Network parameters to detect hubs and bottlenecks in the gene regulatory networks

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Abstract: Gene regulatory networks have implemented in many studies focused on deciphering core regulatory elements and the mechanisms in biological systems. A well adopted pipeline in constructing such networks starts with profiling gene expression, followed by identification of individual regulatory components including transcription factors, miRNAs, protein-protein and protein-gene interactions. With these information, a network of interactions could be constructed in which the elements would be nodes and the interactions make the edges. The network then undergoes different types of analysis to identify and introduce the most important elements including TFs, miRNAs or genes. Then after, centrality analysis are applied to find the most important individuals among aforementioned elements. Parameters including, degree, betweenness, stress, closeness, and eccentricity would be evaluated and the results are expressed as a list of genes that some are at the top in some of these evaluations. However, we found these methods rather ambiguous and case-dependent. Such that the method in one study could not be applied in other similar cases. To address this issue here we have tested the validity of each centrality parameters to detect biologically known hubs and bottlenecks in previously described yeast gene regulatory networks. We have included some of these known networks including, auto regulation, multi-component loop, feedforward loop, single input motif, multi-input motif, regulator chain. Our findings indicated that among centrality analysis parameters, degree is the best detector of for detecting hub nodes, while to detect bottlenecks, betweenness should be used. These findings would be helpful in developing a more comprehensive approach for biological network analysis.

Keywords: Bottlenecks; Centrality Parameters; Degree; Gene Regulatory Network (GRN); Hubs