Scientific Meeting
AuPS | ASB
HOBART · 2022

AUSTRALIAN SOCIETY FOR BIOPHYSICS

Abstract: 111O

A multi-scale kinetic and spatial model of yeast replication and prion transmission

Damien Hall[&,#]

[&] *WPI Nano Life Science Institute. Kanazawa University, Kakumamachi, Kanazawa, Ishikawa 920-1164. Japan.*
[#]*Department of Applied Physics, Aalto University. FI-00076 Aalto. Finland.*

The single celled baker's yeast, Saccharomyces cerevisiae, can be infected by a number of amyloid-based prions, with the three most prominent examples being [PSI+] – formed from the Sup35 protein (yeast translation termination factor), [URE3] – formed from the Ure2 protein (regulator of nitrogen catabolism), and [PIN+] formed from the Rnq1 protein (of as yet unknown function) **[1]**. In a laboratory environment, haploid S. cerevisiae cells of a single mating type can acquire an amyloid prion in one of two ways (i.) Spontaneous nucleation of the prion within the yeast cell, and (ii.) Infection via mother-to-daughter transmission during the cell division cycle. Here we model these two general processes using a multiscale approach that describes spatial and kinetic [**2-4**] aspects of both the yeast life cycle, and the amyloid-prion behavior. The yeast growth cycle is considered in two stages, a mature yeast that is competent to bud (M) and a distinct daughter yeast (D) defined as a fully separated and detached bud. In the virtual plate experiment each transition in yeast growth is stochastically regulated. Between the relatively coarse time-points used for the particle level description a set of differential equations, describing the nucleation, growth, fragmentation and clumping of amyloid fibrils, is solved numerically, for each individual yeast cell. Distribution of amyloid between the mother and the daughter is carried out by solving a set of kinetic partition equations between mother and the newly forming daughter (the yeast budding stage). In this talk I describe the workings of the model, the assumptions upon which it is based and some interesting simulation results that pertain to wave-like spread of the epigenetic prion elements through the yeast population.

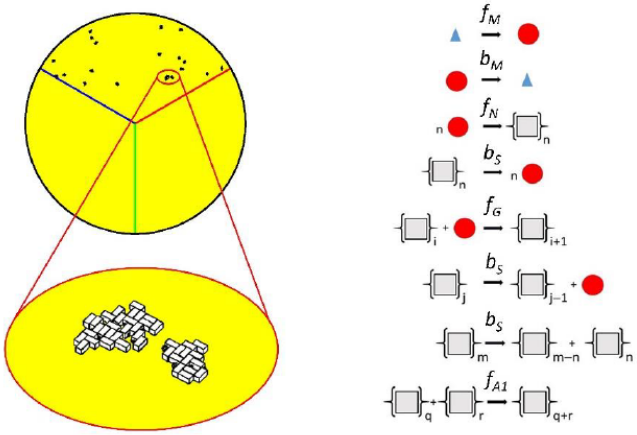

Fig. 1: ***Multiscale modelling of yeast epigenetics.*** A multiscale model of the yeast life cycle is presented that combines continuous cell growth with the growth and division of an amyloid based epigenetic element known as a yeast prion. This talk discusses the basis of the model and three important results developed within these studies.

[1] Wickner RB, Kryndushkin D, Shewmaker F, McGlinchey R and Edskes HK. (2018) Study of Amyloids Using Yeast. Methods in Molecular Biology. 1779:313-339. doi:10.1007/978-1-4939-7816-8_19
[2] Hall D. (2020). A simple method for modeling amyloid kinetics featuring position biased fiber breakage. Biophysics and Physicobiology, 17, 30-35. doi: 10.2142/biophysico.BSJ-2020003
[3] Hall D. and Edskes H. (2009). A model of amyloid's role in disease based on fibril fracture. Biophysical Chemistry, 145, 17-28. doi:10.1016/j.bpc.2009.08.004
[4] Hall, D. and Edskes, H., 2004. Silent prions lying in wait: a two-hit model of prion/amyloid formation and infection. Journal of molecular biology, 336(3), pp.775-786. doi:10.1016/j.jmb.2003.12.