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Computational modelling of mycobacterium infection and innate immune response in zebrafish

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Computational Modeling of *Mycobacterium* Infection and Innate Immune Response in Zebrafish

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Preface

Modeling biological systems is an important process in the endeavor of investigations in the life-sciences. Many studies rely on construction, simulation and analysis of models applying methods, which vary from schematic drawings to complex systems of equations, in order to understand function and behavior of biological phenomena. It is a challenge to model the complex interplay of the cause-and-effect among components that represents a specific biological behavior, e.g. regulatory pathways. It requires an analysis of *in vivo* and *in vitro* experiments, gathering information and data by category, such as concentration over time in response to a certain stimulus. Therefore it is possible to create reductive methods to represent the biological system.

Computational biology has provided tools and methods to investigate how these interactions give rise to the function and behavior of that system. In this thesis we consider computational methods to model biological behavior, in particular the *mycobacterium* infection process. The scope of this thesis is to model and simulate the dynamics of the infection and the interactions between its components from a macro level (i.e. cell) to a micro level (i.e. molecular, protein). In addition, we analyze qualitative and quantitative the model, providing simulation of different scenarios of specific testable hypotheses about a biological system. The aim of this thesis is to provide and validate a computational method for modeling and simulate biological process, considering its functionalism, scalability and portability. Throughout the thesis one particular application domain is used, *Mycobacterium marinum* infection in zebrafish and the innate immune response.

This dissertation presents the modeling aspects of the mycobacterial infection process and innate immune response. From the choice of the modeling formalism, addressing the qualitative and quantitative aspects of the model as well as simulation results from different scenarios. The goal is to create an accurate model that represents the early stage of the infection process. In the first chapter an overview is given of modeling methods used to represent a biological behavior. Their relevance and characteristics are presented followed by a description on the technique used in the models presented on the followed chapters. The first chapter establishes a context for the subsequent chapters, 2 to 5, in which a series of models are presented, describing characteristics and scenarios of the infection process.

