

Quantifying Uncertainty in Kinetics of Within-Host West Nile Virus Infection

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Short Abstract — We use mathematical models to investigate West Nile Virus infection in mice and birds. We set up a framework to explore large model parameter spaces after imposing constraints from biology. We then use a computationally intensive method to quantify the uncertainty in parameter estimates given uncertainty in input parameters.

Keywords — West Nile Virus, mathematical model, uncertainty in parameter estimates, hierarchical Bayesian model, complex systems modeling.

I. ABSTRACT

West Nile virus (WNV) is a flavivirus that has emerged globally as a significant cause of viral encephalitis [1]. Currently, little is known about the within-host viral kinetics of WNV during infection. We used a series of mathematical models of increasing complexity to examine WNV dynamics in mice and birds. To the best of our knowledge, this is the first effort to model within-host dynamics of WNV.

We set up a computational framework to explore large model parameter spaces after imposing constraints from biology. We use a computationally intensive method to quantify the uncertainty in parameter estimates given uncertainty in input parameters.

Our analysis yields estimates of a variety of biologically relevant parameters of WNV infection in mice, e.g., the average number of infectious virions released over the lifespan of an infected cell and the within-host basic reproductive ratio (R_0) or average number of second generation infections produced by a single infected cell.

Using a hierarchical Bayesian model, we infer novel patterns from sparse experimental data of WNV infection in birds. We found that the within-host basic reproductive ratio in a species of birds that are WNV reservoirs is an order of magnitude higher than in birds that are dead-end hosts.

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Our method of quantifying uncertainty in estimates of model parameters in terms of uncertainty in input parameters from sparse experimental data could be more generally applicable to modeling of emerging pathogens and other complex systems like intracellular signaling networks.

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