The Role of Systems Biology and Synthetic Biology

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Description

Over the past decade the biological sciences have been widely embracing Systems Biology and its various data integration approaches to discover new knowledge. Molecular Systems Biology aims to develop hypotheses based on integrated, or modelled data. These hypotheses can be subsequently used to design new experiments for testing, leading to an improved understanding of the biology; a more accurate model of the biological system and therefore an improved ability to develop hypotheses. During the same period the biosciences have also eagerly taken up the emerging Semantic Web as evidenced by the dedicated exploitation of Semantic Web technologies for data integration and sharing in the Life Sciences. We describe how these two approaches merged in Semantic Systems Biology: A data integration and analysis approach complementary to model-based Systems Biology. Semantic Systems Biology augments the integration and sharing of knowledge, and opens new avenues for computational support in quality checking and automated reasoning, and to develop new, testable hypotheses.

Synthetic Biology

Synthetic biology provides numerous great opportunities for chemical engineers in the development of new processes for large-scale production of biofuels, value-added chemicals, and protein therapeutics. However, challenges across all scales abound. In particular, the modularization and standardization of the components in a biological system, so-called biological parts, remains the biggest obstacle in synthetic biology. In this perspective, we will discuss the main challenges and opportunities in the rapidly growing synthetic biology field and the important roles that chemical engineers can play in its advancement.

Top-down systems biology approaches attempt to identify the networks and the logic behind a biological function by the analysis of genome-wide data sets. In other words, these approaches start with a comprehensive set of data generated by one or more of the echnologies and aim to identify networks and components that are participating in the generation of a phenotype or a disease often even without the necessity of prior knowledge. Scientists often refer to these as 'top-down' systems biology approaches. In this class belong gene-set enrichment analysis, pathway mapping, disease classification, reverse causal reasoning and network inference approaches. From the perspective of drug discovery, the top-down systems biology methods aim at a deeper understanding of the causes of a disease, to stratify patients and to identify the right molecular targets.

Bottom-up systems biology approaches try to copy nature by generating computational models of cells, tissues and organs. Here, individual components are assembled into a network with the goal to simulate the dynamic properties of the resulting system. For several biological processes these so-called molecular-mechanistic models are available, which capture and simulate cellular signalling processes

At the start of this century, the time appeared ripe for a call to adopt systems biology approaches to further our understanding of biological form and function. The Human Genome Project had just produced the first of a series of drafts of the complete human DNA sequence, and knowledge about the genetic potential of genomes had provided a tremendous boost to the development and use of high throughput genome wide functional genomics data production approaches.

Systems Biology

Systems biology aims to provide a holistic and in many cases dynamic picture of biological function and malfunction, in case of disease. Technology developments in the generation of genome-wide datasets and massive improvements in computer power now allow to obtain new insights into complex biological networks and to copy nature by computing these interactions and their kinetics and by generating in silico models of cells, tissues and organs. The expectations are high that systems biology will pave the way to the identification of novel disease genes, to the selection of successful drug candidates that do not fail in clinical studies due to toxicity or lack of human efficacy and finally to a more successful discovery of novel therapeutics. However, further research is necessary to fully unleash the potential of systems biology. Within this review we aim to highlight the most important and promising top-down and bottom-up systems biology applications in drug discovery.

Biological functionality like the secretion of insulin from the

pancreatic beta cell to control blood glucose or the contraction of cardiomyocytes to pace the rhythm of the heart beat emerges from interactions among several hundred genes and proteins within the cellular environment. In order to understand living cells, understanding these networks, identifying the most important nodes and their connections, appears to be a pre-requisite.

Systems biology approaches attempt to provide a more holistic and in many cases dynamic picture of biological processes. It is all about understanding biology in a context to address the right targets and the right biological mechanism by a pharmacological treatment.

Technology developments in the area of, for example, Next Generation Sequencing (NGS), transcriptomics, metabolomics and (phospho) proteomics enable parallel and high throughput characterization of biological systems. The available massive improvements in computer power allow the analysis of these genome-wide data sets to derive complex network views of biological systems and to infer the logic behind a biological function or malfunction. The computational improvements also allow copying nature by computing these interactions and their kinetics and by generating in silico models of cells, tissues and organs.