1145-92-1473Elizabeth M. Gilchrist* (egilchrist140@g.rwu.edu), Abigail T. Small and Edward T.
Dougherty. A Computational Approach for Constructing an Intracellular Signaling Pathway
Mathematical Model with Application to Parkinson's Disease. Preliminary report.

Parkinson's disease (PD) is the second most common neurodegenerative disorder. Despite this, there is no cure and the exact cellular level pathogenesis remains elusive. In an attempt to gain new insights, we created a mathematical model of the intracellular signaling pathway of a dopaminergic neuron cell with application to PD. A comprehensive literature search was conducted to construct a signaling wiring diagram, which was used to generate a system of ordinary differential equations using the law of mass action and the Michaelis-Menten equation. Many of the kinetics are presently unknown, so a novel computationally-based reverse engineering method was used to identify them; this approach uses the expected system behavior and the Metropolis Algorithm to numerically determine appropriate values. Suitable rates were ranked based on performance in a phenotype-based computational assessment, and then robustly screened using a k-means clustering assessment, sensitivity analyses, and an eigen-analysis. The result is a mathematical model that efficiently emulates the signaling network of a dopaminergic neuron model. We also showcase the ability of the model to emulate the intracellular processes of both a healthy dopaminergic neuron and one that presents with PD. (Received September 22, 2018)