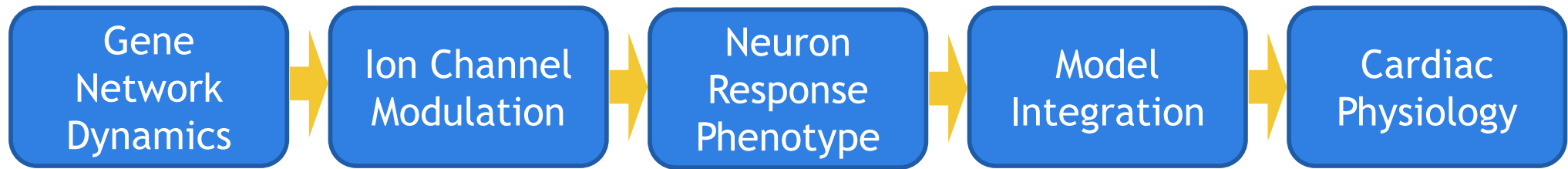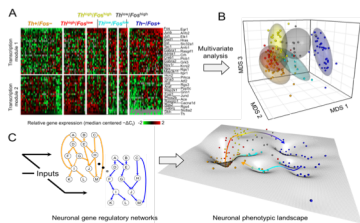# Multiscale Model of the Vagal Outflow to the Heart

James S. Schwaber and Rajanikanth Vadigepalli

Daniel Baugh Institute for Functional Genomics and Computational Biology
Department of Pathology, Anatomy, and Cell Biology
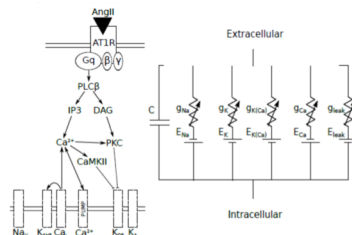Thomas Jefferson University, Philadelphia, Pennsylvania

Modeling the Cardiac Vagal Control Loop
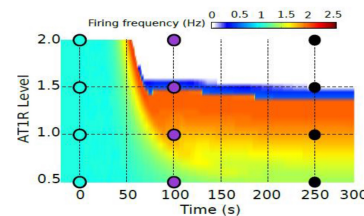# from Neuronal Gene Expression to Cardiac Physiology

Gene Network Dynamics → **Ion Channel Modulation** → **Neuron Response Phenotype** → **Model Integration** → **Cardiac Physiology**
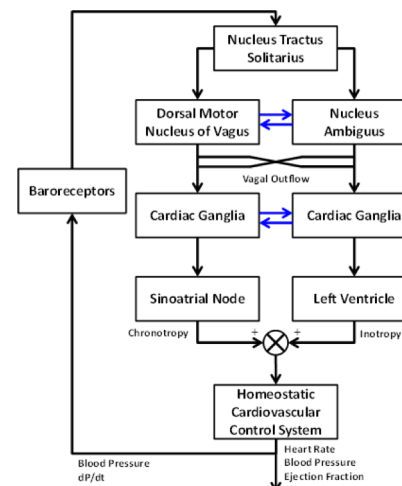

Co-expression networks

Signaling Pathways
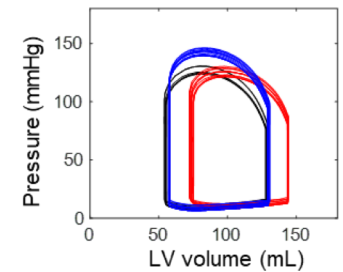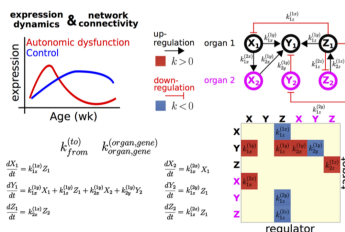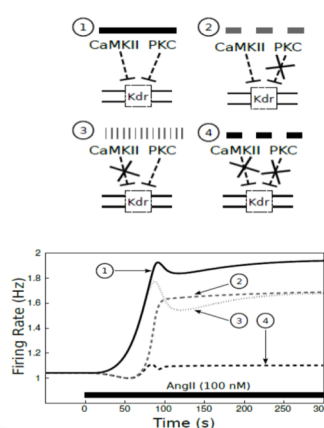
Single Gene Separatrix

Conceptual Framework

Cardiac Performance

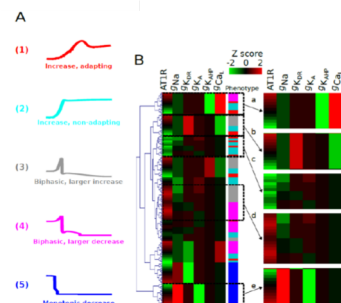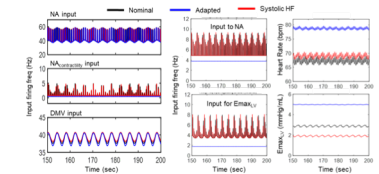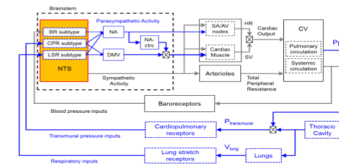Expression Dynamics

Modeling Influence

Gene Network Influences Firing Phenotype

Actual Implementation

Underlying Neuronal Firing Behavior

Credibility Plan – organized along Ten Simple Rules*

1	Define Context	Vagal control of cardiac function by neuronal populations that constitute the multilevel closed loop control circuit. Specific details in the manuscripts.
2	Appropriate data	Single neuron gene expression; Connectivity from tract tracing; Physiological data on cardiac functional parameters
3	Evaluate within context	Evaluate computational model for match to physiological data from essential hypertension and heart failure animal models.
4	List Limitations	Assumptions and expected applicability are detailed in the manuscripts

* Committee on Credible Practice of Modeling and Simulation in Healthcare

Credibility Plan – organized along Ten Simple Rules*

5	Version Control	Manual and Limited; Need to systematize
6	Documentation	Manual and developer-dependent; Need to systematize
7	Dissemination	Model code and documentation will be made available via ModelDB during and after peer review, as well as manuscript supplement
8	Independent Review	New members of the lab routinely review prior models as part of their initial training; Need to establish a systematic workflow for independent external review
9	Test Implementations	NEURON versus custom software in C++ from Drexel University
10	Conform to Standards	Conform to the best practice standards for ModelDB submission

* Committee on Credible Practice of Modeling and Simulation in Healthcare