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Ensemble modeling of symptoms to human immune response of Influenza A virus infection

Deterministic models of a host-level response to influenza A virus (IAV) infection assume a perfect prediction, while an ensemble approach may account for patient and strain variability, and uncertainty in data used to calibrate the models. We generate an ensemble of parameter sets that represent a calibration to experimental data of viral titers and symptoms measured in humans with IAV infection to a host-level model with innate and adaptive immunities. Systemic, upper respiratory and lower respiratory symptoms are mapped to model interferon levels, and extent of upper and lower respiratory cells damage. In order to differentiate between upper and lower symptoms, we compartmentalize the respiratory tract into upper and lower compartments. We measure clinical factors such as onset and severity of symptoms across our ensemble distribution and obtain biologically relevant distributions while also achieving variability in host responses. Sensitivity analysis across the parameter ensembles is employed in order to characterize population-scale relevant clinical phenotypes (severity of infection, immunogenicity) to model kinetic parameters.