Contribution ID: **25** Type: **Poster Presentation**

Mathematical modelling of cytosolic liquid-liquid phase separation

Monday, 9 July 2018 19:45 (15 minutes)

Intracellular phase transitions are an emerging mechanism for cell organization. These membrane-less compartments are formed via liquid-liquid demixing and subsequent concentration of cellular components in a specific region. By undergoing these localized phase separations, cells are able to create dynamic compartments that help maintain the regulation of biomolecular interactions and localize factors such as RNAs and proteins. The utility of liquid-liquid phase transitions and the assembly of cytosolic compartments is especially critical in large, multinucleate cells. These types of cells are common in the biosphere and include skeletal muscle tissue, the placenta, many filamentous fungi, and certain types of cancer. A powerful model organism for studying liquid-liquid phase separations (LLPS) is the branching, multinucleate fungus *Ashbya gossypii*. In *Ashbya*, Whi3, a polyQ tract-containing RNA binding protein, binds to and localizes multiple different mRNAs by forming liquid-like droplets in the cell. Under normal physiological conditions, Whi3 alone cannot form liquid droplets, *in vitro*, as this is a phenomenon that only occurs once it is able to bind with RNA. However, how Whi3 and RNA combine to form complexes and how these complex influence droplet properties remains elusive. This issue is further complicated due to the many possible subcomplexes of RNA and protein that can exist. Specifically, the target RNAs have multiple binding sites for the Whi3 protein and the Whi3 protein has two possible RNA binding sites and likely interacts with itself using the polyQ tract. This means that there are many possible types of interactions between components. Additionally, while preliminary work within the Gladfelter Lab has shown that there is a fairly consistent average ratio of Whi3 to RNA in each droplet of a population, it is unclear what distribution of the different protein-RNA combinations gives rise to this average ratio. To understand the role that the different combinations of Whi3 and RNA play in the initial phase separation and the properties of the droplet population, such as size, shape and spatial distribution of droplets, we have created a mathematical model that employs the use of the phase field method. With phase variables to represent the volume fractions of Whi3, RNA, and the complexes they form, we propose a model that employs the use of mass action kinetics and a modified double-well free energy to represent the complex dynamics present in the cytosol. We report modelling and experimental progress on these cytosolic liquid-liquid phase separations in *Ashbya* as they help guide our understanding of the mechanisms behind droplet formation in the cytosol, as well as how these droplets function in cellular regulation.

Primary authors: Dr GASIOR, Kelsey (University of North Carolina); Dr ZHAO, Jia (Utah State University); Dr NEWBY, Jay (University of North Carolina); Ms LANGDON, Erin (University of North Carolina); Dr FOREST, Greg (University of North Carolina); Dr GLADFELTER, Amy (University of North Carolina)

Presenter: Dr GASIOR, Kelsey (University of North Carolina)

Session Classification: Poster Session

Track Classification: Biochemistry and Cell Biology