1158-92-192 **Suzanne Sindi***, 5200 North Lake Road, Merced, CA 95340. *A Minimal Model for Prion Aggregate Infectivity Shows Prion Strains Differ by Nucleus Size.*

Prion proteins are responsible for a variety of neurodegenerative diseases in mammals such as Creutzfeldt-Jakob disease in humans and "mad-cow" disease in cattle. While these diseases are fatal to mammals, a host of harmless phenotypes have been associated with prion proteins in *S. cerevisiae*, making yeast an ideal model organism for prion diseases.

The common assumption in prion phenotypes is that the only limiting event is the establishment of a stable prion aggregate of minimal size. We show this model is inconsistent with seeding experiments. We then develop a minimal model of prion phenotype appearance: the first successful amplification of an aggregate. Formally, we develop a chemical master equation of prion aggregate dynamics through conversion (polymerization) and fragmentation under the assumption of a minimal stable size. We frame amplification as a first-arrival time process that must occur on a time-scale consistent with the yeast cell cycle. This model, and subsequent experiments, then establish for the first time that two standard yeast prion strains have different minimally stable aggregate sizes. This suggests an novel approach (albeit entirely theoretical) for managing prion diseases, shifting prion strains towards larger nucleus sizes. (Received March 01, 2020)