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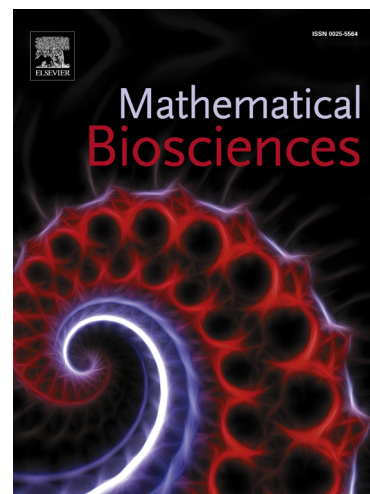
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Mathematical analysis of multiscale models for hepatitis C virus dynamics under therapy with direct-acting antiviral agents

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Abstract

Chronic hepatitis C virus (HCV) infection remains a world-wide public health problem. Therapy with interferon and ribavirin leads to viral elimination in less than 50% of treated patients. New treatment options aiming at a higher cure rate are focused on direct-acting antiviral agents (DAAs), which directly interfere with different steps in the HCV life cycle. In this paper, we describe and analyze a recently developed multiscale model that predicts HCV dynamics under therapy with DAAs. The model includes both intracellular viral RNA replication and extracellular viral infection. We calculate the steady states of the model and perform a detailed stability analysis. With certain assumptions we obtain analytical approximations of the viral load decline after treatment initiation. One approximation agrees well with the prediction of the model, and can conveniently be used to fit patient data and estimate parameter values. We also discuss other possible ways to incorporate intracellular viral dynamics into the multiscale model.

1 Introduction

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease, liver cirrhosis and liver cancer. Approximately 130 to 170 million people are chronically infected with HCV in the world [1]. A combination of pegylated interferon (PEG-IFN) and ribavirin (RBV) has been used to treat HCV infection but only led to sustained viral elimination in less than 50% of treated patients infected with HCV genotype 1, the major genotype affecting North America and Europe [2]. New

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