Chapter 1

Inference of Gene Regulatory Networks by Topological Prior Information and Data Integration

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ABSTRACT

The inference of Gene Regulatory Networks (GRNs) is a very challenging problem which has attracted increasing attention since the development of high-throughput sequencing and gene expression measurement technologies. Many models and algorithms have been developed to identify GRNs using mainly gene expression profile as data source. As the gene expression data usually has limited number of samples and inherent noise, the integration of gene expression with several other sources of information can be vital for accurately inferring GRNs. For instance, some prior information about the overall topological structure of the GRN can guide inference.

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1. INTRODUCTION

Systems Biology is an interdisciplinary research field that aims at the study of complex interactions occurring in living organisms (Snoep & Westerhoff, 2005). Research in this field focuses on the study of biological processes such as cell cycles and the conditions for the origin of certain diseases. The ultimate goal of these studies is to help the development of new treatments and drugs against diseases, biofuel production techniques, among many other applications.

The genome of an organism has a central role in the control of cell processes such as cell response to environmental stimuli, cell differentiation in its respective functional groups, DNA replication for cell division, and many others. An organism can be seen as a network of molecules connected by biochemical reactions (Voet, Voet & Pratt, 2005). Proteins synthesized from genes may work as transcription factors which bind to regulatory sites of other genes, such as enzymes which catalyze metabolic reactions or components of signal transduction pathways. Such regulatory mechanism forms a complex system of sending and receiving signals (RNAs) which can be investigated to identify the control mechanisms of the cell and the relationships among various biological entities like genes, RNAs and proteins. However, there is still much to be discovered about the functional relationships of control mechanisms, e.g., transcription levels and proteins, in the regulatory system (Barabasi, 2002; Fall, Marland, Wagner & Tyson, 2002; Shmulevich & Dougherty, 2007).

With few exceptions, all cells of an organism contain the same genetic material, although cells of different tissues are functionally different. The cell function is partially determined and controlled by gene expression profiles. With the aim of understanding how genes are involved in control of intra and inter cell processes, the scope of the molecular biology studies needs to be enlarged to include not only the discovery of nucleotide sequences that codes for proteins, but also the unraveling of the regulatory systems which determine what genes are expressed, when, where, and to how much extent (Snoep & Westerhoff, 2005). The explanation of these regulatory networks functioning, by means of sending and receiving signals, is currently one of the main objectives of the systems biology studies.
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