Representing Metabolic Networks by the Substrate-Product Relationships

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1 Introduction

One major player in the post-sequencing biology is the metabolome, i.e. comprehensive study on metabolism. Although there are established on-line pathway databases [4], they are not designed to be research-cooperative: the typical usage is to *browse* the on-line data, and not to *work* on them. To facilitate a hands-on metabolic database, we compiled substrate-product atomic correspondents for enzymatic reactions. **The substrate-product structure relationships are indispensable information in reliable pathway reconstruction.** For a sequence of reactions, its validity as a pathway depends on two factors: 1) the atom under focus, and 2) the conserved structural moiety in the reactions. In deducing or predicting pathways from reactions, it is therefore essential to consider the atomic level correspondence of metabolites to guarantee that some moiety is conveyed through the reactions.

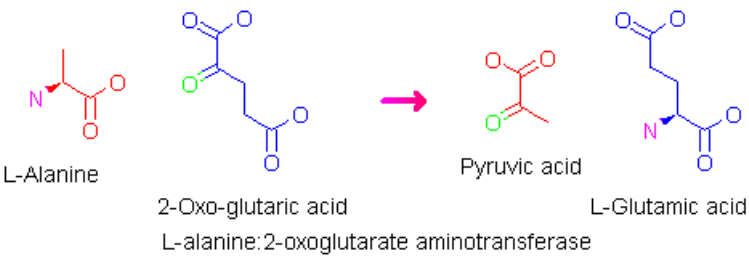

Figure 1: EC 2.6.1.2 aminotransferase.

Figure 1 is an example reaction among four metabolites. In the nitrogen metabolism, the reaction is considered a link between L-Alanine and L-Glutamic acid, but in the carbon metabolism, L-Alanine is linked with Pyruvic acid. Since most metabolic reactions involve three or four metabolites, interpretation of each reaction must change depending on its context.

2 Method and Results

The Atomic Reconstruction of Metabolism (ARM) software can computationally reproduce biochemical radioisotope-tracer experiments. The system consists of three main components: a mapping database of substrate-product atomic correspondents derived from known reaction formulas as color-coded in Fig. 1, a tracing engine that can compute all pathways between two given compounds by using the mapping database, and a graphical user interface. The system can facilitate the display of

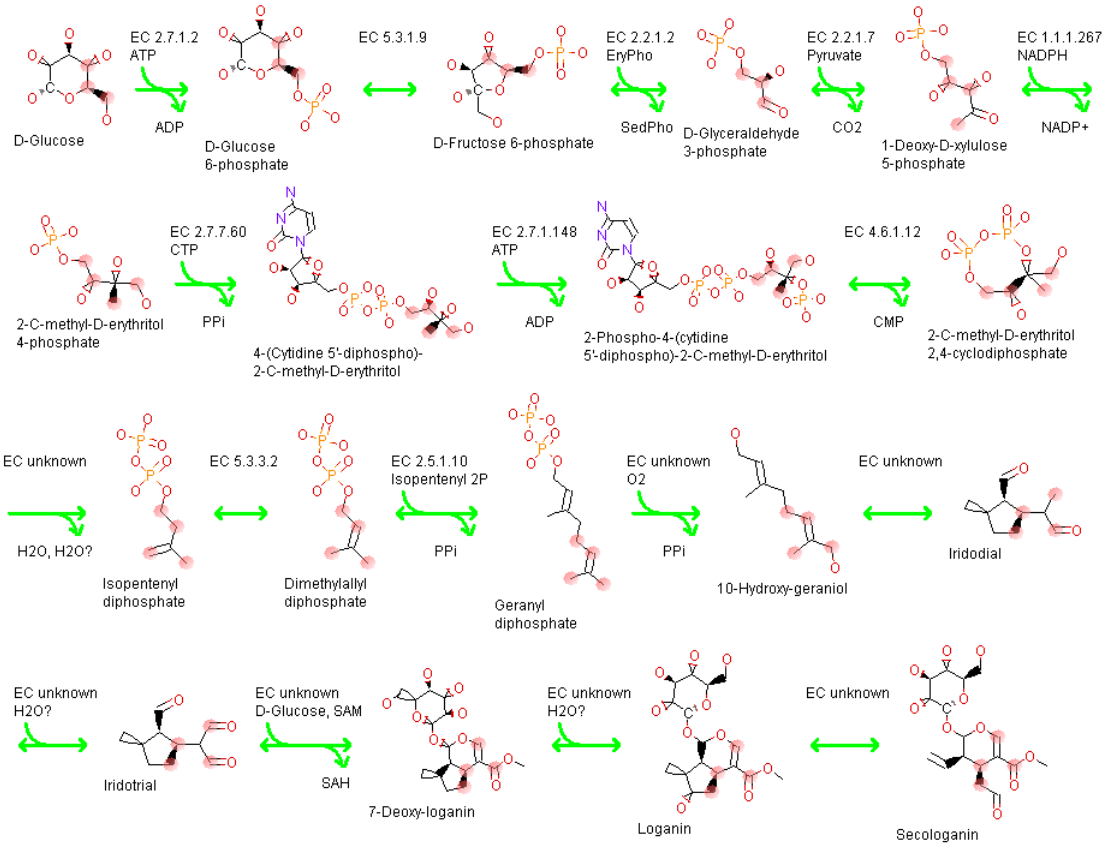

Figure 2: An example pathway from D-glucose to secologanin. Highlighted positions indicate carbon atoms from glucose along this pathway. Symmetric molecules may distribute these atoms to equivalent positions. (This figure is a reproduction from [1].)

possible pathways between any two compounds and the tracing of every single carbon, nitrogen, or sulfur atom in the metabolism (Fig. 2). Users can interactively search or edit metabolites, reactions, and pathways on demand. The curated and precompiled data-set represents the metabolism of more than 2700 reactions in about 1700 EC sub-subclasses. Although this is far short of the spectrum of catalytic activities, it essentially covers reactions in the basic metabolism in bacteria. With this information, we can reassess and compare the global properties of metabolic networks [2, 3]. The software tools and data are freely available at `http://www.metabolome.jp/`.

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