Name(s)	Project Number
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Project Title

Model Order Reduction of Cell Signalling Pathways: An Investigation of the Invasive Mechanism of Ebola Virus

Abstract

Objectives/Goals

To formulate and implement a mathematical algorithm which reduces the dimensionality of kinetic models of cell signalling pathways while still preserving their most important dynamic features.

Methods/Materials

This algorithm (executed at the command-line interface through a Python interpreter) combines the techniques of proper orthogonal decomposition, trajectory piecewise-linearization, and Krylov subspace reduction in an effort to identify a best-fit subspace for the model trajectories that accurately approximates the mapping between the model input and outputs. The algorithm will be implemented on a kinetic model of the IFNG-JAK-STAT-EVP24 network, which will be constructed using the Simmune Modeler and Simulator. Once the reduction procedure has been successfully executed on the kinetic model, correlations between the reduced and full-order bases will be analyzed in order to reveal novel dynamical relationships between the species participating in the signalling cascade.

Results

The algorithm successfully reduced the dimensionality of a kinetic model of the IFNG-JAK-STAT-EVP24 network from 45 to 5. In addition, the algorithm revealed strong positive correlations within four groups of participating species, which divided the mechanism into four distinct temporal phases.

Conclusions/Discussion

The developed model reduction algorithm enables cell biologists to effectively employ kinetic models to analyze the mechanisms of complex diseases. Further work may involve obtaining an a priori error estimation of the accuracy of the reduction procedure and incorporating the algorithm as an accessible front-end tool in the Simmune graphical user interface.

Summary Statement

This project designs a mathematical algorithm for reducing the dimensionality of kinetic models of cell signalling pathways.

Help Received