

## Two-strain multi-scale dengue model structured by dynamic host antibody level.

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Infection by distinct Dengue virus serotypes and host immunity are intricately linked. In particular, certain levels of cross-reactive antibodies in the host may actually enhance infection severity. The coupled immunological and epidemiological dynamics of Dengue calls for a multi-scale modeling approach. In this work, we formulate a within-host model which mechanistically recapitulates characteristics of antibody dependent enhancement (ADE) in Dengue infection. The within-host scale is then linked to epidemiological spread by a vector-host partial differential equation model structured by host antibody level. The coupling allows for dynamic population wide antibody levels to be tracked through primary and secondary infections by distinct Dengue strains, along with waning of cross-protective immunity after primary infection. Analysis of both the within-host and between-host systems are conducted. Stability results in the epidemic model are formulated via basic and invasion reproduction numbers as a function of immunological variables. Additionally, we develop numerical methods in order to simulate the multi-scale model and assess the influence of ADE on disease spread and burden in the population.

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