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Validation of a Large-Scale Dynamical Model of Macrophage/HIV Interaction for the Mathematical Analysis of Methamphetamine Emergent/Epigenetic Effects on HIV/AIDS Disease Progression Using Visual Statistical Inference

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Large-scale, complex biological systems have been shown to display emergent properties—epigenetic phenomena that arise in the dynamics of biochemical networks that are not discernable at the individual gene or protein level. To investigate the influence of methamphetamine on the emergent properties of macrophage biochemistry, we created a large-scale (713 components, 1583 edges, and 38 external inputs) dynamical model of HIV/macrophage interaction. The model correctly simulates the dynamics of over 50 different known phenomena, but no matter how many phenomena are replicated, there is always a question as to the validity of the model. In this work, we introduce a new validation method that allows the assignment of a p -value to the accuracy of a model. The method uses an extension of visual statistical inferential procedure, a cutting-edge method that assigns a p -value based on lineup evaluation by human experts on the subject. The extension of the method involves creating lineups of word lists, where the words are the names of the components of the network and the sorting is based on the determinative power of the components. The development of these types of validations is critical to the creation of useful models of systems in which the mechanisms of action are not well-known, such as the effects of drugs on biochemical systems. The model and the new validation methods opens the possibility of identifying the effects of drugs on the emergent functions of the biochemical systems—a key form of epigenetic effects of drug usage.