Multiscale Modeling of Vector-Borne Diseases

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Background

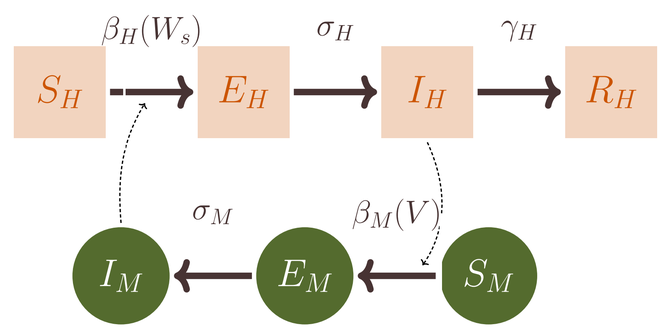
- Infectious diseases, especially vector-borne diseases, spread in a complex manner involving several biological scales
- Within-host viral dynamics do play a role in population-level transmission
- Multiscale models can link epidemiology and within-host dynamics, but face challenges of complexity and limited data

Aims

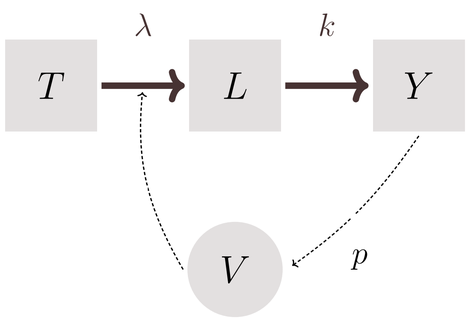
- Develop and analyze a mechanistic multiscale model linking within-host/vector dynamics to population-level transmission
- To assess the role of dose-response functions linking viral load to transmission
- Investigate when multiscale modeling is essential for understanding vector-borne diseases

Model Overview

Between-host (BH): SEIR hosts + SEI mosquitoes



Within-host (WH): Target-cell model with eclipse phase (T, L, Y, V)



Within-vector (WV): Logistic growth in the *midgut* $\mathbf{W_m}$ and *salivary glands* $\mathbf{W_s}$. ODE system:

$$\frac{dW_m}{d\tau} = r_m W_m \left(1 - \frac{W_m}{K_m}\right) - \nu W_m,$$
$$\frac{dW_s}{d\tau} = \frac{\nu W_m^2}{A + W_m^2} + r_s W_s \left(1 - \frac{W_s}{K_s}\right).$$

midgut→saliva flow mimics the extrinsic incubation period

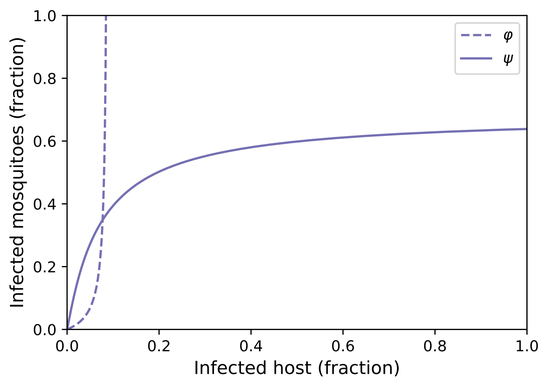
Between-host to within-host link

Attempt to incorporate epidemiological factors into WH dynamics:

- host prevalence i_H increases initial inoculum and the carrying capacity in the salivary glands via a function g_M where: $g_M(0) = 0$, $g_M(i_H) \geq 0$, $g'_M(i_H) > 0$
- abundance of infected mosquitoes i_M increases the within-host viral load via a function $g_H(i_M)$ where: $g_H(0) = 0$, $g_H(i_M) \geq 0$, $g'_H(i_M) > 0$

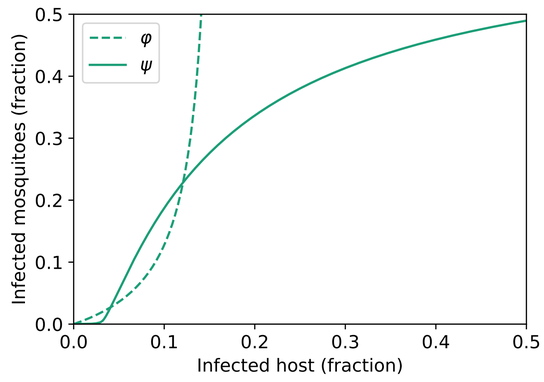
Main Results: Linear vs Nonlinear coupling

Linear coupling ⇒ *same bifurcation structure as uncoupled BH model*; at most one endemic equilibrium



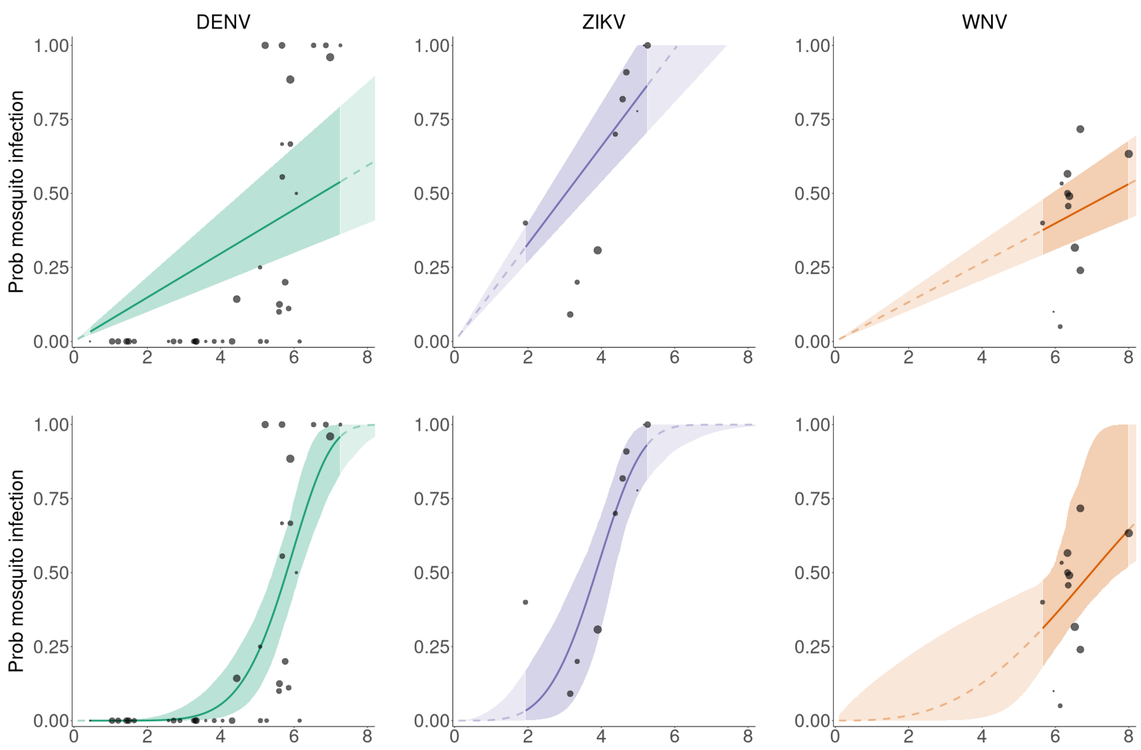
Methods: Center manifold theory

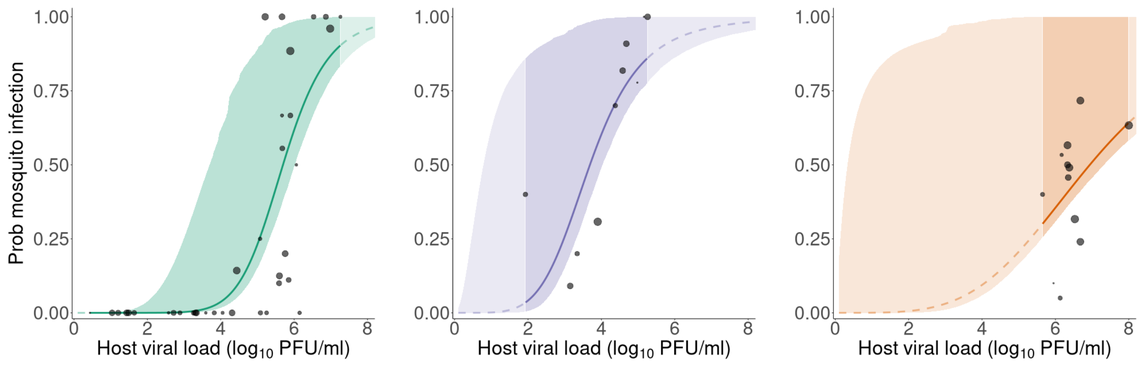
Nonlinear (sigmoidal) coupling ⇒ possible *multiple endemic equilibria* and backward bifurcations



Methods: Monte Carlo simulations

Coupling via dose-response estimation

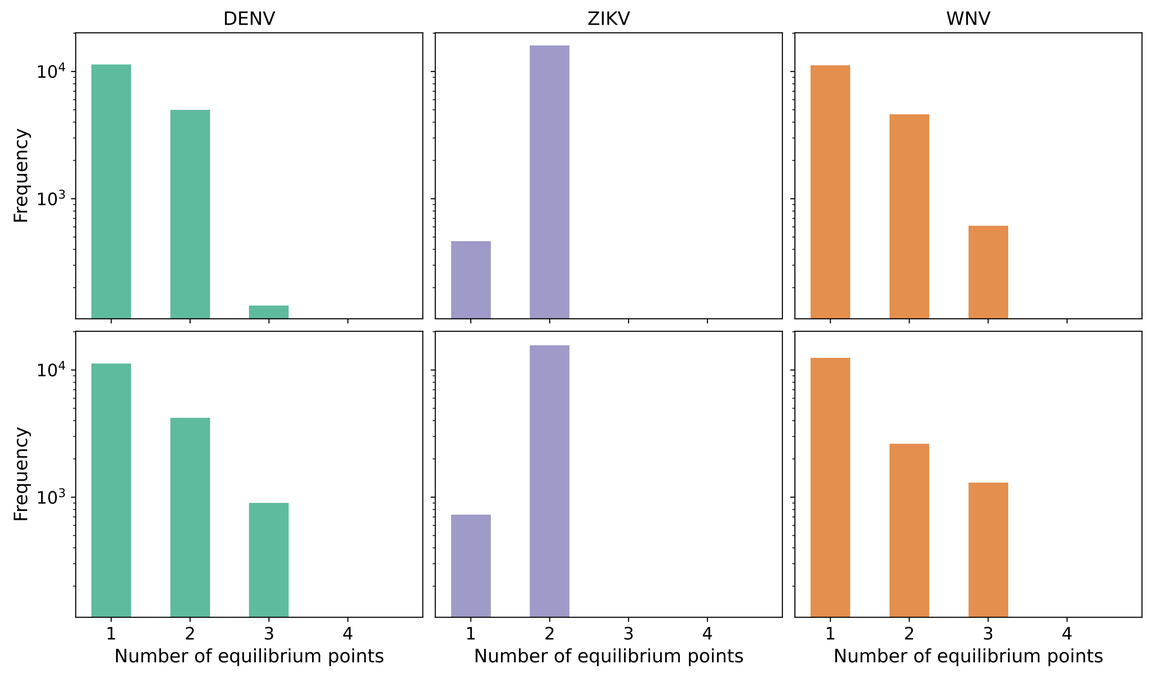




From top to bottom:

$$\beta_{linear}(V) = aV, \quad \beta_{Ferguson}(V) = 1 - \exp\left(-(V/\theta_0)^{\theta_1}\right), \quad \beta_{Hill}(V) = \frac{V^{\gamma_1}}{\gamma_0 + V^{\gamma_1}}.$$

Histograms quantifying the number of equilibrium points (including DFE) for Ferguson (top row) and Hill (bottom row) coupling functions.



Sampling: $\pm 50\%$ parameter perturbations (key parameters) across 2^{14} sets

Takeaways

- If dose–response is **linear**, a simpler single-scale model may suffice for long-term behavior
- If dose–response is **nonlinear/sigmoidal**, multiscale explicitly matters: expect multistability, backward bifurcation, & stronger sensitivity to initial conditions

Future directions

- Include within-host heterogeneity via an individual-based model
- Consider the influence of within-host scale on virulence and recovery

See our preprint here!

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