Virus maturity effects in a within-host dengue infection model

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Introduction

Cleavage of the precursor membrane (prM) protein is required to activate DENV infectivity. DENV-infected cells secrete $\approx 30\%$ of prM-containing immature virus particles[1]. Anti-prM antibodies markedly increase the specific infectivity of immature DENV[2]. Cells releasing immature particles trigger plasmocytoid dendritic cells (pDCs) interferon response more potently than cells producing fusion-competent mature virus[4].

A within-host compartmental model differentiating virus particles according to maturation status is proposed to study whether pDC activation by DENV-infected cells leads to viral replication suppression or to subsequent recruitment of DENV permissive cells and systemic viral spread.

Materials and Methods

Mathematical model, primary infection

$$
\begin{aligned}
S' &= S_0 - \beta S V_m - d_S S + \xi N \quad \text{target cells}\\
I' &= \beta S V_m - kI \quad \text{infected cells in } \textit{eclipse phase}\\
I'_m &= (1-\alpha)kI - d_I I_m - \delta_m I_m N \quad \text{cells releasing } \textit{mature} \text{ particles}\\
I'_i &= \alpha k I - d_I I_i - \delta_i I_i N \quad \text{cells releasing } \textit{immature} \text{ particles}\\
V'_m &= p_m I_m - \beta V_m S - d_m V_m \quad \textit{mature} \text{ virus particles}\\
V'_i &= p_i I_i - d_i V_i \quad \textit{immature} \text{ virus particles}\\
D'_i &= D_0 - q D_i I_i - d_D D_i \quad \text{inactive pDCs}\\
D'_a &= q D_i I_i - d_D D_a \quad \text{activated pDCs}\\
N' &= \varrho D_a - (d_N + \xi) N \quad \text{other immune cells, activated by pDCs}
\end{aligned}
$$

Results

Basic reproduction number

$$R_0 = \frac{(1-\alpha) p_m \beta S_0}{d_I (d_m d_S + \beta S_0)}$$

At most two non-negative steady states other than DFE when

$$
\begin{aligned}
\frac{d_D^2 d_I (\xi + d_N)}{\varrho D_0 q \xi} &< \alpha < 1 - \frac{1}{p_m}\left(d_I + \frac{\varrho D_0}{d_D(\xi + d_N)}\delta_m\right)\\
g'(0) &< f'(0)
\end{aligned}
$$

Outlook

Locally stable positive viral load for $R_0 < 1$ which may be below the *limit of detection*.

Future work: to perform a parameter scan, to incorporate antibody response and immune complexes and to consider a secondary DENV infection.

References

[1] J. Gen. Virol. (2008) 89: 3047.
[2] Curr. Opin. Virol. (2012) 2: 168.
[3] Trends Microbiol. (2011) 19: 248.
[4] PLoS Pathog (2014) 10: e1004434.

The research has been partially supported by the Bulgarian National Science Fund under grant contract FNI-DKOST01/29.

DENV infectivity

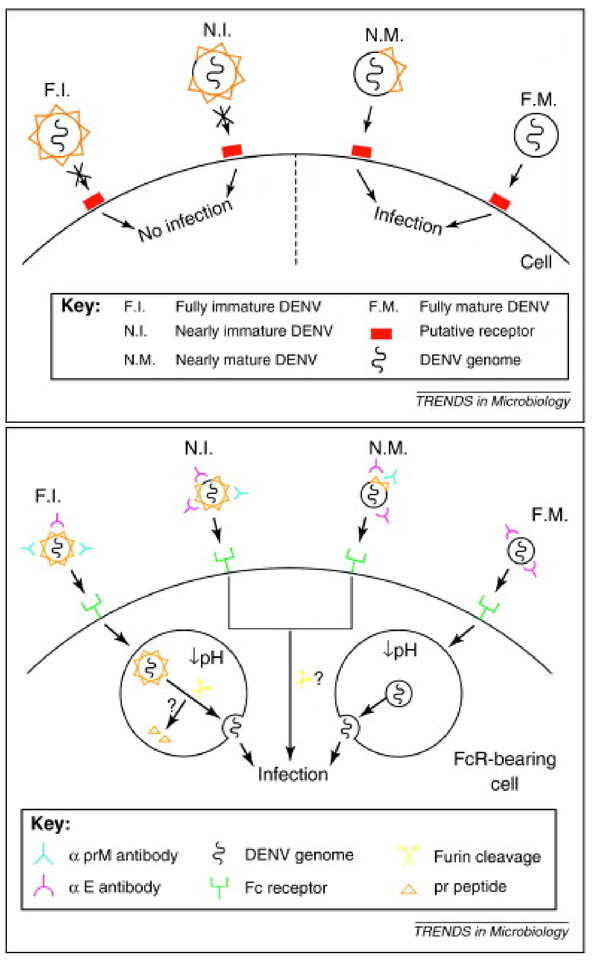

Figure 1: DENV infectivity in the absence and presence of antibodies[3].

Bifurcation

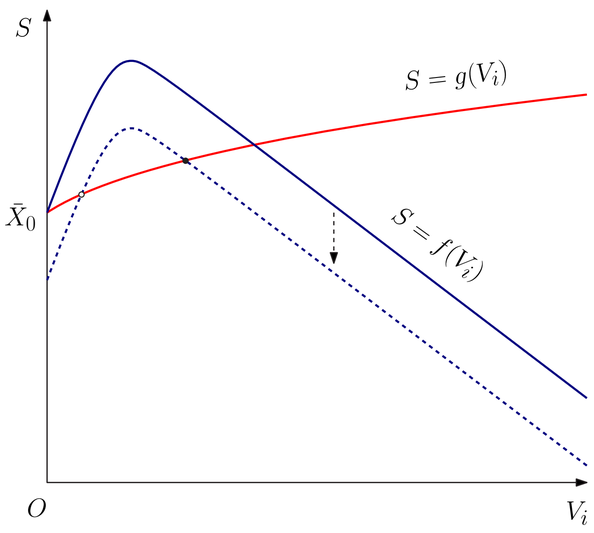

Figure 2: Algebraic transformation to a planar system in S, V_i.

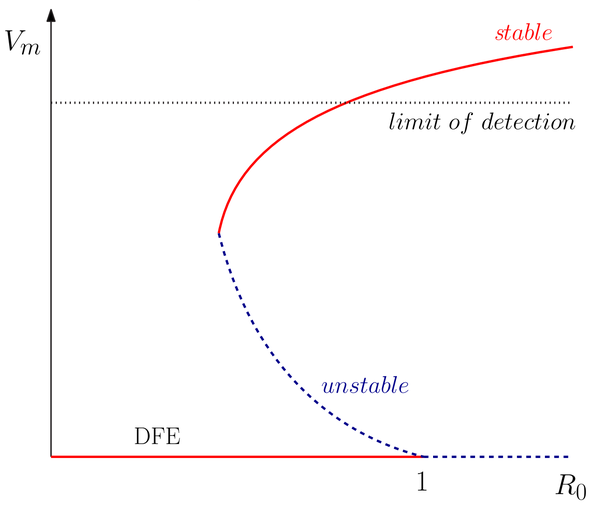

Figure 3: Possible backward bifurcation with R_0 decreasing through 1.