

Summary

In order to construct a complete model of the cell and hence fulfil one of the promises of systems biology, we need to include data on cellular components that are not directly encoded in the genome. This includes small molecules.

The chapters of this dissertation consider interactions between cells and small molecules at different levels of cellular organisation. After the introductory chapter, Chapter 2 considers small molecule-cell interactions at the atomic level, Chapter 3 at the pathway level, Chapter 4 at the proteome level, and Chapter 5 at the whole-cell level.

Chapter 1: An introduction to the concepts related to small molecule-cell interactions.

Chapter 2: I introduce Spial (Specificity in alignments), a tool for the computational analysis of subtype-specific features in multiple sequence alignments of proteins. I show that it can be used to gain understanding of both protein-small molecule interactions and protein-protein interactions.

Chapter 3: The topic of this chapter is quorum sensing, or cell-to-cell communication between unicellular organisms. I use a combination of computational methods to identify quorum sensing systems in sequenced bacterial genomes. Furthermore, I establish a framework for the identification of transcription factors involved in the quorum sensing response in the yeast *Saccharomyces cerevisiae*.

Chapter 4: This chapter provides a broader view of small molecule-cell interactions. It is about chemogenomics, a field of high-throughput biology that probes the reactions of cells to a large number of different small molecules. I develop computational methods for the analysis of chemogenomic data that can assist in the identification of leads for drug development.

Chapter 5: Recent years have seen a rapid increase in the number of high-throughput experiments in the fields of genomics, cell and evolutionary biology, pharmacology, epigenetics, and functional genomics. I assembled 236 gene-centric descriptors from such high-throughput experiments in *S. cerevisiae* and characterised the global set of relationships between them. By assembling a large number of diverse descriptors of various aspects of the cell, the methods I outline allow an unbiased integrative investigation of a wide variety of data types. I also report several novel associations between cellular descriptors that were not known before.

Chapter 6: The dissertation ends with a chapter that highlights the important aspects of the findings presented and their practical implications.

Overall, this dissertation presents a framework for the investigation of the interactions between small molecules and cells at different levels of resolution.