

Modeling Pathogenesis of Viral Infections: Statistical Inverse Problems for ODE Models

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Abstract

In this presentation, I will review the history of HIV dynamics modeling and its impact to AIDS research. Differential equation models have been used to model epidemics and pathogenesis of HIV infection since late 1980s. In mid-1990s, applications of mathematical modeling and statistical estimation methods to AIDS clinical data led a major breakthrough in understanding of pathogenesis of HIV infections and made a great impact to AIDS research. Although biomathematicians and modelers have made significant contributions to biomedical dynamic systems, very few statisticians have dedicated to this field. It is very challenging to solve the so-called “inverse problem” for dynamic systems (ODE models), i.e., parameter estimation based on the measurements of outcome variables. In the past 10 years, we have developed various strategies and methods to deal with the statistical inverse problems that include (i) simplifying the nonlinear ODE model to obtain an approximate closed-form solution to the ODE model so that we can fit the closed-form model using standard regression approaches; (ii) using Bayesian approach to incorporate prior information in order to solve the identifiability problem; (iii) exploring global search techniques to find a robust least squares estimator; and (iv) employing local smoothing approaches to avoid numerically solving the ODE models. In this talk, I will review these techniques. I will also discuss how to deal with identifiability problems of ODE models from both theoretical perspective and practical perspective. Real data examples from AIDS studies and influenza infections will be used to illustrate the modeling and estimation methods. I will briefly mention our effort in user-friendly software development for dynamic model simulations and parameter estimation.