Mathematical, Computational and Systems Biology
Graduate Programs

Ph.D. DISSERTATION DEFENSE

Thursday, November 15, 2018
10:00AM
Dale Melbourne Herklotz Conference Center

(Building 506 on the campus map)

Conference facility usage provided by the Center for the Neurobiology of Learning and Memory

Kathryn Manakou

Professor Jun Allard, Chair, Dept. of Mathematics

Title: Modeling membrane-network assemblies: dynamics and disease.

Biological membranes are essential to life as we know it. One of the most important roles of membranes is to provide a stable barrier between two aqueous environments maintaining spatially localized chemical environments to facilitate the occurrence of biochemical reactions necessary for life. To accomplish this, membranes must remain stable under a variety of external and internal stresses. Thus, membranes are often structurally reinforced with networks of proteins or polysaccharides. Here, we present three models of metazoan membranes and their associated protein networks. We first investigated the plasma membrane, under which lies a dense network of actin filaments known as the cortex. Disruptions in the cortex lead to transient membrane protrusions known as blebs, which are implicated in a variety of cellular functions. Here, we developed a model which recapitulates the bleb life cycle and provides conditions under which blebbing occurs. Furthermore, our model can give rise to traveling blebs, a mysterious behavior observed in some cell lines, and predicts traveling velocity, which had not been established by other models. We derived a previously unknown necessary condition for traveling wave solutions to exist in such a system, and demonstrate sufficiency numerically. Next, we present two models of the nuclear envelope which is internally associated with a network of lamin proteins known as the nuclear lamina. In the first model, we investigated nuclear shape defects resulting from mutations in the gene encoding for lamin A/C, a major component of the nuclear lamina. Our model serves as a pipeline to determine unknown biophysical properties, presented as parameters in the model, of the lamina. Our second model explored the scaling relationship between nuclear size and cell size. We combined equations for the transport of nuclear elements, including surface factor elements (e.g. lamins) and volume factor elements (e.g. NuMA), across the cell and into the nucleus with a mechanical force-balance equation establishing the size of the nucleus. This model predicts that nuclear size is regulated by a combination of surface factor and volume factor elements with a non-negligible contribution from genomic content.

Center for Complex Biological Systems
University of California, Irvine

UC Irvine