Atom-Atom Maps and Electron Pushing Diagrams

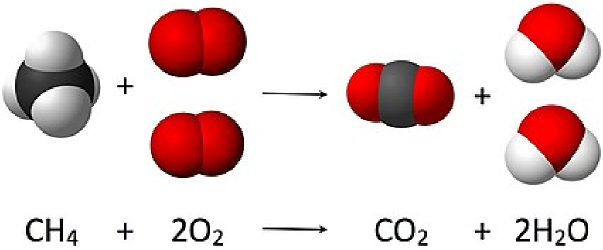
Peter F. Stadler

Bioinformatics Group, Dept. of Computer Science & Interdisciplinary Center for Bioinformatics,
Leipzig University
The Santa Fe Institute (external faculty)
Max Planck Institute for Mathematics in the Sciences, Leipzig
Institute for Theoretical Chemistry, Univ. of Vienna (external faculty)
Center for non-coding RNA in Technology and Health, Copenhagen, DK
Facultad de Ciencias, Universidad Nacional de Colombia, Bogotá, COL

joint work with
Christoph Flamm & Stefan Müller

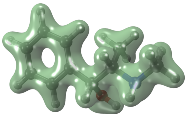
Bled, Feb 12-17 2024

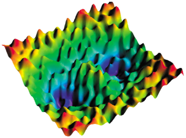
Chemical Reactions



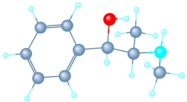
$$A + 2B \to C + 2D$$

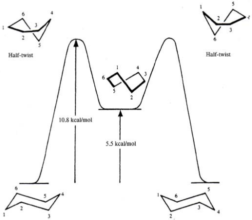
Levels of Abstraction in Chemistry



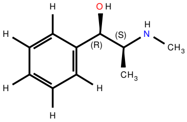


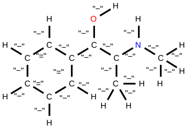
Potential energy surface





Reaction coordinate





$L \leftarrow K \rightarrow R$

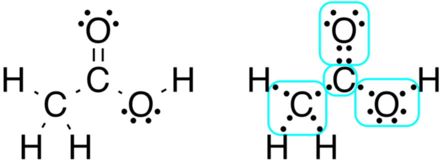
Large Hypergraphs

Chemical Reaction Networks

- Not every directed hypergraph is a “chemical” reaction network
- Necessary conditions:
  - every reaction preserves mass $\iff$ there is strictly positive reaction invariant $\mathbf{mS} = \mathbf{o}$
  - no directed cycles of forward reactions, i.e., $\mathbf{Sv} = \mathbf{o}$ implies $\mathbf{v} \not> \mathbf{o}$
- in this case there is a representation of the reactants as Lewis structures

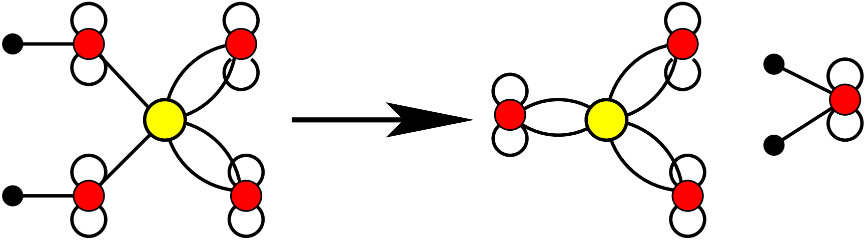
Different compounds can have the same atomic composition,
... different Isomers have the same sum formula but different structural formulas.

Lewis formulas: represent atoms and **all** outer-shell electrons



$\Longrightarrow$ labeled multigraphs

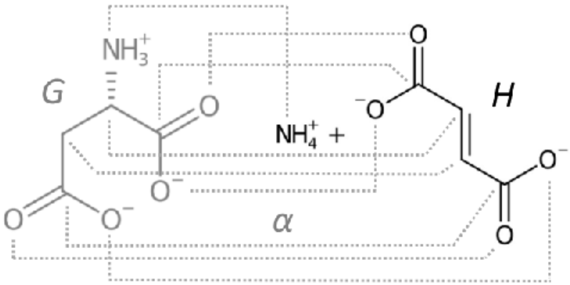
Reactions a Lewis structures



vertices	...	atoms
colors	...	elements
edges	...	bonding electron pairs
loops	...	non-bonding electrons pairs

degree(v) = # edges + 2# loops

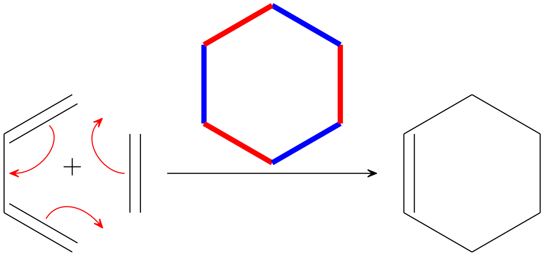
Mechanistic Level: Atom-Atom Maps



The atom-atom map of a reaction is the bijection between educt and product graph that preserves atom types.
In Lewis formulas, the vertex degree is defined by the atom types.
$\Longrightarrow$ Atom-atom maps preserve vertex degrees

ITS graphs

obtained by gluing together product and educt graph along the atom-atom map (and marking changes in bond orders)



In the simplest case: EPD corresponds to a cycle with alternating increase and decrease of the bond order
Difference graph: restriction of ITS graph to edges with changing bond orders.

Difference graphs

For a vertex x let $d_+(x)$ and $d_-(x)$ be the number of bonds whose order increases and descreases, respectively.

Lemma

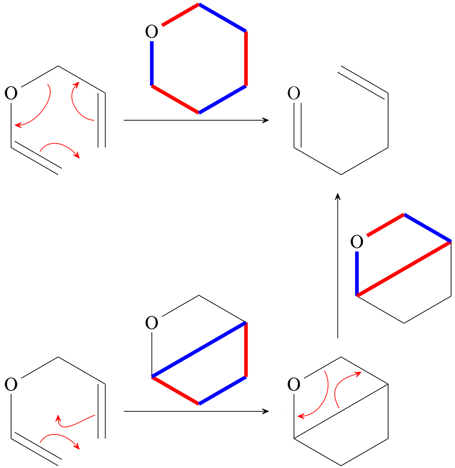
The difference graph of every atom-atom map satisfies $d_+(x) = d_-(x)$ at each vertex x.

Theorem

Every difference graph of an atom-atom map is the edge-disjoint union of closed alternating walks.

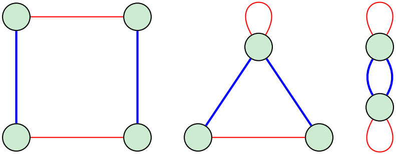
The proof parallels the proof of the famous Euler bridge theorem.
Every alternating closed walk can be interpreted as a cyclic electron punishing diagram

Subdivision of long electron pushing cycles



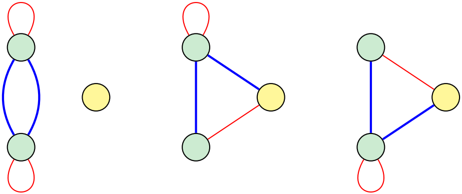
Claisen rearrangement of vinyl-allyl ethers. The 6-cyclic imaginary transition state can be decomposed into two 4-cyclic imaginary transition states.

Subdivision of long electron pushing cycles



Lemma

Every alternating closed walk can be decomposed into a sequence of alternating closed walks of length 4*.*



The unrealistic 4-walk can be explained by two steps with a catalyst.

Take Home Message

Theorem

Every atom-atom-map can be explained by a sequence of short electron punishing diagrams.
Moreover, each step may be restricted to an elementary reaction comprising no more than 2 educts and products.

The existence of a “chemically reasonable” reaction mechanism therefore does not impose additional restrictions on the realizability of chemical reactions networks.

Open Question

Is this still true when electron pushing requires some sort of a charge gradient?