Visualization of Metabolic Networks as Networks of Atoms by Pajek: An Application of Connectivity Matrix Method

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1 Introduction

Many studies have been conducted about the global topological nature of metabolic networks since the report by Barabasi's group [3]. Topological nature of networks depends on the definition of nodes and edges/arcs. In most of such studies, metabolites are assumed as nodes either in the studies conducted with or without the care of atomic tracing [1,3,4,5]. This is acceptable because the main function of metabolism is consumption and production of metabolites. However, it should be noted that the definition of the edges varied depending on the researches. On the other hand, instead of metabolites, atoms can be assumed as nodes, where metabolic networks are defined by inter-metabolite atom-level connectivity through enzymatic reactions and by intra-metabolite atom-level connectivity through chemical bonds without variation of the edge definition [6,7]. Understanding metabolic networks as networks of atoms seems to have certain value because it provides an insight about evolution of metabolic networks, that is, co-evolution of inter- and intra-metabolite atom-level connectivities corresponding to evolutionary emergences of new compounds associated with those of new reactions. Possible correlation between 2 types of connectivities seems to deserve investigation.

Connectivity matrix method [6] has been proposed for analyses of biological networks, where all the connectivities of interest in a given network are expressed in a matrix, connectivity matrix, and then a variety of analyses can be conducted on Octave or Matlab using functions or script files written by researchers. Whereas calculation of topological indices based on connectivity matrix would produce valuable information about network structure, graphical representation of the network makes it easy to understand the nature of the network. In the present study, both inter- and intra-metabolite connectivities in a model network of carbohydrate metabolism were expressed in a connectivity matrix. Then, based on this matrix, the file for Pajek [9] was generated and the atom network structure was visualized.

2 Method

2.1 The Model Network of Carbohydrate Metabolism

The model metabolic network used in the present study was composed of the reactions for glycolysis, oxidative decarboxylation of pyruvate, citric acid cycle, pentose phosphate pathway, and gluconeogenesis, where cytosolic compartment were distinguished from the mitochondrial compartment.

2.2 Description of Atom-Level Connectivity in the Model Network

Each atom in the network was expressed as a row vector. Information about connectivity or edge itself was also expressed as a row vector. A vector for inter-metabolite connectivity included 1 as a connectivity-type number and reaction number, whereas a vector for intra-metabolite connectivity included 0 as a connectivity-type number. In the present study, valences of chemical bond were not expressed in the vector for the connectivity. Thus, conversion of atom va1 to atom va2 through connectivity vc is expressed as (va1, va2, vc), a row vector formed by the combination of 3 row vectors. Using this format, all the atom-level connectivities in the network were expressed as a matrix, connectivity matrix, each row of which
corresponded to one connectivity [6]. Metabolites and reactions were numbered based on the LIGAND [2].

### 2.3 Construction of Connectivity Matrix and Generation of the Pajek Files

Construction of connectivity matrix from IMAC [8] and generation of the Pajek file were conducted on GNU Octave or Matlab by functions or scripts written for the present study.

### 3 Results and Discussion

The model network was successfully visualized. Various layout options supplied by Pajek were tested to observe the network clearly. ‘Kamada-Kawai’ method under ‘Energy’ generally worked well for this purpose. The network seems to be coarse rather than dense. Figure 1 is a visualization, where only inter-metabolite C-C connectivities (dotted lines) and intra-metabolite connectivities in the metabolites of glucose (solid lines) were written to the file.

Visualization of atomic tracing between 2 metabolites was reported [1] and visualization of chemical structure is established. Whilst those visualizations are not global, they are very useful in understanding metabolism. In the present study, the entire network was visualized although its size was small. Highlighting specific atom(s) or edge(s) were possible by script files and can be applied, for example, to mapping 6 carbons of glucose, movement of isotope etc. Mapping parts in the entire network will contribute to the understanding of organization of the entire of a metabolic network.

### References


