Foreword

Systems biology has been in the focus of intense public and private research in recent years evoking high expectations and hopes with regard to the solution of emerging problems in the health care sector. The notion of systems biology is rather broad agglomerating mathematical and computational methods, experimental techniques and biomedical applications. At its core, systems biology aims at the explanation of physiology and disease from the level of interacting components such as molecular pathways, regulatory networks, cells, organs and, ultimately, the entire organism. This is complementary to the single-protein (-target) approach that had been the primary research paradigm for a long time condensed in the term "reductionism". However, with the increasing amount and heterogeneity of data generated by modern experimental techniques and the increasing power of computational hardware, it has become evident that such reductionism can no longer be maintained as the primary research paradigm.

The essential tool of systems biology research is the computer. With the use of computational methods systems biology aims at an understanding of biological processes using mathematical models of different granularity. The purpose of these models is the generation of *in silico* predictions, for example on the state of a particular disease or the effect of the therapy on the individual patient. With the use of data integration methods systems biology utilises a comprehensive experimental read-out on different levels of cellular information in order to fit the parameters in these models. And, finally, at the intersection of several key research disciplines systems biology links these mathematical models to practically relevant research questions and contributes to the generation and testing of hypotheses and the planning of experiments. These new approaches are about to revolutionize our knowledge on disease mechanisms and on the interpretation of data from high-throughput technologies.

Systems biology approaches are necessary in several respects. First, with respect to the increasing complexity of research, it is very likely that systems biology contributes to the formulation and solution of new paradigms able to describe the underlying complex biological problems. Secondly, with respect to the increasing complexity of experimental techniques, new problems arise that must be solved by integration rules. For example, in practice often several laboratories are working with different experimental techniques at the same research question. A fundamental challenge is thus to search through the exhaustive set of data and extract meaningful information. Thirdly, with respect to these increasing demands on the mathematical modelling it becomes more and more evident that the development of computational modelling approaches itself must be connected much closer to the experimental observations in order to proof usefulness and relevant predictive power of these approaches.

Having acknowledged that systems biology holds such high promises for future biomedical research, I am delighted to write the Foreword to this "Handbook of Research on Systems Biology Applications in Medicine" as its scope and content provide both, students and researchers, from various disciplines with a broad introduction of systems biology methodologies and show their usefulness on a multitude of applications. The book targets systems biology on a rather practical level from two directions – from an experimental and a methodological direction.

The experimental path contributes articles that highlight applications in important problem domains, for example human diseases such as cancer, type-2 diabetes mellitus, infectious diseases, influenza and ageing, among others, as well as in specific processes such as apoptosis and photosynthesis and with respect to specific experimental techniques such as chip analyses, interference microscopy, protein-protein interactions, synthetic biology, de novo peptide design and photodynamic therapy. The reader approaching the book from this path will find in-depth descriptions of these biological phenomena, of the practical problems in analysing these phenomena along with a description of computational solutions for these analyses.

The methodological path contributes articles that describe multivariate statistical methods such as clustering, gene expression analysis, normalisation methods as well as analysis methods for kinetic models such as metabolic flux analysis, metabolic control analysis among others and, additionally data integration methods in terms of experimental data, pathways and mathematical models. The reader approaching the book from this path will find introduction and description of relevant computational methods and a demonstration how these methods are applied to practical problems. Taken together both paths allow researchers from different disciplines to catch a common basis.

In summary, by presenting such a broad mixture of articles the book gives relevant insights into the different research disciplines that are touched by systems biology such as mathematics, biology, chemistry, medicine and information theory. Students and researchers from these fields might get interested in a specialisation towards this new discipline. On the other hand, researchers coming from the systems biology field will get valuable information on real practical problems and potential approaches to these problems that could benefit from systems biology methods. Thus, the book gives both sides a good starting point to walk on further on this fascinating new road.

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Ralf Herwig studied physics and mathematics at the Technical and the Free University Berlin and finished his PhD in 2001 on clustering methods for gene expression data. He was awarded for the Heinz-Billing-Price for Scientific Computation of the Max-Planck Society in 1999 and was an honor student of the American Academy of Achievement in 2000. Since 2001 he is group leader at the Max-Planck-Institute for Molecular Genetics. His research focuses on multivariate statistical methods, data integration systems and computational modelling. Ralf Herwig has contributed to 50 scientific publications and was co-author of the first textbook on systems biology in 2005.