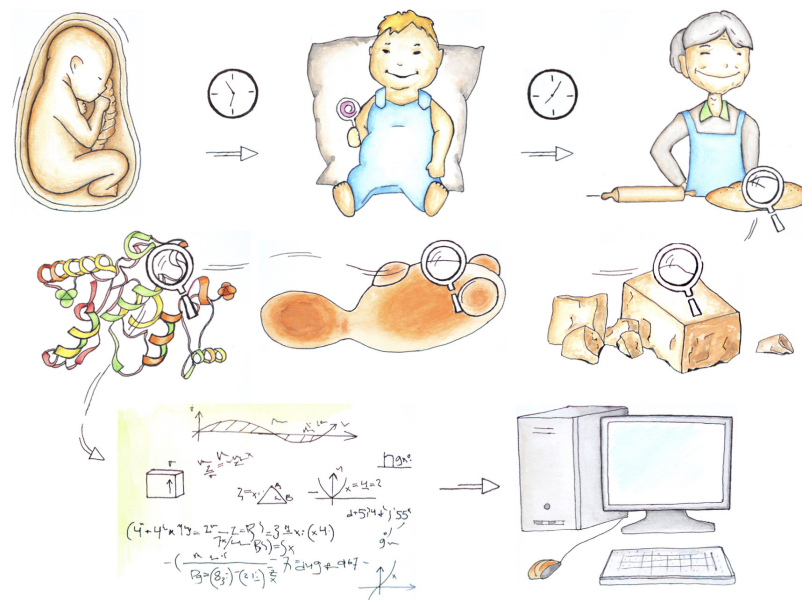# The Construction, Analysis and Validation of Mechanistic Mathematical Models of Protein Kinetics in the Context of Replicative Ageing in Budding Yeast

Age-related conditions such as Huntington's, Parkinson's and Alzheimer's diseases impose severe problems in terms of human suffering as well as financial costs on a societal level. These are caused by malfunctioning proteins and the underlying processes of these illnesses can be studied in the baker's yeast Saccharomyces cerevisiae. The work presented in this thesis consists of the construction, validation and analysis of mechanistic mathematical models of ageing in baker's yeast. In this context, the focus is the kinetics of specific proteins which is modelled by both ordinary and partial differential equations. Moreover, the ageing phenomena is modelled on two timescales, namely a long and a short one. On the long timescale corresponding to the entire lifespan of yeast cells, a model of the accumulation of damaged proteins is constructed. On the short timescale corresponding to an isolated part of the cell division, the activity of a particular protein called Cdc42 is described through a spatiotemporal reaction diffusion model taking the 3D geometry of the cell into account. Lastly, a common theme on both these timescales is the difficulty of validating a particular model. To address this problem, a mathematical tool called symmetry methods is introduced into kinetic modelling in order to be able to deduce ``hidden information'' in the models which can be used to differentiate between candidate model structures. The overall conclusion is that novel mathematical tools are required in order to improve the capacity for constructing and validating mechanistic models and one concrete example of such a tool is symmetry methods.

Johannes Borgqvist is an M.Sc. in Engineering Mathematics and Computational Science from Chalmers University of Technology. In this thesis, his work from his PhD studies at the department of Mathematical Sciences at the University of Gothenburg is presented.

The Construction, Analysis and Validation of Mechanistic Mathematical Models of Protein Kinetics in the Context of Replicative Ageing in Budding Yeast

Johannes Borgqvist

DEPARTMENT OF MATHEMATICAL SCIENCES

UNIVERSITY OF GOTHENBURG