NIMBioS

National Institute for Mathematical and Biological Synthesis

presents an Interdisciplinary Seminar with

DR. MARY ANN HORN

on

Using mathematical modeling to understand the role of diacylglycerol (DAG) as a second messenger

12:40 PM*, APRIL 16, 2019

Hallam Auditorium, Room 206@NIMBioS · 1122 Volunteer Blvd.

Reception & refreshments at 12:10 p.m.

Diacylgylcerol (DAG) plays a key role in cellular signaling as a second messenger. In particular, it regulates a variety of cellular processes and the breakdown of the signaling pathway that involves DAG contributes to the development of a variety of diseases, including cancer. A mathematical model of the G-protein signaling pathway in RAW 264.7 macrophages downstream of P2Y6 activation by the ubiquitous signaling nucleotide uridine 5'-diphosphate is presented. The primary goal is to better understand the role of diacylglycerol in the signaling pathway and the underlying biological dynamics that cannot always be easily measured experimentally. The model is based on time-course measurements of P2Y6 surface receptors, inositol trisphosphate, cytosolic calcium, and with a particular focus on differential dynamics of multiple species of diacylglycerol. When using the canonical representation, the mathematical model predicted that key interactions were missing from the current pathway structure. Indeed, the model suggested that to accurately capture experimental observations, an additional branch to the signaling pathway needed to be incorporated, whereby an intracellular pool of diacylglycerol is immediately phosphorylated upon stimulation of an extracellular receptor for uridine 5'-diphosphate and subsequently used to aid replenishment of phosphatidylinositol. As a result of sensitivity analysis of the model parameters, predictions can be made regarding which of these parameters are the most sensitive to perturbations and are therefore most responsible for output uncertainty. (Joint work with Hannah Callender, Univ. of Portland, and the H. Alex Brown Lab, Vanderbilt.)

Dr. Mary Ann Horn is Professor and Chair in the Department of Applied Mathematics and Statistics at Case Western Reserve University. She received a Ph.D. and M.S. in applied mathematics from the University of Virginia and a B.S. in mathematics, with a chemistry emphasis, from the Pennsylvania State University. Her research interests include control of distributed parameter systems, optimal control, nonlinear analysis, partial differential equations, and applications in the biological sciences and medicine. She initially received tenure from Vanderbilt University, then spent over a decade as a program officer at the National Science Foundation, primarily handling programs in Applied Mathematics and Mathematical Biology.

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The seminar will be live streamed & recorded.

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