An Investigation of Poxvirus Response to the Integrated Cellular Stress Mechanism through Steady-State Analysis and Stochastic and Deterministic Models

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While research and experimentation on the viral invasion of the human cell exists, there are few working models of the process itself. This study sought to model and analyze a system of feedback mechanisms active during a poxvirus invasion. The focus of the system lies within the competition between eukaryotic initiation factor eIF2 and viral mimic protein K3L, to bind to protein kinase R (PKR), which, respectively, activates or prevents the activation of the cellular stress response. The study introduces both Gillespie stochastic and deterministic computer models based on the binding affinity and concentration of each protein, as well as mathematical analysis focused on the system's equilibria. In addition to accurately reflecting the results of experimentation performed by other groups, the models were used to investigate the difference in effectiveness between two types of evolution of K3L: increased binding affinity and increased gene copy number amplification, in which the study determined the copy number evolution to be more effective at small amounts while the affinity evolution was more effective at large amounts. The models also determined that with staggered releases of K3L into the system, as the rate of introduction of K3L was held constant, longer pauses between each release resulted in increased probability of activation of the integrated cellular stress response. Steady-state analysis determined that there was always one stable equilibrium within the system. This study presents tools and models to aid future research, as well as analysis proving assumptions about similar systems, such as the intrinsic apoptotic pathway.

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