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Oral Presentation Session

Fuzzy Modularity of Biological Networks

Nathan Menke[1, 2]

[1]Virginia Commonwealth University Reanimation Engineering Shock Center (VCURES), Richmond, VA, USA [2]Department of Emergency Medicine, Virginia Commonwealth University, Richmond, VA, USA
Presenter's email address: nmenke@vcu.edu

Objective: Crisp set theory has provided useful tools for the analysis of biological networks; however, biological networks are better described using the language of fuzzy set theory. Traditionally, algorithms designed to identify modules from networks utilize crisp sets. These algorithms may give arbitrary results and fail to identify nodes with partial membership in multiple modules (gateways). Fuzzy sets are defined as sets whose boundaries are not precise. Fuzzy sets are ideal for to dealing with the uncertainty, imprecision, and complexity of real world systems. Thus, fuzzification of the modularity algorithms provides biological plausibility to the creation of modules

Methods: A small metabolic network composed of molecules involved in glucose metabolism, glucose storage, fatty acid metabolism and protein metabolism was created by assigning a node for every molecule. Chemical reactions were denoted by an undirected edge between molecules. The network was then analyzed using basic network tools and subjected to a modularity analysis algorithm developed by MEJ Newman. The results of the modularity analysis are fuzzified by creating a membership function that is defined as the proportion of edges from a given node to a given module.

Results: The statistics for the network are summarized in Table 1. Applying the modularity algorithm resulted in the creation of seven modules (Table 2). The fuzzification of the modularity analysis allowed the gateway molecules to be easily identified (Table 3). For example, glucose-6P provides a gateway between glycolysis, glycogen storage, and the pentose phosphate pathway.

Conclusion: Utilizing fuzzy set theory to analyze biological networks provides an added layer of analysis consistent with real world data. Fuzzy modularity analysis may help predict possible side effects of therapeutic modalities (such as an anti-inflammatory medicine causing myocardial infarctions) and provide insight into abnormal physiology of complex diseases.

Key words: fuzzy, set, modularity, network

Table 1: Network Statistics

number of nodes	62
number of edges	96
average vertex degree	3.10
network connectedness	0.0508

Table 2: Network modules created using Newman's algorithm

Module	Number of Nodes	Function
1	10	Nitrogen Metabolism
2	12	Fatty Acid Metabolism
3	8	Glycolysis & Glycogen Metabolism
4	10	Glycolysis & Pentose Phosphate
5	12	Glycolysis & Citric Acid Cycle
6	3	Glycolysis
7	7	Mixed

Table 3: Fuzzy module membership values of gateway molecules

Molecule Name	Newman-Module	Fuzzy-Module-1	Fuzzy-Module-2	Fuzzy-Module-3	Fuzzy-Module-4	Fuzzy-Module-5	Fuzzy-Module-6	Fuzzy-Module-7
AcetylCoA	5		0.20			0.80		
Alanine	4	0.33				0.67		
α-ketoglutarate	5	0.29				0.57		0.14
Glucose-6P	3			0.75	0.25			