

Molecular Analysis of Metabolic Pathways with Graph Transformation

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Motivation

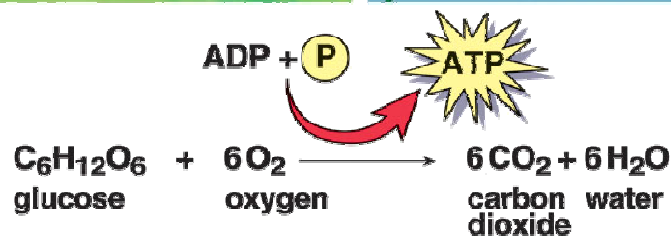
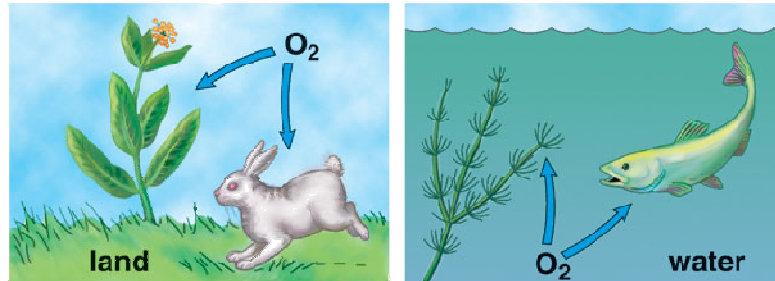
- ✗ Chemical reactions are often described by rules.
- ✗ Different rule-based approaches can be used
 - providing different levels of detail.
 - focussing on different aspects.

What about graph transformation?

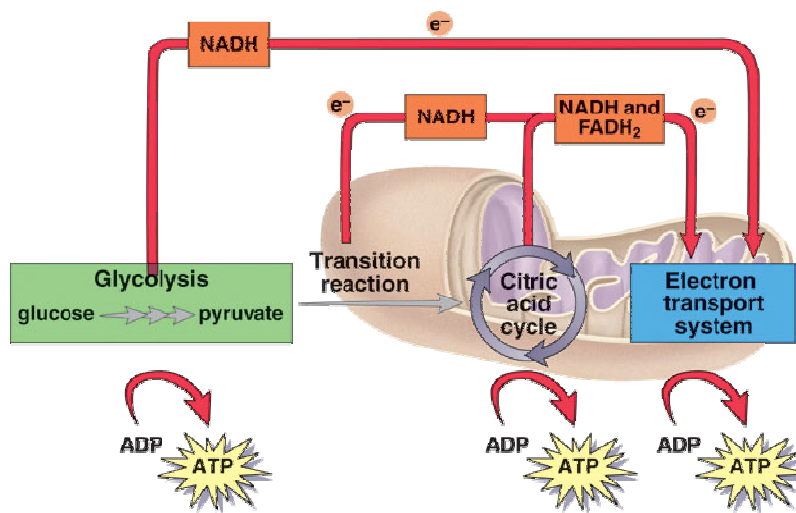
- How do graphs model molecular structure, and what of it can they represent?
- How do transformations model reactions?
- Are our tools and theory any help?

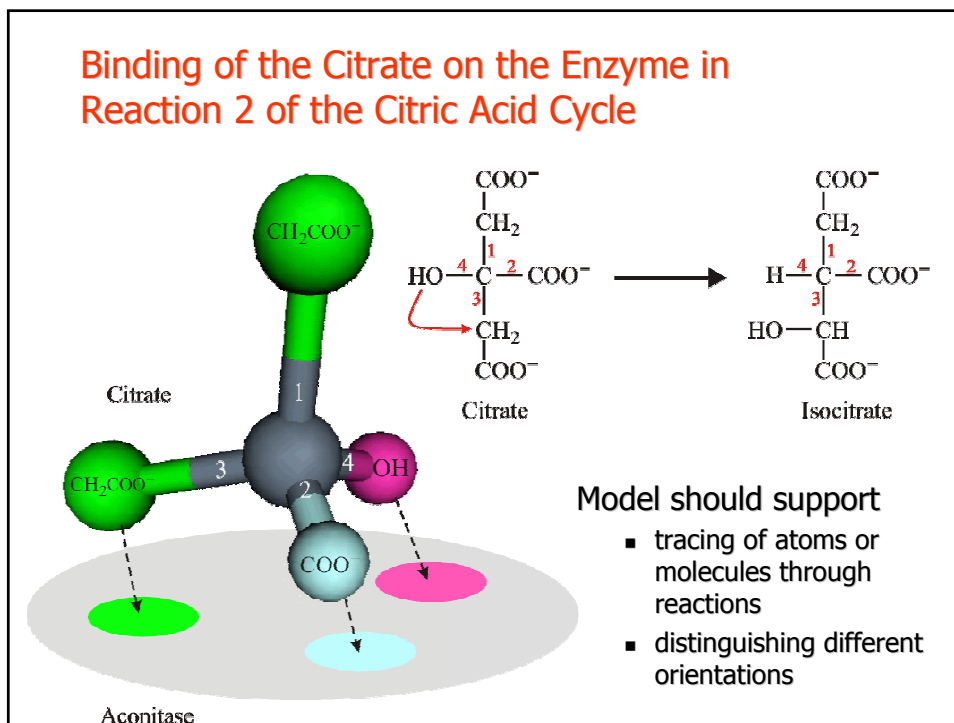
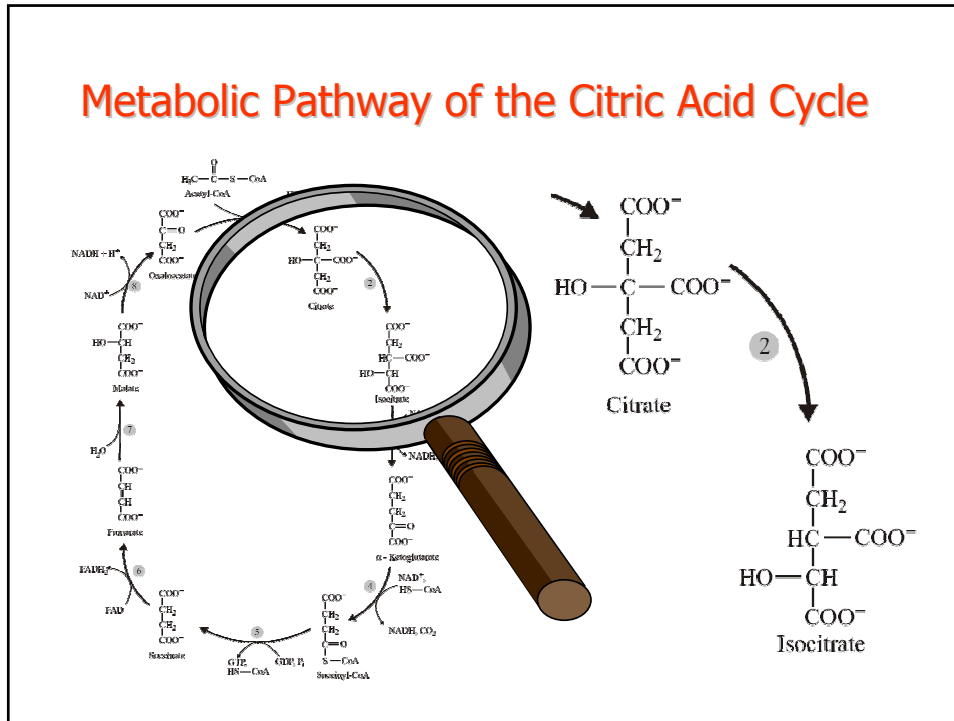
Let's look at a classic example!

Example: Cellular Respiration



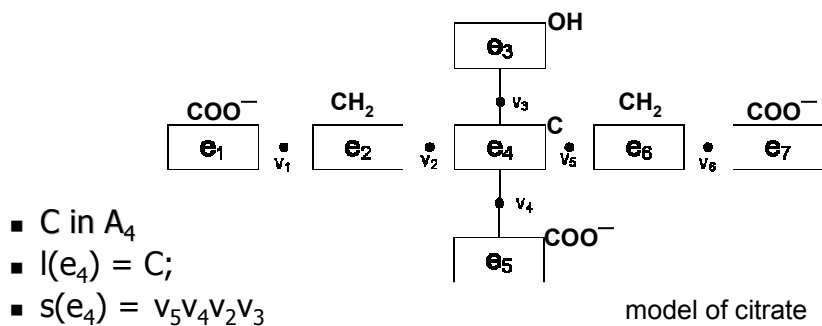
Phases of Respiration



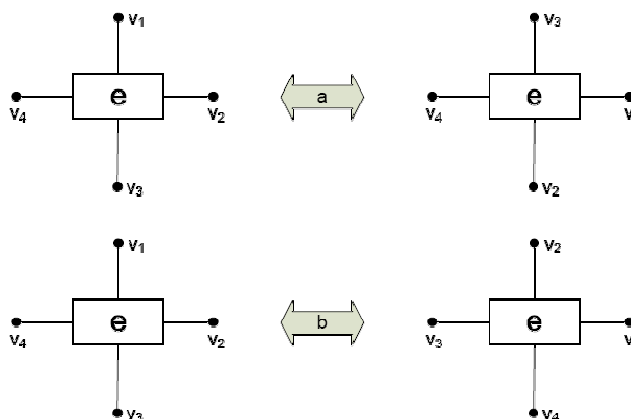


Structural Modelling with Hypergraphs

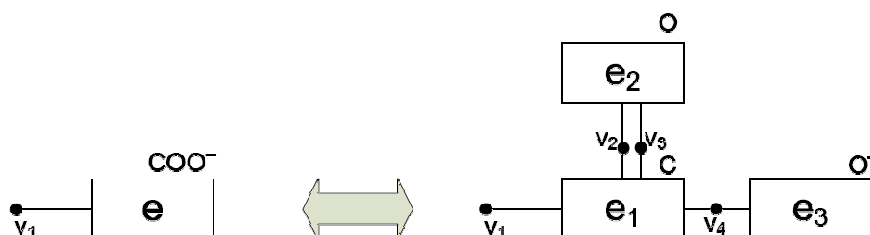
- ✗ Ranked alphabet $A = (A_r)_{r \text{ in } \mathbb{N}}$
 - rank of label models valence of atom or compound
- ✗ Hypergraph (V, E, s, l) ; $s: E \rightarrow V^*$, $l: E \rightarrow A$
 - hyperedges as atoms; nodes as bonds



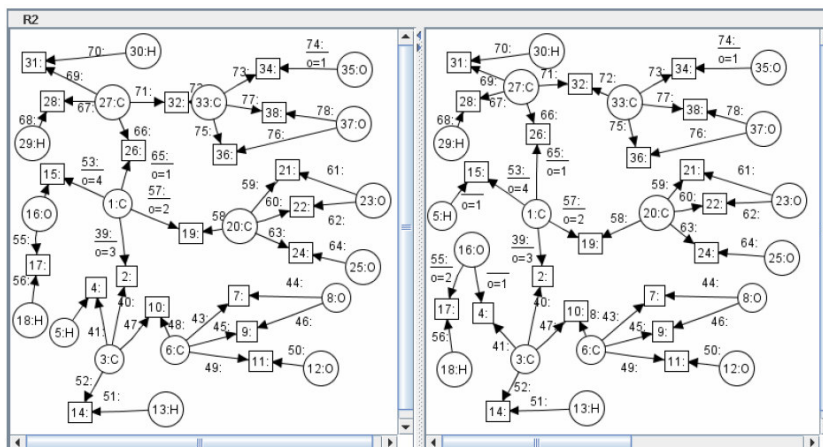
Equivalence Rules



Expansion and Collapsing Rule



Tool Support: Reaction 2 in AGG



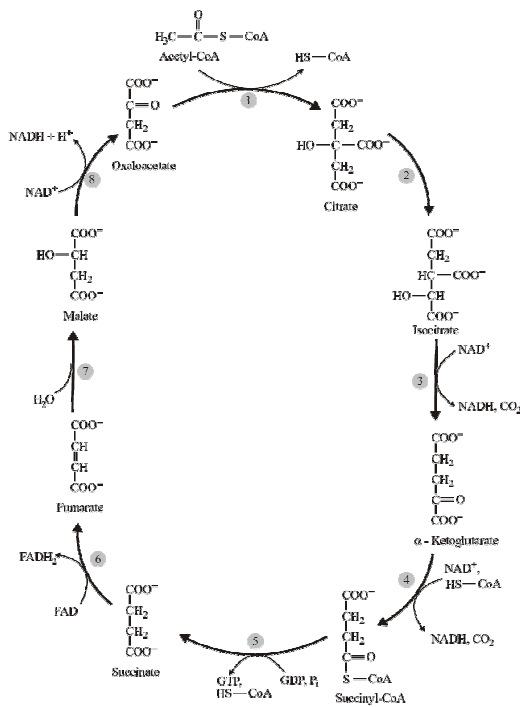
Where have all the C atoms gone?

Hypothesis: into the CO₂ ejected in step 3 or 4 of the cycle

Analysis:

- ✗ both are still in there at the end of the cycle
- ✗ they are ejected only in the 2nd cycle

Explanation: the enzyme in step 2 distinguishes the 'old' from the 'new' COO-CH₂ group by the chirality of the citrate molecule



Conclusion

- ✗ Molecular analysis of metabolic pathway reactions using hypergraph transformation
- ✗ Metabolic pathway analysis requires
 - to trace the history of particular atoms or molecules
 - to represent spatial orientation (chirality) of molecules
- ✗ Tool support for simulation in AGG via representation as bipartite graphs
 - in the citric acid cycle at least two turns have to be considered to understand the metabolism of the agents

Outlook

Theory: study properties of the model and apply existing results

- rewriting on normal forms of equivalent classes of graphs, representing the same molecule
- static analysis techniques: confluence, reachability
- stochastic models

Application: analysis of not so well-known reaction pathways in living cells

- analysis of the effect of drugs on cells
- tracing of (radioactive) compounds in cancer diagnosis and treatment