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Dengue Fever Modeling with Virus Load and Antibody Levels

Paulo Amorim[1], Maria S. Aronna[2], Débora O. Medeiros[3]
FGV-EMAp, Rio de Janeiro, RJ

Dengue fever is an arboviral disease transmitted from human to human by the *Aedes aegypti* mosquito, which has rapidly become one of the most concerning tropical diseases, affecting millions of people every year. The realistic modeling of Dengue transmission and epidemiology presents several challenges [6]: First, being a vector-borne disease, it is important to model the mosquito population in addition to the host (human) population. Second, there are four serotypes of the virus, complicating the epidemiological dynamics [3]. Finally, so-called antibody-dependent enhancment (ADE) can occur [4], in which the presence of multivalent antibodies from a previous infection can, in certain situations, enhance a new infection. Therefore, it has become apparent that modeling the within-host antibody dynamics can be an important aspect of dengue modeling.

Motivated by these observations and the related works [1, 2, 5], we introduce a new dengue transmission model, taking the form of a system of structured (transport) equations and ODEs. The model acts on the following dynamical variables: $F(t,s,y)$ is the infected (human) host population with virus level higher than some detectable threshold s_0, distributed by virus load $s > s_0$ and antibody (Ab) titer $y > 0$. $S(t,y)$ is the recovered host population distributed by Ab titer $y > y_0$, where y_0 is an Ab detection threshold. $E(t)$ is the quantity of hosts in the incubation period, and $P(t)$ is the quantity of susceptible hosts. E_v and I_v represent the vector (mosquito) dynamics, with incubation and infected compartments. The system takes the following form:

$$
\begin{aligned}
&\partial_t F(t,s,y) + \partial_s \left(a_1 F(t,s,y)s - a_2 F(t,s,y)y\right) \\
&\qquad + \partial_y \left(-a_3 F(t,s,y)y + a_4 F(t,s,y)s\right) = 0, \\
&\partial_t S(t,y) + \partial_y \left(-a_3 S(t,y)y\right) = -F(t,s_0,y)\big(a_1 s_0 - a_2 y\big)_-, \\
&\dot{E}(t) = bI_v(t)P(t) - \frac{a_1 s_0}{\tau_h} E(t), \\
&\dot{P}(t) = -bI_v(t)P(t) + a_3 y_0 S(t,y_0), \\
&\dot{E}_v(t) = \left(\int_0^\infty \int_{s_0}^\infty F(t,z,y)\gamma(z)dzdy\right)(1 - E_v(t) - I_v(t)) - \frac{1}{\tau_v} E_v(t), \\
&\dot{I}_v(t) = \frac{1}{\tau_v} E_v(t) - \mu_v I_v(t),
\end{aligned}
\tag{1}
$$

The system must be supplemented with some boundary conditions which we omit here for the sake of brevity. The constants appearing in (1) are explained in Table 1.

The transport terms in the first equation of (1) represent the within-host virus reproduction, the Ab effect on the virus, the Ab decay rate, and the Ab production in the presence of virus. The transport term on the second equation represents the natural Ab decay in individuals with

[1]paulo.amorim@fgv.br
[2]soledad.aronna@fgv.br
[3]debora.medeiros@fgv.br

Table 1: Variables and parameters in the system (1).

Notation	Definition	Value
s_0	Minimum detectable viral load	$s_0 > 0$
y_0	Minimum detectable Ab titer	$y_0 > 0$
a_1	Virus growth rate in host	≥ 0
a_2	viral load decay rate in presence of antibody	≥ 0
a_3	Ab titer decay rate	≥ 0
a_4	Ab titer production rate in presence of virus	≥ 0
b	Vector to host transmission rate	≥ 0
μ_h	Natural host death rate	≥ 0
μ_v	Natural vector death rate	≥ 0
$\gamma(\cdot)$	Efficiency of host to vector transmission	≥ 0
τ_v	virus incubation period in the vector	$\tau_v \in [8, 12]$
τ_h	virus incubation period in the host	$\tau_h \approx 7$

little or no viral load. The right-hand side of the second equation represents the flow from the infected population F as infected individuals reach the threshold viral load s_0 by recuperation. the remaining equations follow standard SIS/SIR type dynamics, except that the exposure rate of vectors is a (nonlocal) function of the total infected population.

Partial results for this system include numerical simulations, which we will report, and a numerical estimate of the reproduction number R_0. Mathematical questions related to this model include the existence of an endemic equilibrium (which is not immediate due to the PDE nature and the couplings), and the stability of the disease-free equilibrium.

Thus, the goal of this work is to determine if the above system can serve as a reasonable modeling framework for dengue dynamics, with the aim of later introducing more specific terms related to ADE, multiple virus strains, and vaccines.

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