125. A Computational Approach for Constructing an Intracellular Signaling Pathway Mathematical Model with Application to Parkinson's Disease

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Parkinsons disease (PD) is the second most common neurodegenerative disorder. Despite this, there is no cure and the 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 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 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; it showcases the intracellular processes of both a healthy and PD-like dopaminergic neuron.