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MATHEMATICAL ANALYSIS OF AGE-STRUCTURED HIV-1 DYNAMICS WITH COMBINATION ANTIRETROVIRAL THERAPY*

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Abstract. Various classes of antiretroviral drugs are used to treat HIV infection, and they target different stages of the viral life cycle. Age-structured models can be employed to study the impact of these drugs on viral dynamics. We consider two models with age-of-infection and combination therapies involving reverse transcriptase, protease, and entry/fusion inhibitors. The reproductive number $\mathcal{R}$ is obtained, and a detailed stability analysis is provided for each model. Interestingly, we find in the age-structured model a different functional dependence of $\mathcal{R}$ on ϵ_{RT}, the efficacy of a reverse transcriptase inhibitor, than that found previously in nonage-structured models, which has significant implications in predicting the effects of drug therapy. The influence of drug therapy on the within-host viral fitness and the possible development of drug-resistant strains are also discussed. Numerical simulations are performed to study the dynamical behavior of solutions of the models, and the effects of different combinations of antiretroviral drugs on viral dynamics are compared.

Key words. human immunodeficiency virus type 1, antiretroviral therapy, drug resistance, optimal viral fitness, age-structured model, stability analysis

AMS subject classifications. 35L60, 45D05, 92C37, 92C45, 92C50

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1. Introduction.

Since the discovery of the human immunodeficiency virus type 1 (HIV-1) in the early 1980s, the disease has spread in successive waves to most regions around the globe. It is reported that HIV has infected more than 60 million people, and over a third of them subsequently died [10]. Considerable scientific effort has been devoted to the understanding of viral pathogenesis, host/virus interactions, immune response to infection, and antiretroviral therapy.

Over the last decade, there has been a great effort in the mathematical modeling of HIV infection and treatment strategies. These models mainly investigated the dynamics of the target cells and infected cells, viral production and clearance, and the effects of antiretroviral drugs treatment. Perelson et al. [44] and Ho et al. [22] used a simple mathematical model to analyze a set of viral load data collected from infected patients after the administration of a protease inhibitor, and the virion clearance rate, the rate of loss of productively cells, and the viral production rate were estimated. These estimates were minimal estimates since the effects of antiretroviral drugs were assumed to be 100% effective, and cells were assumed to produce new virus immedi-

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