$\mathbf{T}_{\text{EMPLE}} \; \mathbf{U}_{\text{NIVERSITY}} \; \mathbf{M}_{\text{ATHEMATICS}} \; \mathbf{C}_{\text{OLLOQUIUM}}$

Jeffrey Saltzman

Merck, Department of Applied Computer Science and Mathematics will speak on Modeling HCV Antivirals

ABSTRACT: Hepatitis C affects between 4 and 5 million people in the United States with nearly 75% suffering chronic infection. Further, current estimates indicate 170 million people are infected, worldwide, with the Hepatitis C virus (HCV). Pegylated interferon and ribavirin combination therapy is currently the standard of care for treatment of HCV but is considered less than optimal. For example, sustained virologic response (SVR) for genotype 1 virus is observed in pivotal clinical trials for only 54% of treated patients. SVR is defined as undetectable HCV RNA in plasma on the order of 6 months after cessation of treatment. This combination therapy is also associated with a high incidence of significant side effects suffered over a treatment interval of at least six months. Identification of better treatment alternatives is the goal of a vigorous antiviral program at Merck.

In this talk we describe mathematical models explaining HCV infection and response to treatment. The model equations and resultant simulations were chiefly derived from the literature. Simulations have already provided support for the antiviral drug development program at Merck. Mathematical modeling gives evidence of target engagement and drug efficacy. Using accumulated simulation experience gained from basic research, preclinical data, and the literature, design optimizations for early clinical studies may be proposed. As internal modeling expertise is enhanced by experience gained in early development, this mathematical knowledgebase may help optimize costly phase III trials by guiding key decisions such as dose selection and length of dosing.

Joint work with Robert Nachbar, Ansu Bagchi, Arthur Fridman (Department of Applied Computer Science and Mathematics) and Steven S. Carroll, David Olsen (Department of Antiviral Research)

> Monday, 29 October 2007 Lecture at 4:00 pm Coffee, tea, and refreshments from 3-5 pm Room 617, Wachman Building Department of Mathematics