ESTIMATING THE NUMBER OF PRION SEEDS IN YEAST: A STOCHASTIC MODELLING APPROACH

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Prions are unique, protein-only infectious agents that underlie certain neurological diseases (e.g. BSE in cattle and CJD in humans) and are also involved in the inheritance of several epigenetic states in the yeast *Saccharomyces cerevisiae*. The conformationally altered, infectious forms of these proteins are efficiently replicated and transmitted to daughter yeast cells during cell division. This propagation process can be reversibly blocked by the addition of the chemical guanidine hydrochloride (GdnHCl), which effectively inhibits new prion seed generation within the yeast cell. This results in the elimination ('curing') of the prion from the cells by dilution of the pre-existing prion seeds as the cells divide. The kinetics of GdnHCl-induced prion curing can be analysed by a simple dilution based model, which we have extended to derive a more accurate model of the underlying process. Important extensions include asymmetric division of yeast, unequal prion segregation and an allowance for the presence of respiratory-defective petite cells. The results from the model have aided our research into the molecular entities associated with yeast prion propagation. Additional support for our model is provided by the inclusion of experimental data obtained by studying the effects of adding other chemicals, such as α-factor, which reduce the growth rate.