

Interdisciplinary Mathematical Statistical Techniques (Shanghai 2007), May 20–23, 2007,
University of Science and Technology of China, Hefei, Anhui, P.R.China

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**A BAYESIAN APPROACH FOR DIFFERENTIAL EQUATION
MODELS WITH APPLICATION TO AIDS CLINICAL STUDIES**

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A virologic marker, the number of HIV RNA copies or viral load, is currently used to evaluate antiretroviral (ARV) therapies in AIDS clinical trials. This marker can be used to assess the antiviral potency of therapies, but is easily affected by drug exposures, drug resistance and other factors during the long-term treatment evaluation process. HIV dynamic studies have significantly contributed to the understanding of HIV pathogenesis and ARV treatment strategies. However, the models of these studies are only used to quantify short-term HIV dynamics (less than one month), and are not applicable to describe long-term virological response to ARV treatment due to the difficulty of establishing a relationship of antiviral response with multiple treatment factors such as drug exposure and drug susceptibility during long-term treatment. Long-term therapy with ARV agents in HIV-infected patients often results in failure to suppress the viral load. Pharmacokinetics, drug resistance and imperfect adherence to prescribed antiviral drugs are important factors explaining the resurgence of virus. To better understanding of the factors responsible for the virological failure, this paper develops a mechanism-based nonlinear differential equation models for characterizing long-term viral dynamics with ARV therapy. In this model we directly incorporate pharmacokinetics, drug adherence and drug susceptibility into a function of treatment efficacy. A Bayesian nonlinear mixed-effects modeling approach is investigated for estimating dynamic parameters by fitting the model to viral load data from an AIDS clinical trial. The correlations of baseline factors with estimated dynamic parameters are explored and some biologically significant results are presented. Further, the estimated dynamic parameters in patients with virologic success were compared to those in patients with virologic failure and important findings were summarized. These results suggest that viral dynamic parameters may play an important role in understanding HIV pathogenesis, designing new treatment strategies for long-term care of AIDS patients.

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