Research Experiences for Undergraduates (REU) 2012 Abstract

HENNESSEY, K., MUTAMBUKA, V., RHOADS, A., GAO, F., SONG, H., NGONGHALA, C., GANUSOV, V.V. Estimating rates of HIV recombination during first months post infection. National Institute for Mathematical and Biological Synthesis, Knoxville, TN, Departments of Biology and Mathematics, St. Olaf College, Northfield, MN, Department of Mathematics and Systems Engineering, University of Arkansas, Little Rock, AR, Department of Mathematics, McKendree University, Lebanon, IL, School of Medicine, Duke University, Durham, NC, Department of Microbiology, University of Tennessee, Knoxville, TN.

In 2010, an estimated 34 million people worldwide were living with Human Immunodeficiency Virus (HIV) (1). HIV establishes a lifelong infection in the host that leads to the development of AIDS and almost certain death if left untreated (2). The ability of the virus to persist in the host despite a strong immune response is thought to be driven by its high mutation rate and potential to form new genetic sequences via recombination. In vitro recombination of HIV has been frequently observed, but the rate of HIV recombination in vivo remains poorly estimated. While recombination can be beneficial to the virus by bringing together advantageous mutations, it can also impede evolution by destroying fit viral genotypes. In approximately 20 percent of heterosexual transmissions, HIV infection is initiated by 2 or more transmitted/founder (T/F) viruses. In this study, we track changes in the frequency of the T/F viruses in several such patients. We develop mathematical models of different levels of complexity that predict HIV evolution by recombination and estimate parameters of these models using experimental data. We constructed several systems of differential equations representing a range of biological complexity. We also study the role of stochasticity in early HIV dynamics for the kinetics of different T/F viruses and their recombinant progeny. Our preliminary results suggest that recombinants should possess a substantial fitness advantage over T/F viruses in order to replace the original strains within months post-infection. Our results also provide a minimal estimate of the effective rate of virus recombination which can be used to predict the effects and potential failures of antiretroviral therapy in acute HIV infection.