Study of the effect of individual cell behaviors on prion protein aggregation and colony organization in yeast

Mikahl Banwarth-Kuhn*, Jordan Collignon, Suzanne S. Sindi

Department of Applied Mathematics, University California Merced, Merced, CA

mbanwarth-kuhn@ucmerced.edu

Prion proteins are most commonly associated with fatal neurodegenerative diseases in mammals, but they are also responsible for causing a number of harmless phenotypes in yeast. The diseased state (or phenotype) in yeast arises when a misfolded form of a protein, i.e. prion, appears and, rather than be removed by cellular quality control mechanisms, persists. Mathematical models have previously been developed for studying prion aggregate dynamics in isolation. However, a major open question in prion biology is to understand how prion aggregates spread between cells within a whole colony or tissue. Living cells are constantly exhibiting different behaviors such as growth, diffusion, and division, that impact the abundance and concentration of normal proteins and aggregates. These behaviors are thought to have a large impact on prion protein aggregation and propagation. We introduce a novel, two-dimensional agent-based model of a budding yeast colony with detailed representation of cell-type specific biological processes, including budding, variation in cell-cycle length, and asymmetric protein segregation. The model is used to study how individual cell behaviors impact yeast colony structure and organization as well as protein aggregation and propagation in an entire yeast colony. In the model, spatial arrangement of cells is modeled using a center-based modeling approach that accounts for the affect of biophysical properties such as increased adhesion between a mother and daughter cell during budding. In addition, prion dynamics are simulated within each individual cell using simplified intracellular dynamics. The unified model may have the potential to predict mechanisms underlying experimentally observed phenomena such as sectored prion phenotypes in yeast colonies in addition to serving as a tool for future hypothesis generation and testing.