Name: Pilhwa Lee, Ph.D. Email: pilhwa.lee@morgan.edu

Comparison of microglial-dopaminergic interaction between development and disease through time-course profiles

We target HIV-1 infection and administration of the psychostimulant METH, and aim for deconvolution of gene regulation with time course data, and those in the representation of the interaction between glial and dopaminergic neurons in the striatum. We especially focus on the gene regulation related to mTOR signaling with upstream of the cytokine SPP1. We hypothesize that SPP1 and mTOR signaling in neuroinflammation is, in part, reflected in the canonical development.

We apply a method designed to infer a "physical-time" differential equation-based model for transcription factor expression and regulation from time-series data on multiple transcripts. We deconvolve gene-to-gene connectivity by treating the transcriptomic ensemble as a kinetic dynamical system on randomized networks and projecting it to empirical time-series data. Theoretically, this is a non-polynomial (NP) hard problem, that is, generally not possible to solve exactly. We have approximately handled this difficulty by decomposing a network into subnetworks with one-to-many relationships, utilizing GPU ODE-based parallel reconstruction of the subnetworks. Those

sub-networks are compared to kinetic data by a hybrid approach of global and gradient-based optimizations. By scoring gene-to-gene interaction and deriving p-values from multiple conditions, we identify commonly inferred directly associated genes and differentially inferred pathways from external differential cues. Here, the external

cues are determined by the glial-dopaminergic interaction, mainly in the mechanism of receptor-ligand interaction. The selection of random networks for testing is unbiased in bootstrapping. i.e., there is no incorporation of a priori confirmed gene-to-gene interactions. The result is a set of likely dynamic network interactions that are informed solely by the time-course data and not by prior knowledge.

We are currently interrogating OPN/SPP1 and mTOR signaling in the canonical development, and in comparison with some known regulations of neuroprotection in HIV-1 infection and substance use disorder.

Authors:
Submitter: Pilhwa Lee, Lecturer and Graduate Faculty, Morgan State University, Baltimore
Bose Iyiola, MS, Morgan State University
Godgift Ndiwari, MS, Morgan State University
Olusola Olabanjo, Ph.D., Morgan State University
Olusola Olabanjo, Ph.D., Morgan State University

DRAFT