

Identifiability in Mathematical Models of Infectious Disease Dynamics

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Abstract

Parameter estimation connects mathematical models of infectious diseases with observed data, but agreement between model output and data does not necessarily imply that the underlying parameters can be determined reliably. This dissertation examines structural and practical identifiability in three infectious disease models that differ in biological scale, mathematical structure, and the observations available for parameter estimation.

The first study investigates a within-host HIV model that includes immune response dynamics. The equilibria and stability properties of the model are analyzed, followed by structural and practical identifiability analyses under different observation schemes. The model is structurally identifiable under the assumed observations, while practical identifiability is affected by measurement noise and the frequency of data collection.

The second study develops a multiscale HIV model that couples within-host viral dynamics with treatment-age-structured population dynamics, allowing viral load to influence infectiousness and progression to AIDS. Within-host parameters are estimated using viral-load and target cell data from treated individuals, while population-level parameters are estimated using U.S. surveillance data on HIV incidence, diagnoses, and AIDS classifications. Structural and practical identifiability analyses are used to determine which parameters can be identified and reliably estimated from the available observations. The fitted model is then used to study HIV epidemic dynamics in the United States and progress toward the Ending the HIV Epidemic incidence targets.

The third study develops an epidemiological–evolutionary model of tuberculosis that couples disease transmission and treatment with pathogen genetic adaptation. The model is fitted to U.S. TB incidence and mortality data together with SNP-based genetic divergence data. Structural and practical identifiability analyses are used to determine which parameters can be identified and reliably estimated from the epidemiological and genetic observations. Sensitivity and elasticity analyses are then used to examine the influence of evolutionary parameters on projected TB incidence.

Across the three studies, parameter identifiability depends on model structure, the quantities observed, and the amount and quality of the available data. The within-host HIV study shows how measurement noise and sampling frequency affect parameter recovery, while the multiscale HIV and epidemiological–evolutionary TB studies extend the identifiability problem to models that combine different biological processes and data sources. Together, these studies demonstrate how identifiability analysis can be used to determine which parameter-based conclusions are supported by the available data across within-host, multiscale, and epidemiological–evolutionary infectious disease models.