Abstract

A fully functional gene regulatory network can be formed using gene-gene and/or gene-protein interactive patterns. To maintain a healthy cell cycle, it is necessary to have a proper control of the regulatory proteins in the network. Excess protein concentration may lead to beyond control division of the healthy cells causing cancer. Microarray gene expression profiles are frequently explored to understand the causal factors of regulation associated with some disease. Most of the significant research to interpret the regulations in a gene regulatory network is restricted to comparison of gene expression values across more than one condition or the discovery of genes having altered interaction levels with neighbours across conditions. Therefore, differential expression (DE), gene correlation and differential co-expression have been intensively studied using microarray gene expression profiles. In other words, the regulatory action of a gene in a complex network is guided by the differential functionalities of the gene acting under varied conditions. To gain better insight significant state of the art methodologies primarily explore the existence of differential co-expression patterns, where the co-expression level between genes alters across different states. Rigorous researches via such methodologies help in comparing the expression samples over normal and diseased states making us understand the pattern of various diseases.

Exploring the complex interactive mechanism in a Gene Regulatory Network (GRN) developed using transcriptome data obtained from standard microarray and/or RNA-seq experiments helps us to understand the triggering factors in diseased pathways. In this regard, the Transcription Factor (TF) genes generate protein complexes which affect the transcription of various target genes. These TF genes play a pivotal role in a Gene Regulatory Network (GRN) by differentially regulating genes across conditions. In some cases, it requires coordinated regulation of multiple TFs to control a Differentially Expressed (DE) gene. This form of regulation can be restricted to simple pairwise structures and may extend involving multiple TF genes regulating a target DE gene. This form of differential regulation can be expected to occur in

between two levels or even beyond following multiple hierarchical paths of regulation to the target DE gene. These regulatory situations helping in the reconstruction of differential TF regulatory networks (TRNs; can be considered as a subset of GRNs) emulating the biologically significant KEGG (Kyoto Encyclopaedia of Genes and Genomes) pathways can be designed through various forms of transcriptome data utilizing static or time series expression profiles. Further extension of these approaches helps us in identifying the therapeutic targets, which happens to be open challenge in systems biology. In this regard, indirect gene regulatory hierarchical architectures may be promising enough considering varied topological structures and unknown gene regulation factors. Such causal regulations can be investigated, keeping in force all perturbation experiments of a dataset. Contemporary state of research primarily highlights direct interaction networks which mostly forego the inevitable presence of a third entity, if any, towards varied forms of causal regulations.