Graph Modeling of Metabolism

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1 Introduction

Metabolism is a network of chemical reactions catalyzed by enzymes. In a cell, ingested sugars and proteins are metabolized to basic compounds such as amino or fatty acids, and they are used to construct cellular structures in turn. This paper proposes the graph modeling of metabolism. It is possible to describe metabolism as a circulation of atoms by representing all reactions with the chemical structures of small compounds (metabolites). Enzymatic reactions are regarded as the rearrangement of chemicals, and the mapping information of atoms between structures are stored in a database. In fact, the tracer experiment in biochemistry is based on this model, although the mapping information is referenced with the traditional metabolic map on paper. This tracing effort should be minimized by the digitization of metabolism as in our project.

2 Method and Results

As in Fig. 1, the metabolism is represented as a graph, in which nodes and edges correspond to atoms and their mapping information in the chemical reactions, respectively. The graph is automatically generated from a set of chemical reactions (Fig. 2) [1]. The application of k shortest path algorithms [4], and k minimum spanning tree algorithm [3] to this graph produce:

- pathways between any two compounds (in the shortest order), and

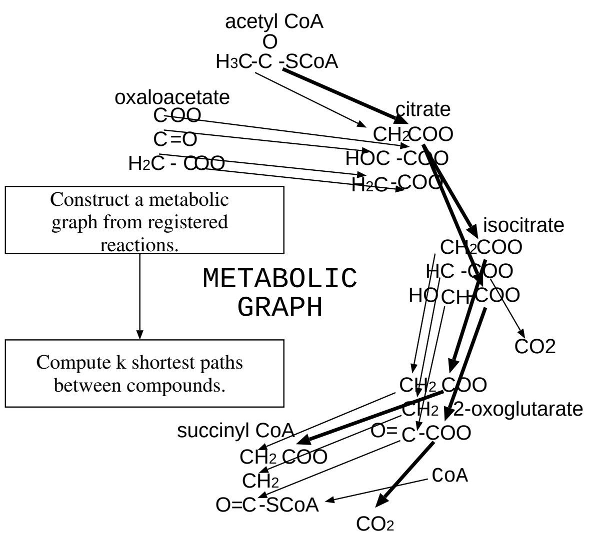

Figure 1: The tracing result of a carbon in acetyl CoA in TCA cycle. Bold arrows represent the movement of the labeled carbon in acetyl CoA. Normal arrows represent other movements of atoms. Note that arrows may split, because of the symmetry of structures. These movements can be computed by a graph matching algorithm, i.e. comparison between chemical structures.

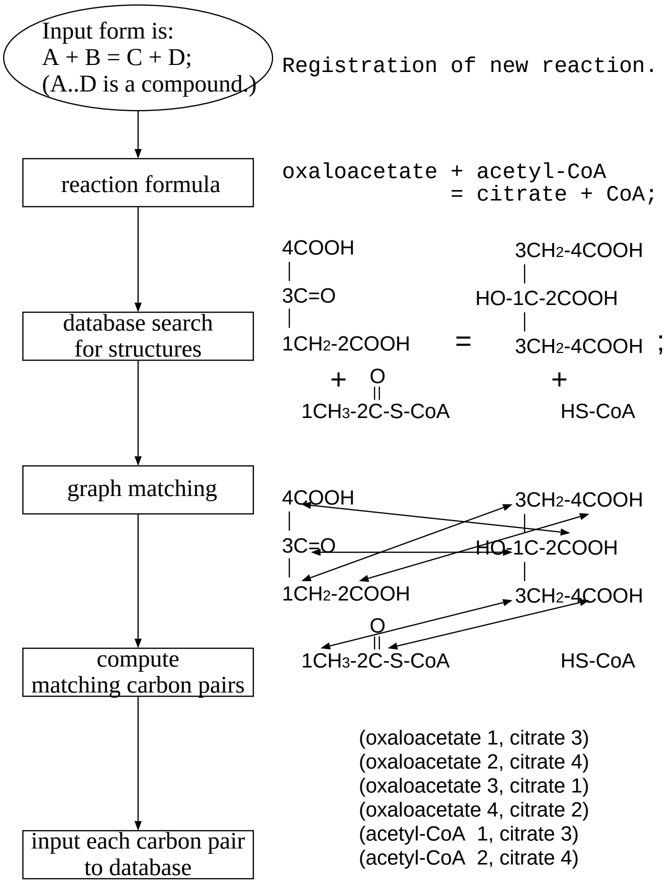

Figure 2: Assume we have a database of chemical compounds. Given a chemical reaction, the structures of compounds are searched in the database. The structures in the left-hand side of the reaction and those in the right side are combinatorially compared, and the best matching is determined so that the breakage and formation of chemical bonds are minimum. Since many reactions use water, the mapping of hydrogens and oxygens are often ambiguous. We therefore omit hydrogens and oxygens from the mapping information.

- a metabolic map centered at any given compound.

With this method, it is easy to see why the glycolysis, not the pentose pathway, is necessary for digesting glucose. Although glucose is connected to pyruvate through the pentose pathway, only half of glucose can be turned to pyruvate. In secondary metabolism, we found the relationship between sterols [1, 2]. Prediction of new metabolism is also possible, by comparing with the traditional metabolic map [5].

References

[1] Arita, M., Automated metabolic reconstruction: theory and experiments, Ph.D Thesis, Tokyo Univ, 1999.

[2] Arita, M., Asai, K. and Nishioka, T., Finding precursor compounds in secondary metabolism, *Genome Informatics*, 10:113–120, 1999.

[3] Eppstein, D., Finding the k smallest spanning trees, *BIT*, 32:237–248, 1992.

[4] Eppstein, D., Finding the k Shortest Paths, *Proc 25th Ann. Symp. on Foundations of Comp. Sci. (FOCS'94)*, 154–165, 1994.

[5] Ogata, H., Goto, S., Sato, K., Fujibuchi, W., Bono, H. and Kanehisa, M., KEGG: Kyoto Encyclopedia of Genes and Genomes, *Nucleic Acids Res*, 27(1):29–34, 1999. `http://www.genome.ad.jp/kegg`