Algebraic Comparison of Metabolic Networks

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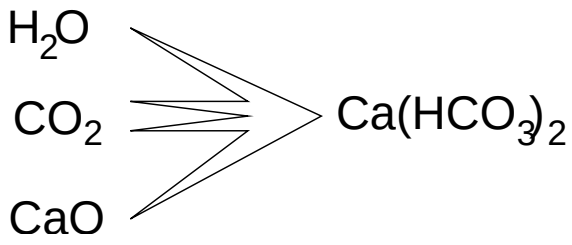
17th January 2006

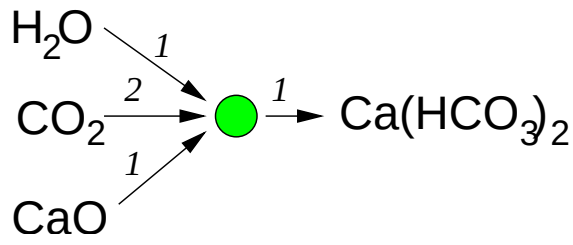
Motivation

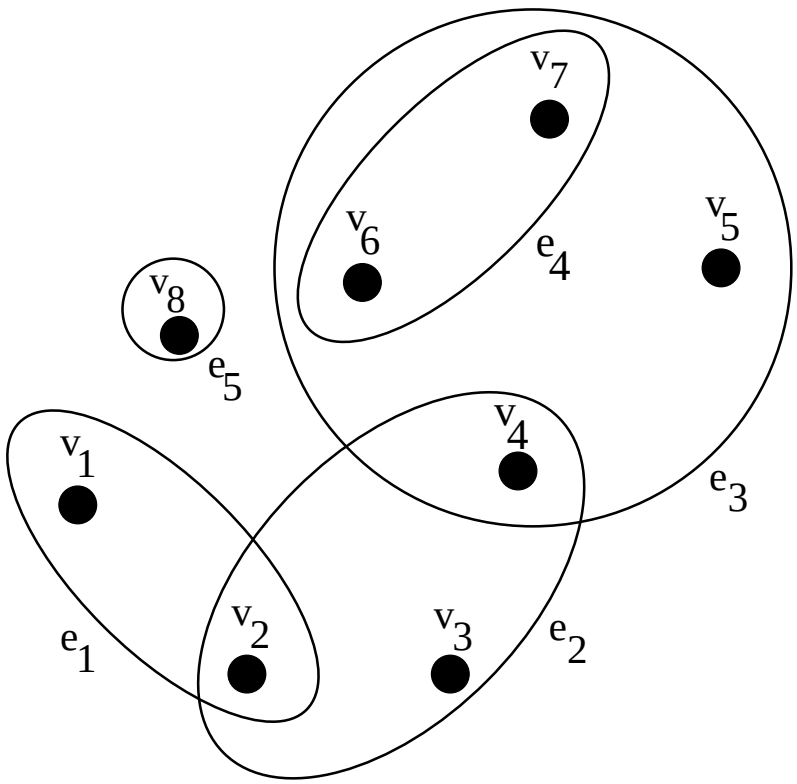
- Advances in experimental techniques in metabolomics.
- Gene based phylogenies have problems with gene transfer, duplication, deletion or functional replacement.
- No tools available for hypergraphs.

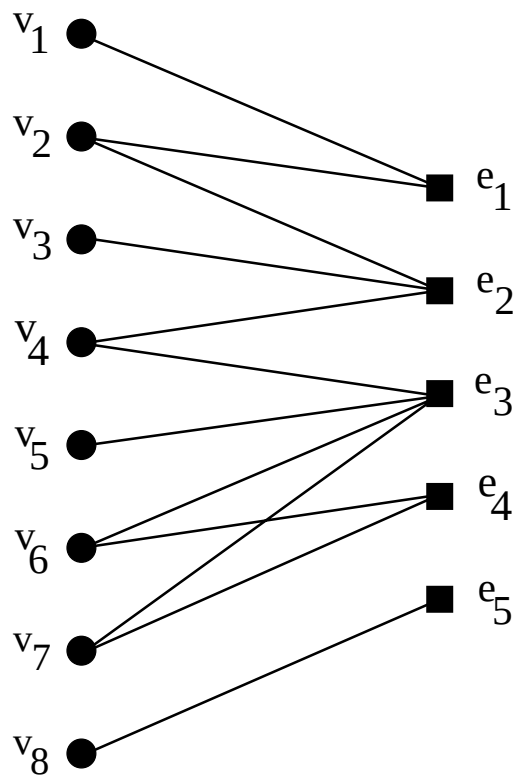
Hypergraphs and Chemical Reactions

$$CaO + 2CO_2 + H_2O \rightarrow Ca(HCO_3)_2$$

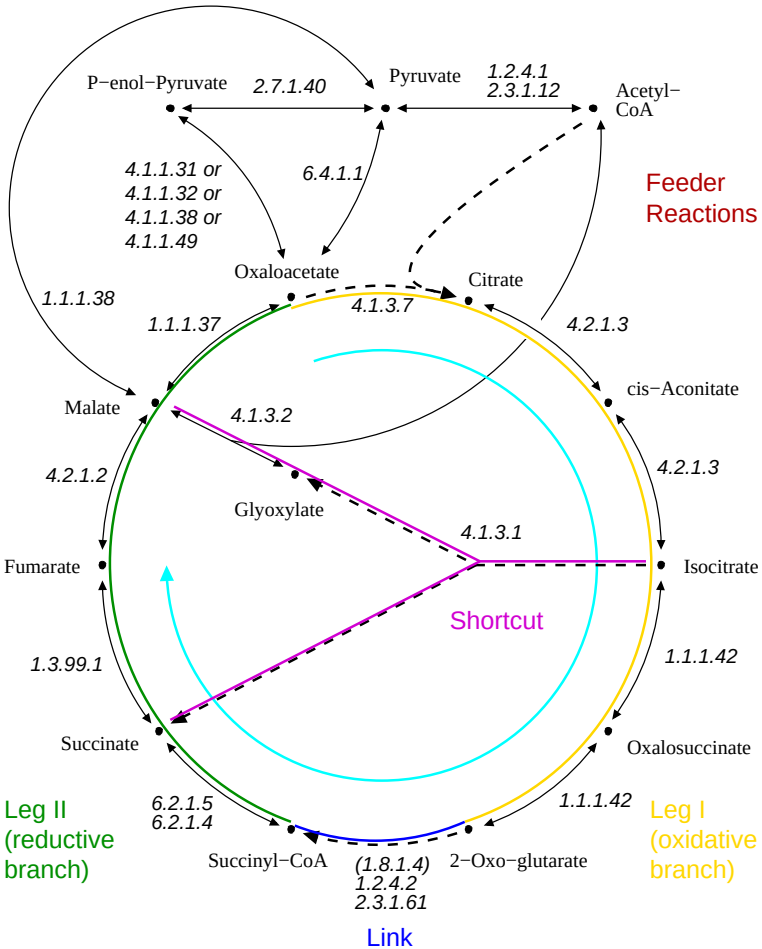


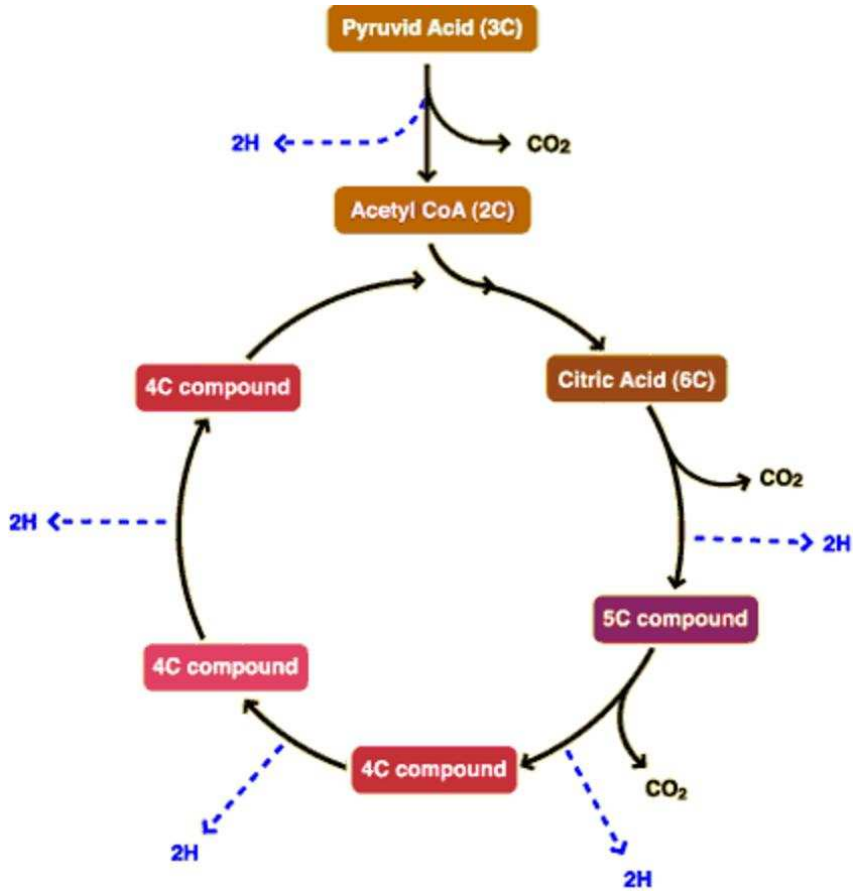




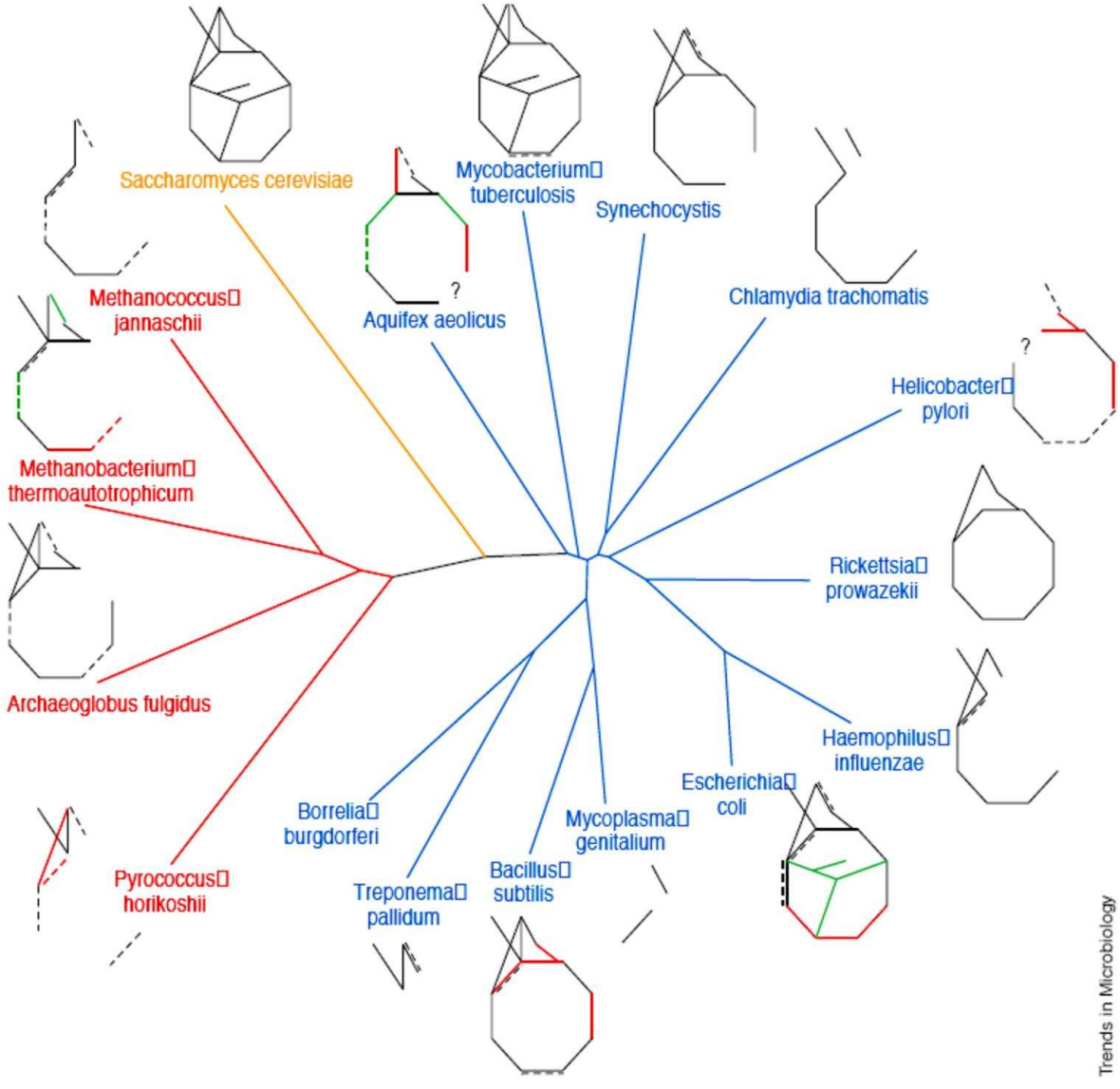


The Krebs Cycle





Variations of the Krebs Cycle



Huynen et. al. Trends Microbiol., 7(7):281-291, 1999

Set Algebra Operations

Intersection

$$\mathfrak{M}' \cap \mathfrak{M}'' = \lfloor\!\lfloor (X' \cap X'', \mathcal{E}' \cap \mathcal{E}'') \rfloor\!\rfloor$$

Difference

$$\mathfrak{M}' \setminus \mathfrak{M}'' = \lfloor\!\lfloor (\mathrm{supp}(\mathcal{E}' \setminus \mathcal{E}''), \mathcal{E}' \setminus \mathcal{E}'') \rfloor\!\rfloor$$

strict Difference

$$\mathfrak{M}' \backslash\backslash \mathfrak{M}'' = \lfloor\!\lfloor (X' \setminus X'', (\mathcal{E}' \setminus \mathcal{E}'')[X' \setminus X'']) \rfloor\!\rfloor$$

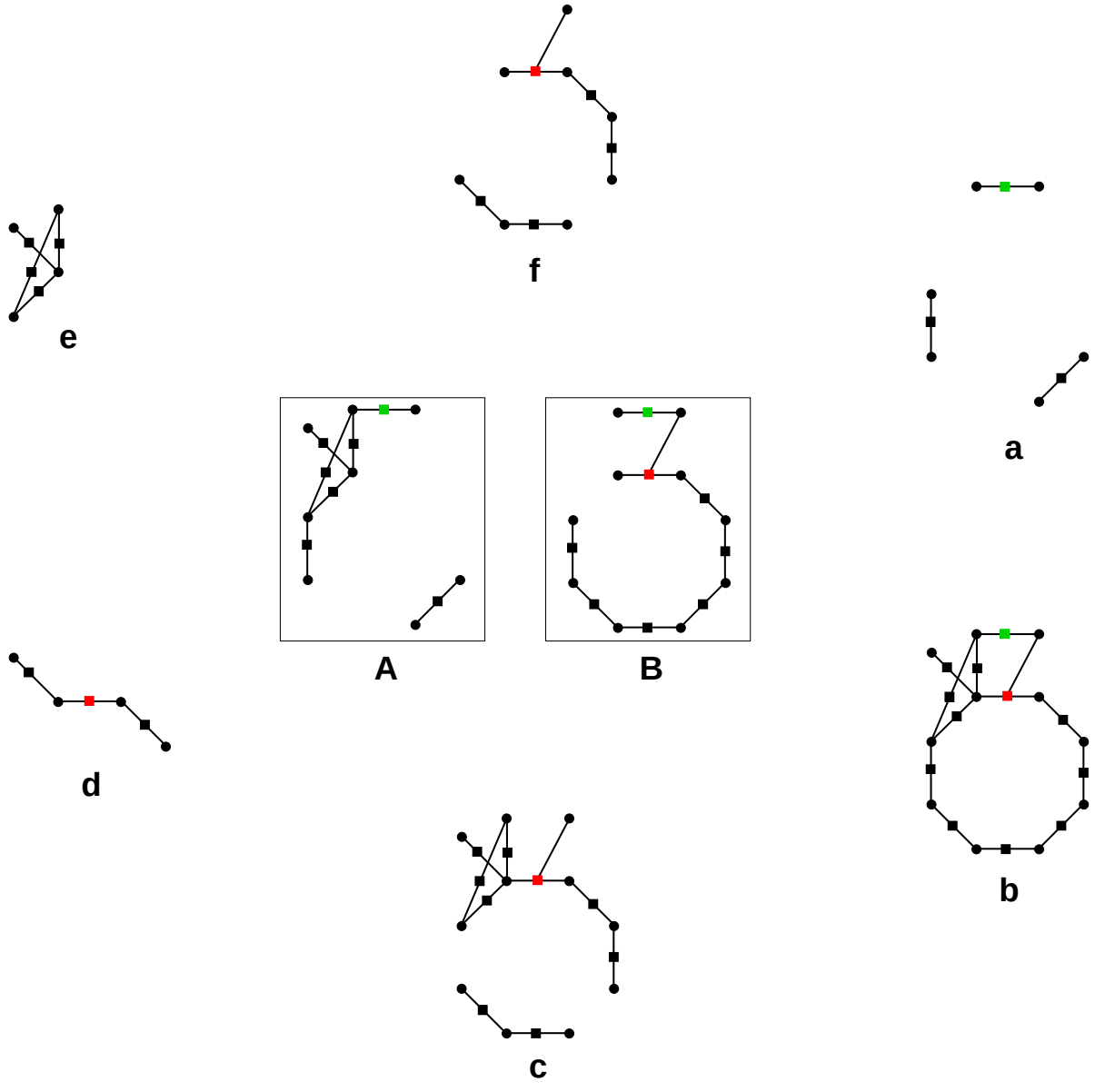
symmetric Difference

$$\mathfrak{M}' \triangle \mathfrak{M}'' = \lfloor (\mathfrak{M}' \cup \mathfrak{M}'') \setminus (\mathfrak{M}' \cap \mathfrak{M}'') \rfloor$$

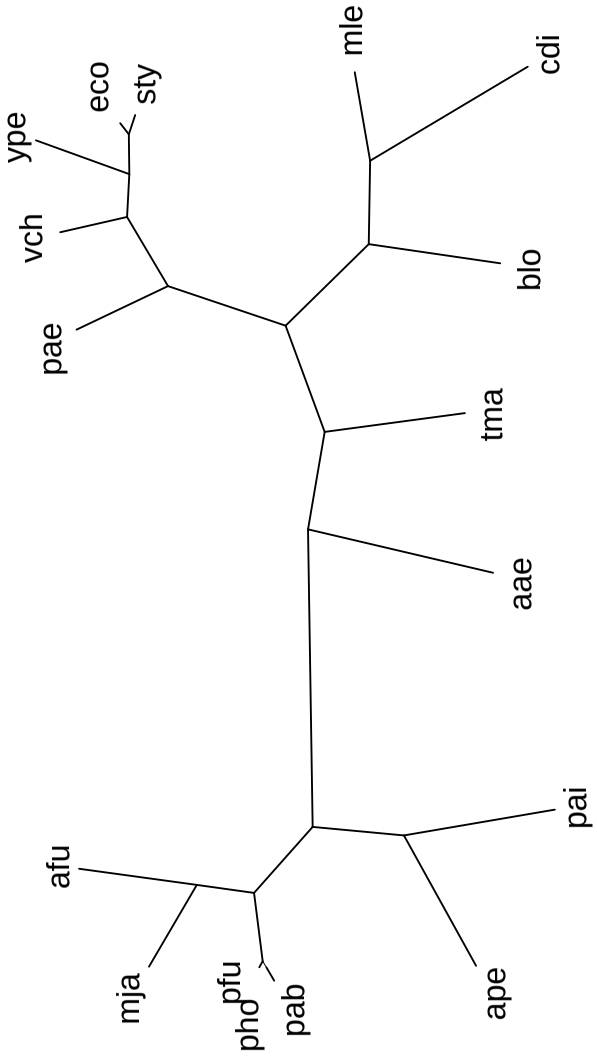
strict symmetric Difference:

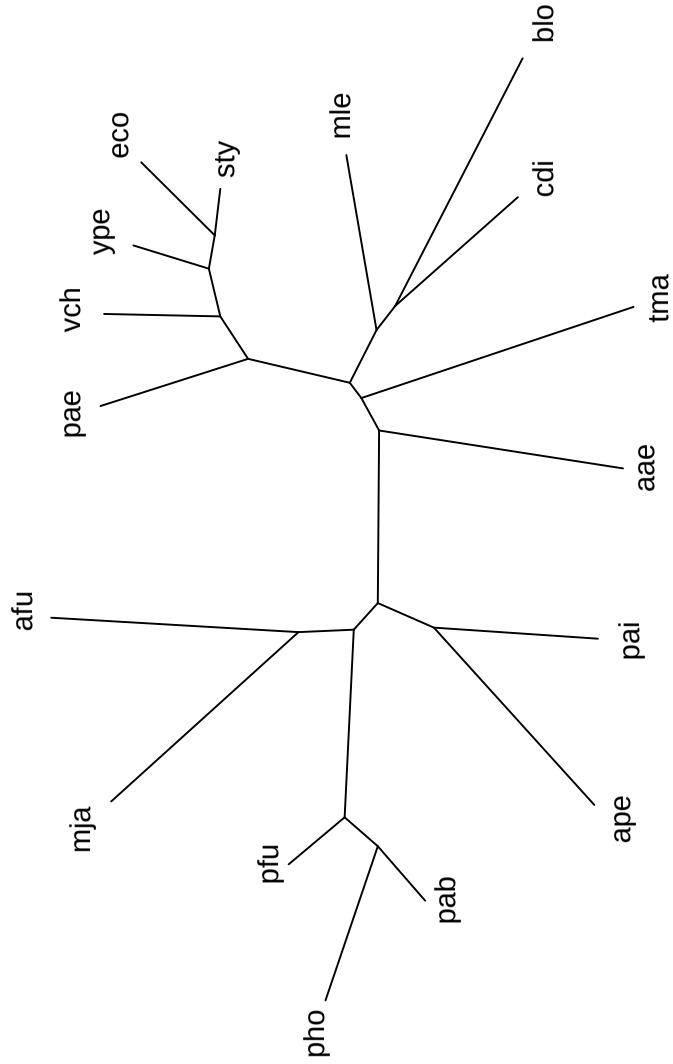
$$\mathfrak{M}' \diamondsuit \mathfrak{M}'' = \lfloor (\mathfrak{M}' \cup \mathfrak{M}'') \backslash\backslash (\mathfrak{M}' \cap \mathfrak{M}'') \rfloor$$

Examples of the Set Algebra Operations



Phylogenies from Networks





$$d(\mathfrak{M}', \mathfrak{M}'') = \frac{\|\mathfrak{M}' \triangle \mathfrak{M}''\|}{\|\mathfrak{M}'\| + \|\mathfrak{M}''\| - \|\mathfrak{M}' \cap \mathfrak{M}''\|} = \frac{\|\mathfrak{M}' \triangle \mathfrak{M}''\|}{\|\mathfrak{M}' \cup \mathfrak{M}''\|}$$

Differential Network

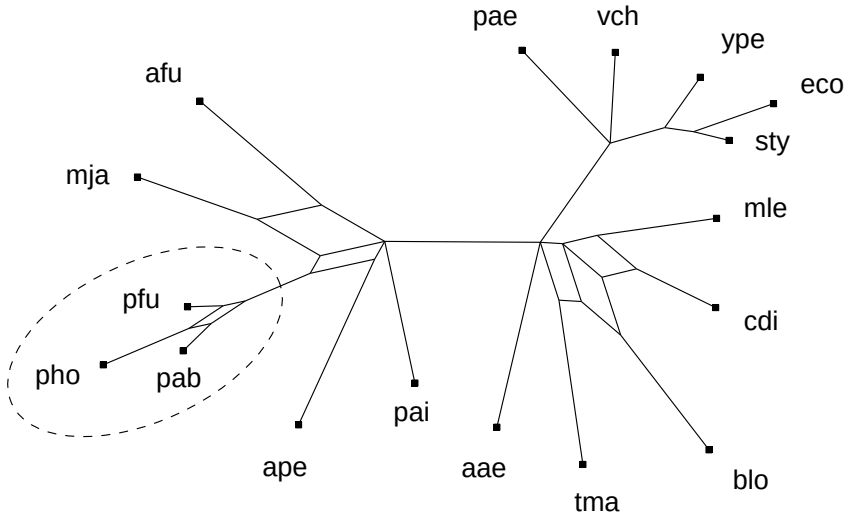
For a split

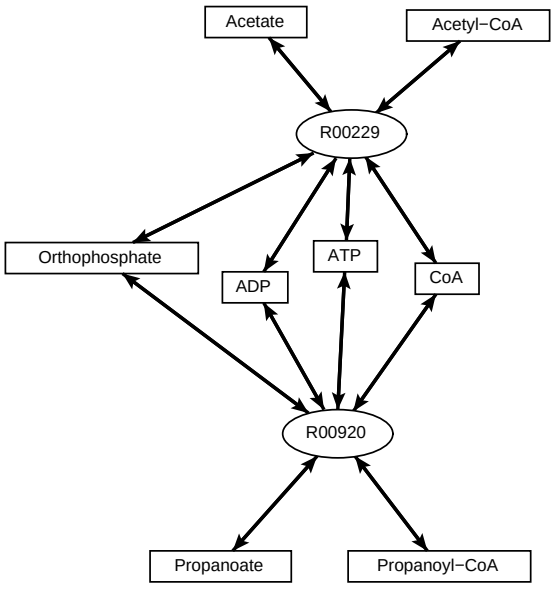
$$\sigma = (U, \bar{U}) \text{ with } U \neq \emptyset, \bar{U} \neq \emptyset, \text{ and } U \cap \bar{U} = \emptyset.$$

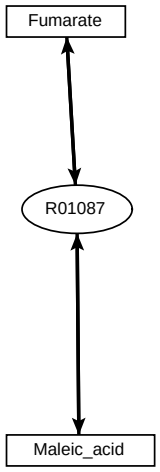
The differential metabolic network can be defined as:

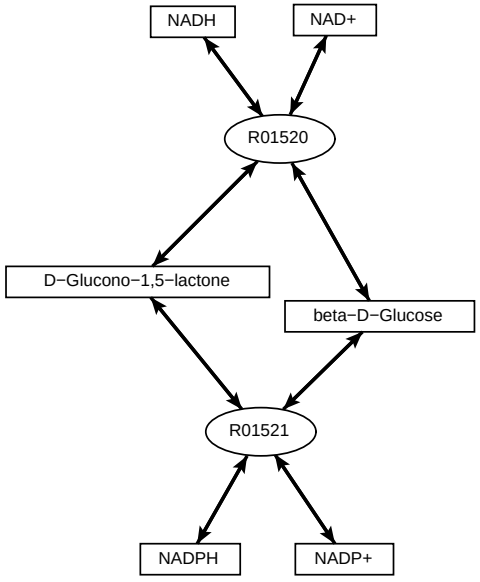
$$\mathfrak{D}(\sigma) = \left(\bigcup_{k \in U} \mathfrak{M}_k \right) \setminus \left(\bigcup_{k \in \bar{U}} \mathfrak{M}_k \right)$$

Metabolic Innovation









Conclusion

- Metabolic networks convey phylogenetic information.
- Network based phylogenies are in good agreement with phylogenies based on other methods.
- Network based phylogenies are insensitive to functional replacement.
- Metabolic innovations can be studied easily among subtrees of a trusted phylogeny.