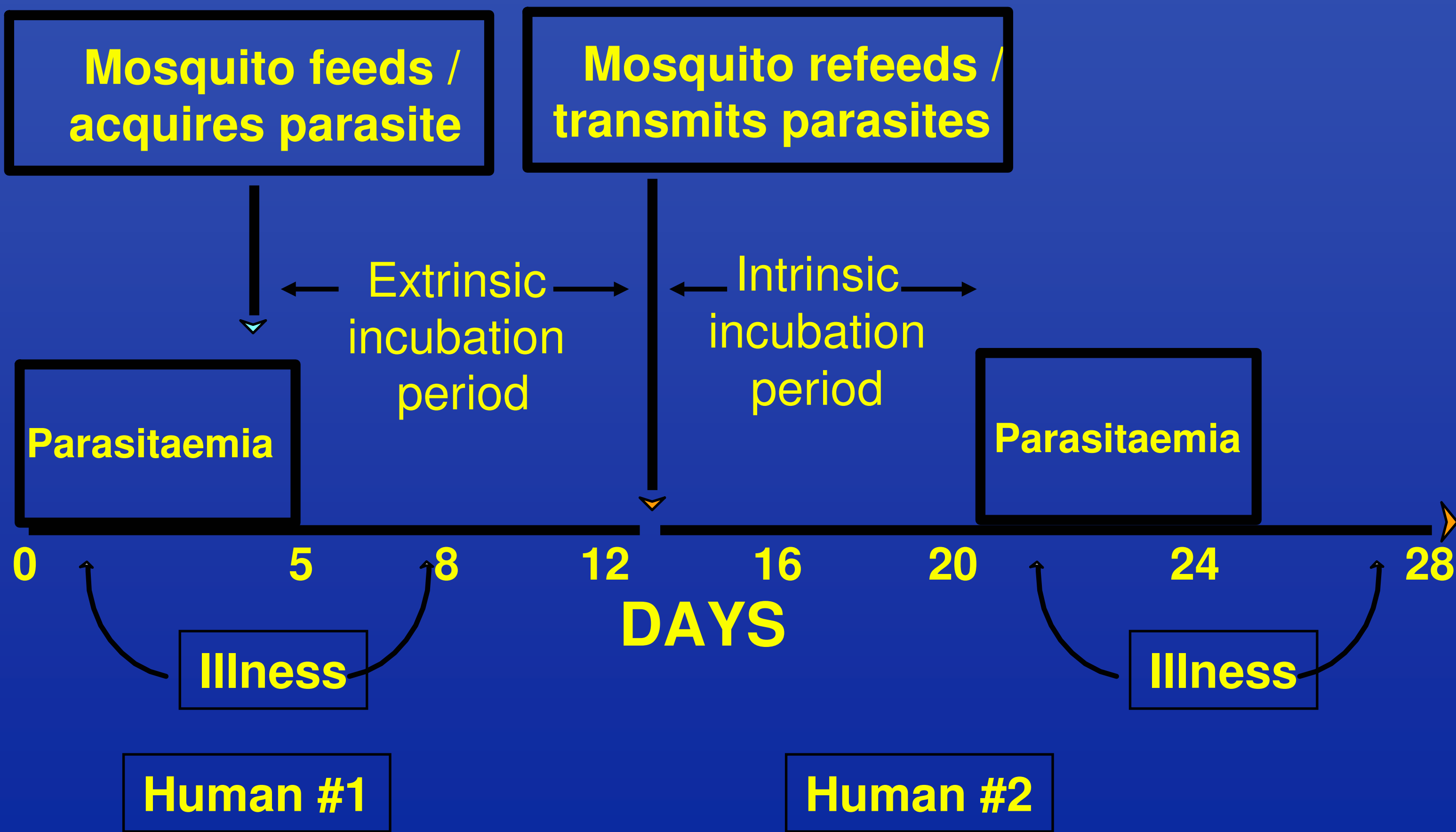
MAXIMUM THEORETICAL PREVALENCE OF VECTOR-BORNE INFECTIONS IN HUMANS

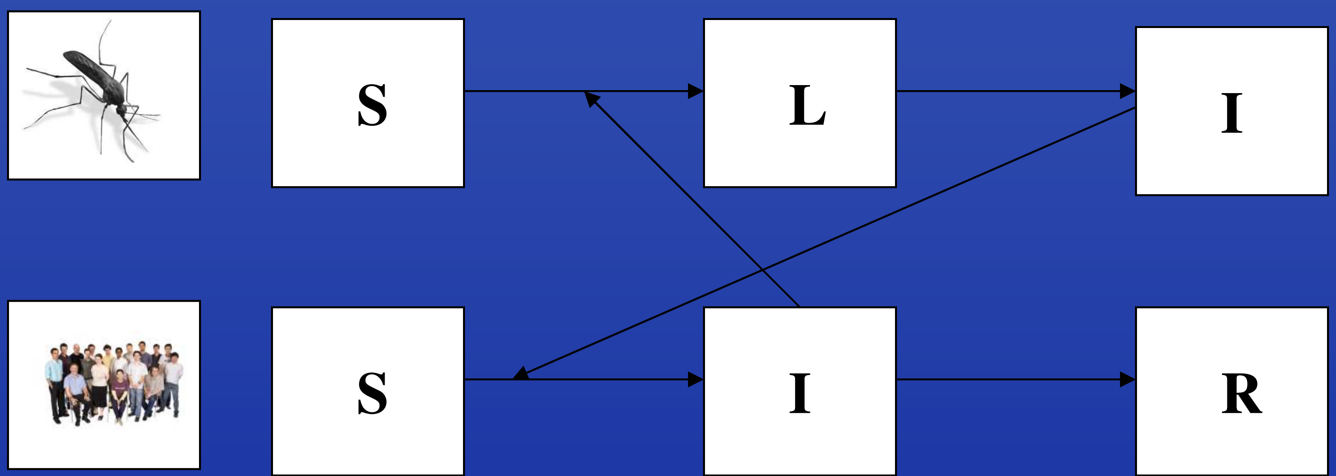
Francisco Antonio Bezerra Coutinho

University of São Paulo, Brazil

coutinho@dim.fm.usp.br

Transmission of Malaria by *Anopheles* mosquitoes




S
L
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S
I
R

$$\frac{dS_H}{dt} = -abI_M \frac{S_H}{N_H} - \mu_H S_H + r_H N_H \left(1 - \frac{N_H}{\kappa_H}\right) + \sigma_H R_H + \theta_H I_H$$

$$\frac{dL_H}{dt} = abI_M \frac{S_H}{N_H} - (\mu_H + \delta_H) L_H$$

$$\frac{dI_H}{dt} = \delta_H L_H - (\mu_H + \alpha_H + \gamma_H + \theta_H) I_H$$

$$\frac{dR_H}{dt} = \gamma_H I_H - \mu_H R_H - \sigma_H R_H$$

$$\frac{dS_M}{dt} = pc_S(t) S_E - \mu_M S_M - acS_M \frac{I_H}{N_H}$$

$$\frac{dL_M}{dt} = acS_M \frac{I_H}{N_H} - \gamma_M L_M - \mu_M L_M$$

$$\frac{dI_M}{dt} = \gamma_M L_M - \mu_M I_M + pc_S(t) I_E$$

$$\frac{dS_E}{dt} = \left[r_M S_M + (1-g) r_M (I_M + L_M)\right]\left(1 - \frac{(S_E + I_E)}{\kappa_E}\right) - \mu_E S_E - pc_S(t) S_E$$

$$\frac{dI_E}{dt} = \left[g r_M (I_M + L_M)\right]\left(1 - \frac{(S_E + I_E)}{\kappa_E}\right) - \mu_E I_E - pc_S(t) I_E$$

where

$$N_H = S_H + L_H + I_H + R_H$$

$$N_M = S_M + L_M + I_M$$

$$N_E = S_E + I_E$$

Table 1. Model variables and their biological meanings.

Variable	Biological Meaning
S_H	Susceptible humans
L_H	Latent humans
I_H	Infectious humans
R_H	Recovered humans
S_M	Uninfected mosquitoes
L_M	Latent mosquitoes
I_M	Infectious mosquitoes
S_E	Uninfected eggs (imm. Stages)
I_E	Infected aquatic forms

Table 2. Model's parameters and their biological significance

Parameter	Biological Meaning
a	Average daily rate of biting
b	Fraction of bites actually infective to humans
σ_H	Loss of immunity rate
δ_H	Latency rate in humans
θ_H	Loss of infectiousness in humans
μ_H	Human natural mortality rate
r_H	Birth rate of humans
κ_H	Carrying capacity of humans
α_H	Dengue mortality in humans
γ_H	Human recovery rate
p	Hatching rate of susceptible eggs
γ_M	Latency rate in mosquitoes
μ_M	Natural mortality rate of mosquitoes
r_M	Oviposition rate
g	Proportion of infected eggs
κ_E	Carrying capacity of eggs
μ_E	Natural mortality rate of eggs
c	Fraction of bites actually infective to mosquitoes
c_S	Climatic factor

Table 3. Model's structure as a function of the parameters

Model's structure	δ_H	γ_H	σ_H	θ_H
SI	$\rightarrow \infty$	0	0	0
SIS	$\rightarrow \infty$	0	0	$\neq 0$
SIR	$\rightarrow \infty$	$\neq 0$	0	0
SIRS	$\rightarrow \infty$	$\neq 0$	$\neq 0$	0
SEIR	$\neq 0$	$\neq 0$	0	0
SEIRS	$\neq 0$	$\neq 0$	$\neq 0$	0

$$I_M^* = \frac{(\delta_H + \mu_H)(\mu_H + \gamma_H + \alpha_H + \sigma_H)I_H^*}{ab\delta_H\left(1 - \left(\frac{(\mu_H + \sigma_H)(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H) + \gamma_H\delta_H}{\delta_H(\mu_H + \sigma_H)}\right)\frac{I_H^*}{N_H^*}\right)}$$

$$\frac{I_H^*}{N_H^*} = \frac{(\gamma_M + g\mu_M)a^2bc\dfrac{N_M^*}{N_H^*} - Q(\mu_M + \gamma_M)\mu_M(1-g)}{(\gamma_M + g\mu_M)a^2bc\delta_H\dfrac{N_M^*}{N_H^*}Z + acQ(\mu_M + \gamma_M)}$$

$$Q = \left(\frac{(\mu_H + \sigma_H)(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H) + \gamma_H \delta_H}{\delta_H (\mu_H + \sigma_H)} \right)$$

$$Z = \left[\frac{((\delta_H + \mu_H)(\mu_H + \gamma_H + \alpha_H + \sigma_H))}{\delta_H} \right]$$

and

$$N_M^* = \frac{pc_S}{\mu_M} \kappa_E \left[1 - \frac{(\mu_M)(\mu_E + pc_S)}{r_M pc_S} \right]$$

$$N_H^* = \frac{-B + \sqrt{B^2 - 4AC}}{2A}$$

where

$$A = acr_H\Omega$$

$$B = -ac\Omega\kappa_H(r_H - \mu_H) + \Gamma Z r_H - \Omega\mu_M(1-g)\alpha_H\kappa_H$$

$$C = -\Gamma\kappa_H(r_H - \mu_H)Z + \Gamma\alpha_H\kappa_H$$

and

$$\Omega = Q(\gamma_M + \mu_M)$$

$$\Gamma = (\gamma_M + g\mu_M)a^2bc\delta_H N_M^*$$

$$R_0 = \frac{(\gamma_M + g\mu_M)a^2bc\dfrac{N_M(0)}{N_H(0)}}{\left(\dfrac{(\mu_H+\sigma_H)(\mu_H+\gamma_H+\alpha_H+\delta_H+\theta_H)+\gamma_H\delta_H}{\delta_H(\mu_H+\sigma_H)}\right)(\mu_M+\gamma_M)\mu_M(1-g)}$$

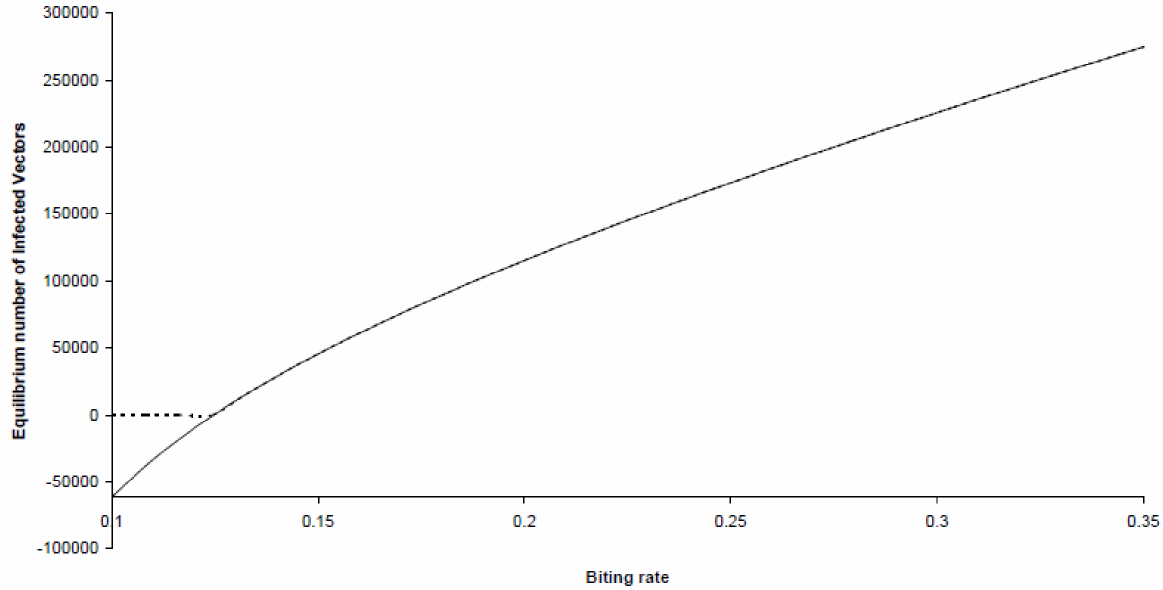
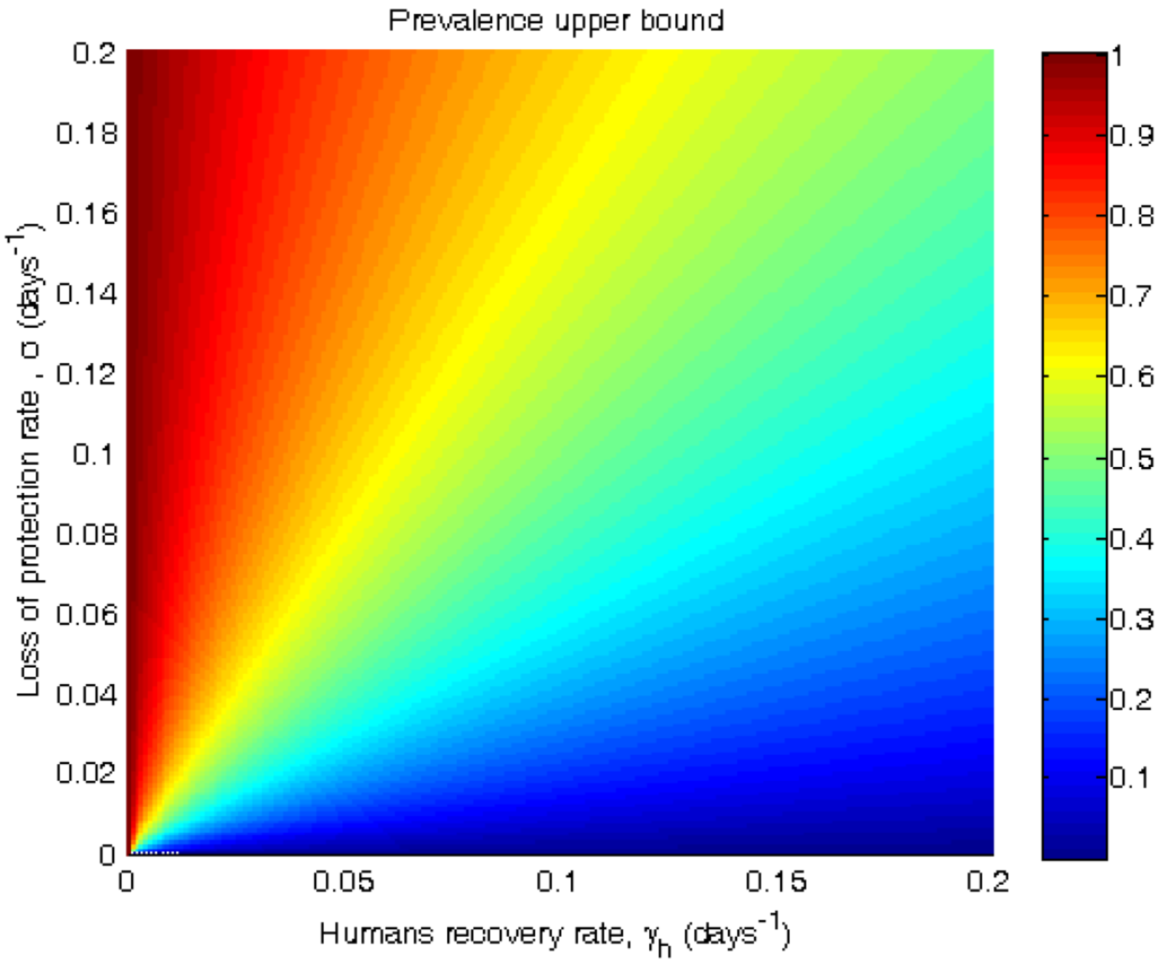


Figure 1. Plot of equation (2) as a function of the biting rate, a, calculated in two ways: in the dotted line the number of infected vectors is calculated with the host prevalence I_H^* / N_H^* directly derived from the dynamics of system (1); in the continuous line I_H^* / N_H^* is calculated from equation (3) and for a such that R_0 can be less than one and, therefore $I_H^* / N_H^* < 0$.

$$\lambda_H^* = ab\frac{I_M^*}{N_H^*}$$

$$\lambda_H^* = \frac{(\delta_H + \mu_H)(\mu_H + \gamma_H + \alpha_H + \sigma_H)\frac{I_H^*}{N_H^*}}{\delta_H\left(1 - \left(\frac{(\mu_H + \sigma_H)(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H) + \gamma_H\delta_H}{\delta_H(\mu_H + \sigma_H)}\right)\frac{I_H^*}{N_H^*}\right)}$$

$$\left(\frac{I_H^*}{N_H^*}\right)_{MAX} = \frac{\delta_H(\mu_H + \sigma_H)}{(\mu_H + \sigma_H)(\mu_H + \gamma_H + \alpha_H + \delta_H + \theta_H) + \gamma_H \delta_H}$$


Prevalence upper bound
0.2
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
Loss of protection rate , σ (days-1)
0
0.05
0.1
0.15
0.2
Humans recovery rate, γh (days-1)
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1

Some Important Pitfalls in Modelling Vector-Borne Infections

Main Variables

Variable	Biological description
S_H	density of susceptible humans
L_H	density of latent humans
I_H	density of infected humans
R_H	density of recovered humans
S_M	density of susceptible mosquitoes
L_M	density of latent mosquitoes
I_M	density of infected mosquitoes

Usual Equations: Wrong!

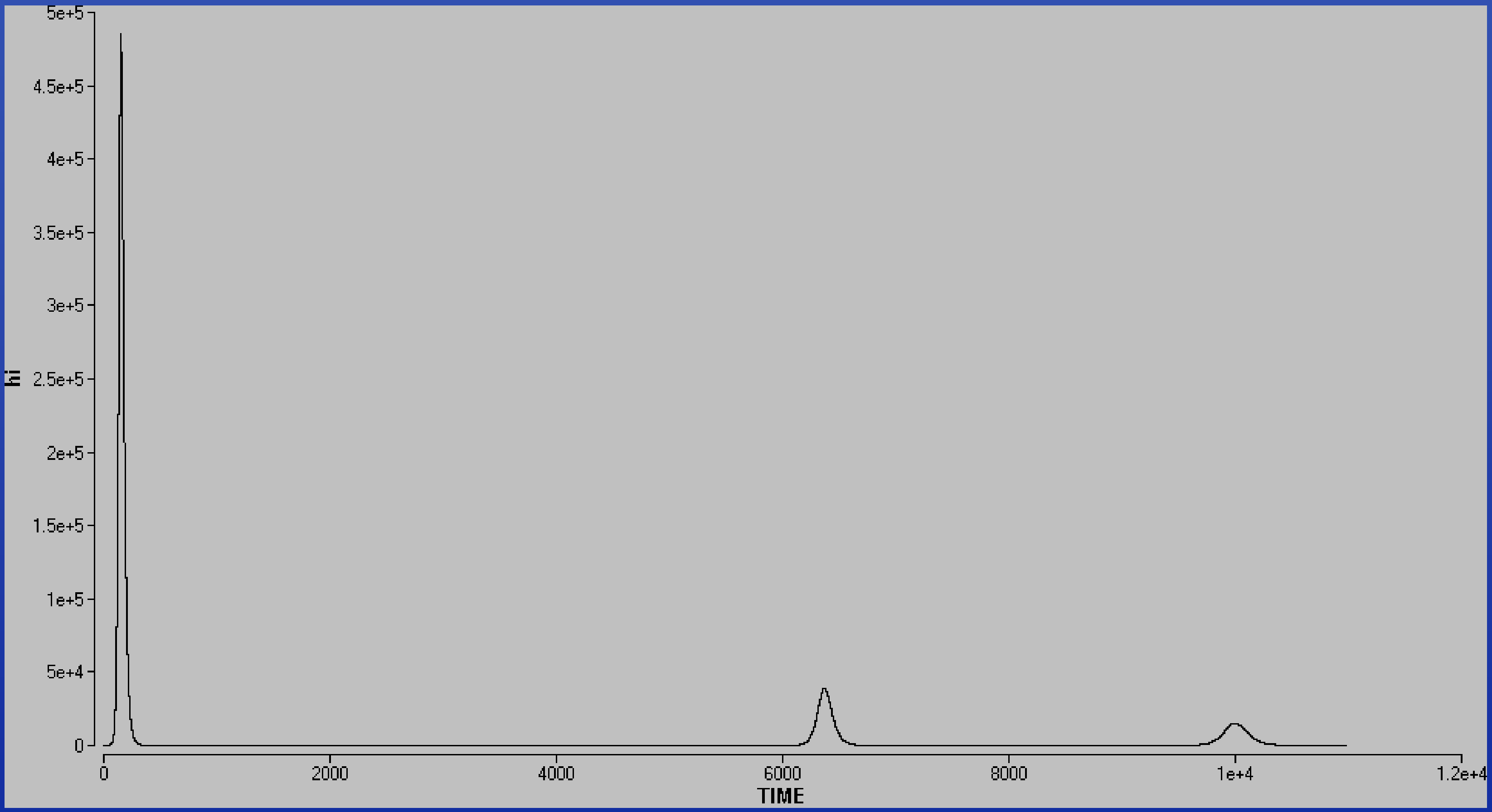
$$\begin{aligned}
\frac{dS_H}{dt} &= -ab(I_M + \eta_M L_M)\frac{S_H}{N_H} - \mu_H S_H + \sigma_H R_H + \theta_H I_H + \Lambda_H \\
\frac{dL_H}{dt} &= ab(I_M + \eta_M L_M)\frac{S_H}{N_H} - (\mu_H + \delta_H)L_H \\
\frac{dI_H}{dt} &= \delta_H L_H - (\mu_H + \alpha_H + \gamma_H + \theta_H)I_H \\
\frac{dR_H}{dt} &= \gamma_H I_H - (\mu_H + \sigma_H)R_H \\
\frac{dS_M}{dt} &= -ac\frac{(I_H + \eta_H L_H)}{N_H}S_M - \mu_M S_M + \Lambda_M \\
\frac{dL_M}{dt} &= ac\frac{(I_H + \eta_H L_H)}{N_H}S_M - (\mu_M + \gamma_M)L_M \\
\frac{dI_M}{dt} &= \gamma_M L_M - \mu_M I_M
\end{aligned}$$

One particular point is raised by the term:

$$ab(I_M + \eta_M L_M)\frac{S_H}{N_H}$$

Let us explain the meaning of this term. The parameter a is a composed quantity. Let A be the area explored by a mosquito by the joint movement of the humans and the mosquitoes. Let ξ be the number of bites a mosquito inflicts per unit time and per unit area in the humans. Then, $\xi A I_M$ is the number of bites that $A I_M$ infected mosquitoes inflict on $N_H A$ people. Hence, the fraction of bites given on susceptible humans is $\xi A I_M \frac{S_H A}{N_H A} = a I_M \frac{S_H}{N_H}$, where $a = \xi A$

Why is this important?


5e+5
4.5e+5
4e+5
3.5e+5
3e+5
2.5e+5
2e+5
1.5e+5
1e+5
5e+4
0
hi
0
2000
4000
6000
8000
1e+4
1.2e+4
TIME

The Correct Equations in 1 dimension

$$\begin{aligned}
\frac{\partial S_H(x,t)}{\partial t} &= -\lambda_H(x,t)S_H(x,t) - \mu_H S_H(x,t) + \Lambda_H(x,t) \\
\frac{\partial L_H(x,t)}{\partial t} &= \lambda_H(x,t)S_H(x,t) - (\mu_H + \gamma_H)L_H(x,t) \\
\frac{\partial I_H(x,t)}{\partial t} &= \gamma_H L_H(x,t) - (\mu_H + \alpha_H + \delta_H)I_H(x,t) \\
\frac{\partial R_H(x,t)}{\partial t} &= \delta_H I_H(x,t) - \mu_H R_H(x,t) \\
\frac{\partial S_M(x,t)}{\partial t} &= -\lambda_M(x,t)S_M(x,t) - \mu_M S_M(x,t) + \Lambda_M(x,t) \\
\frac{\partial L_M(x,t)}{\partial t} &= \lambda_M(x,t)S_M(x,t) - (\mu_M + \gamma_M)L_M(x,t) \\
\frac{\partial I_M(x,t)}{\partial t} &= \gamma_M L_M(x,t) - \mu_M I_M(x,t),
\end{aligned}$$

where

$$\lambda_H(x,t) = \frac{1}{N_H}\int_0^D dx' ab\beta_H(x,x')I_M(x',t)$$

and

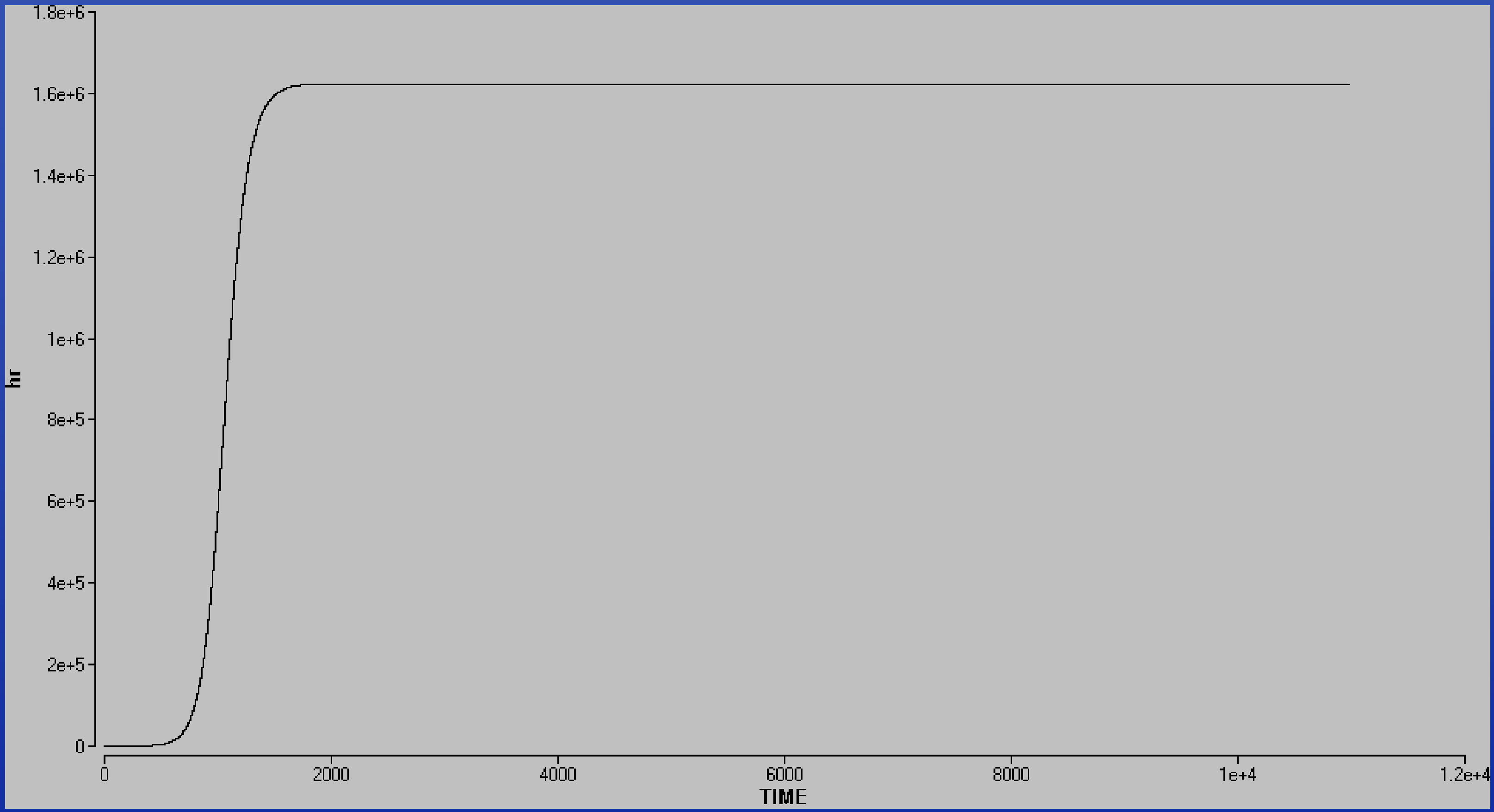
$$\lambda_M(x,t) = \frac{1}{N_H}\int_0^D dx' ac\beta_M(x,x')I_H(x',t).$$

The Correct Equations in 2 dimensions

$$\lambda_H(r,\theta,t) = \frac{1}{N_H}\int_0^D r'dr'\int_0^{2\pi} d\theta' ab\beta_H\left(\sqrt{r^2+r'^2-2rr'\cos(\theta-\theta')}\right) I_M(r',\theta',t) \quad (24)$$

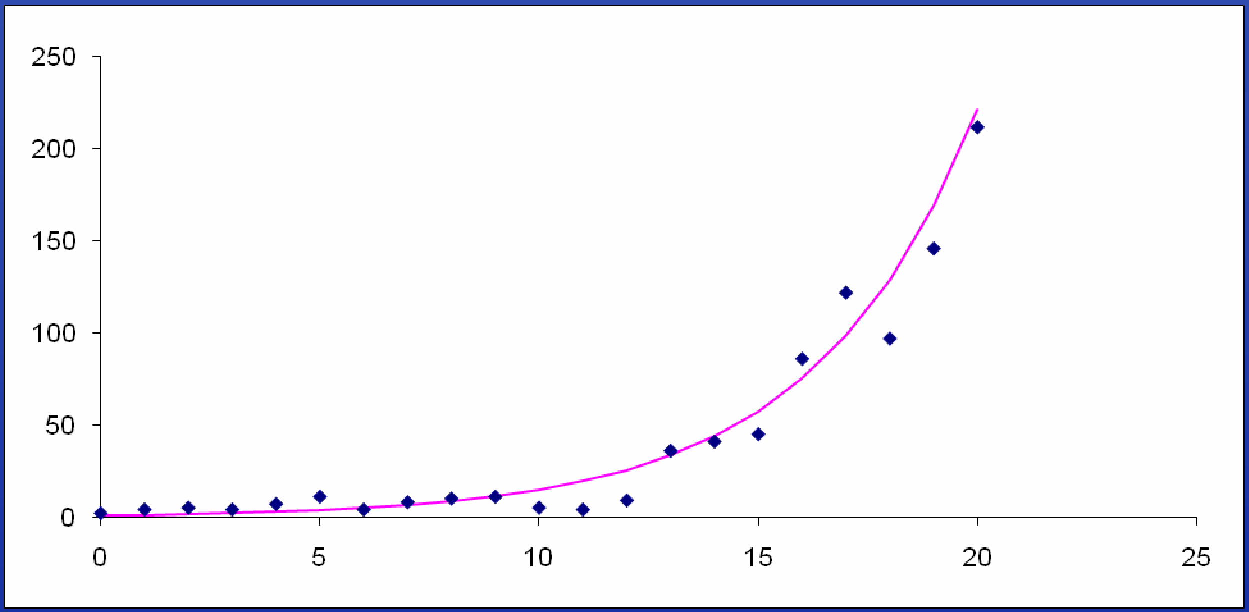
and

$$\lambda_M(r,\theta,t) = \frac{1}{N_H}\int_0^D r'dr'\int_0^{2\pi} d\theta' ac\beta_M\left(\sqrt{r^2+r'^2-2rr'\cos(\theta-\theta')}\right) I_H(r',\theta',t)$$



1.8e+6
1.6e+6
1.4e+6
1.2e+6
1e+6
8e+5
6e+5
4e+5
2e+5
0
hr
0
2000
4000
6000
8000
1e+4
1.2e+4
TIME

A comment on the estimation of the Basic Reproduction Number for vector-borne infections: Another Pitfall


250
200
150
100
50
0
0
5
10
15
20
25

$$R_0 = \left[\frac{\ln(2)}{(\mu+\gamma)t_d} + 1\right]$$

Anderson and May (1991)

$$R_0 = 1 + \frac{\Lambda}{(\mu+\gamma)}$$

Marques *et al.* (1994)

$$R_0 = \left(1 + \frac{\Lambda}{\mu}\right)\left(1 + \frac{\Lambda}{\gamma}\right)$$

Massad *et al.* (2001)

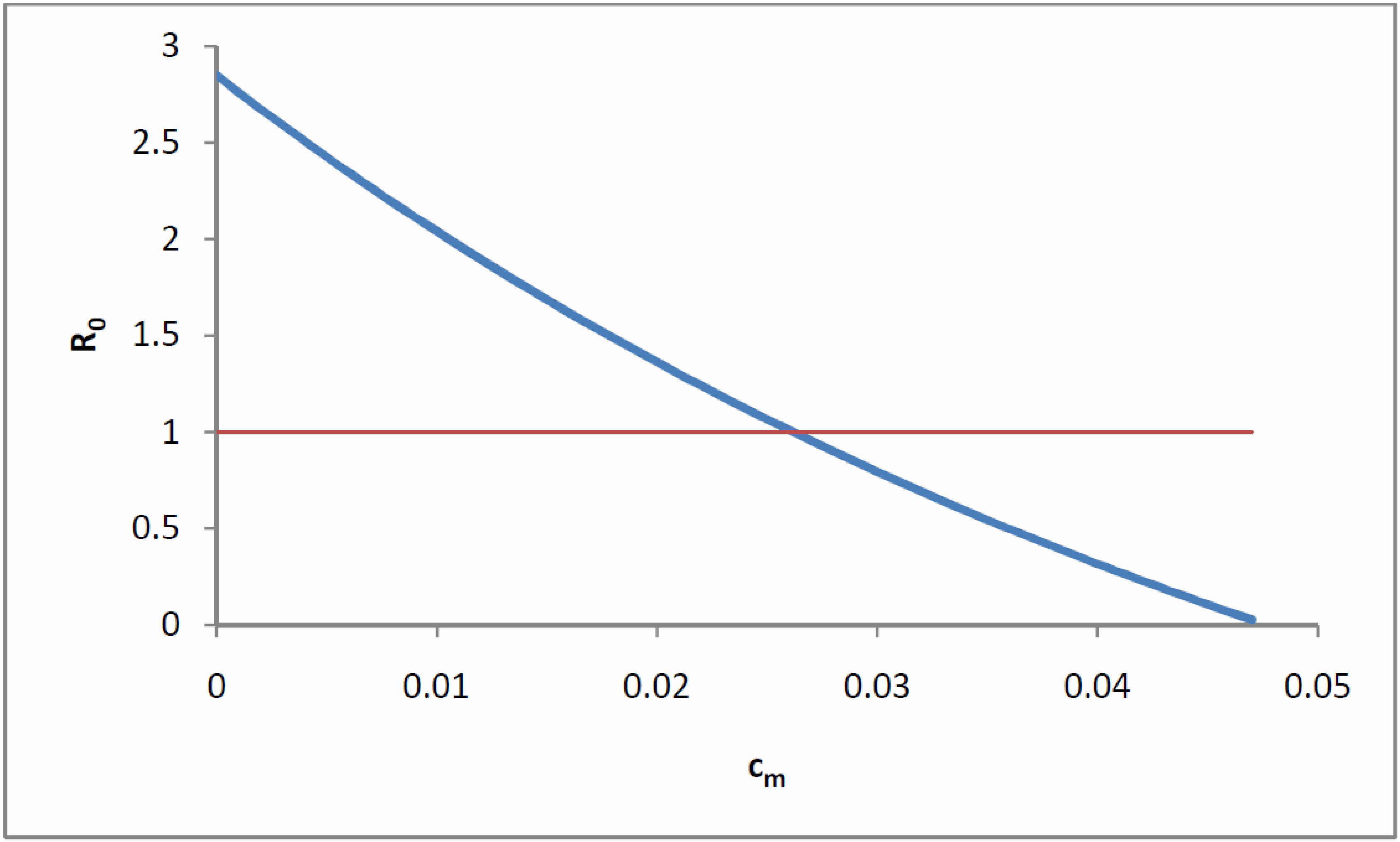
$$R_0 = \left(1 + \frac{\Lambda}{\mu}\right)\left(1 + \frac{\Lambda}{\gamma}\right)e^{\Lambda(\tau_i+\tau_e)}$$

Favier *et al.* (2006)

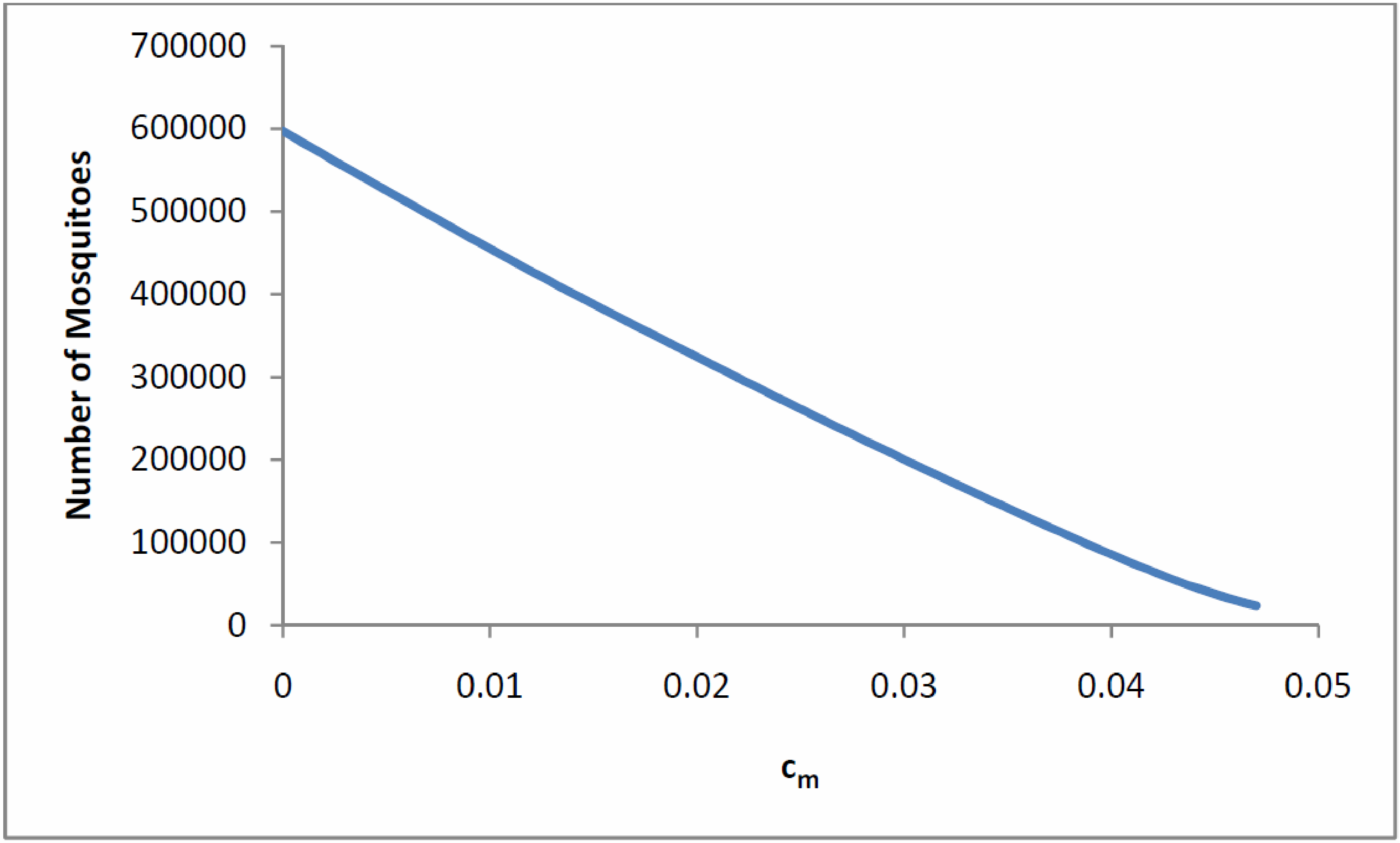
In a paper published in this journal, Pinho et al. (2010) conclude that "The value of R_0 is greater than 1 for the epidemic in 1995-1996 for any chosen value of the vector-control parameter, indicating that other strategies would be necessary besides the adult vector-control, as such as the control of the mosquito's aquatic phase, to reduce its force of infection and therefore to control the epidemic".

Pinho's et al. equation (3.8) assumes, as mentioned above, $\Lambda > 0$ and to get $R_0 < 1$ another method must be used, as described in Massad et al. (2010).

$$R_0^2 = \left(\frac{\Lambda}{\theta_m+\mu_m+c_m} + 1\right)\left(\frac{\Lambda}{\theta_h+\mu_h} + 1\right)\left(\frac{\Lambda}{\theta_m+c_m} + 1\right)\left(\frac{\Lambda}{\alpha_h+\mu_h} + 1\right)$$



3
2.5
2
1.5
1
0.5
0
R0
0
0.01
0.02
0.03
0.04
0.05
cm


700000
600000
500000
400000
300000
200000
100000
0
Number of Mosquitoes
0
0.01
0.02
0.03
0.04
0.05
c_m

Collaborators:

Marcos Amaku
Luis Fernandez Lopez
Marcelo Nascimento Burattini
Claudio José Struchiner
Eduardo Massad