Graph Transformation, Atom Tracing, and Isotope Labelling

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Feb. 12, 2018

About me

- Peter Severin Rasmussen
- University of Southern Denmark (SDU)
- Computer Science student
- Master thesis
- Supervisor: Daniel Merkle

Examples from chemistry

- Isotope labelling experiments
- Mass spectrometry
- Hypothetical (prebiotic) chemistries
- Metabolic engineering
- Synthesis planning
- One-pot synthesis

My master thesis

- Isotope labelling experiments $\leftarrow$
- Mass spectrometry
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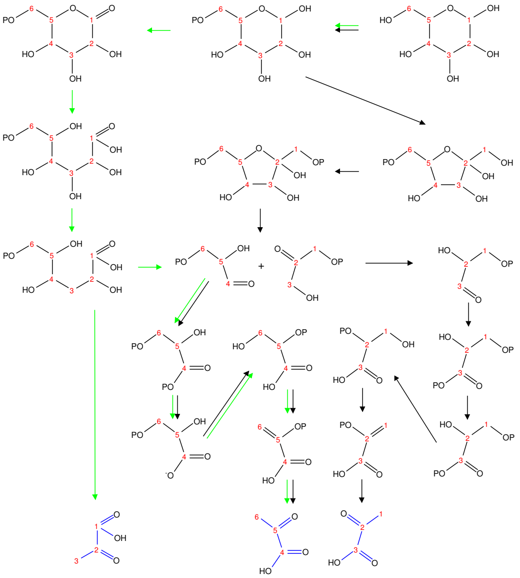
My master thesis

Isotope labbeling experiments & atom tracing

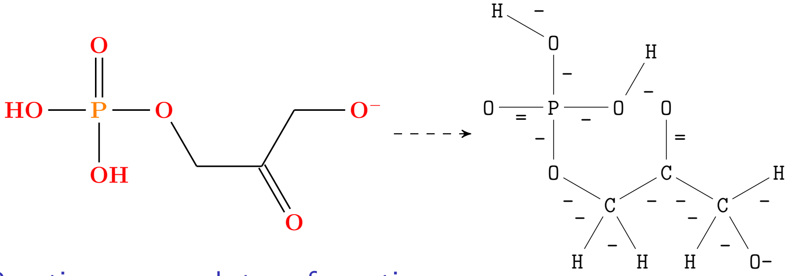


Glycolysis:
ED & EMP
Pathways

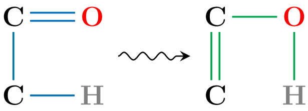
A bit of background

The molecular model

Molecules as graphs

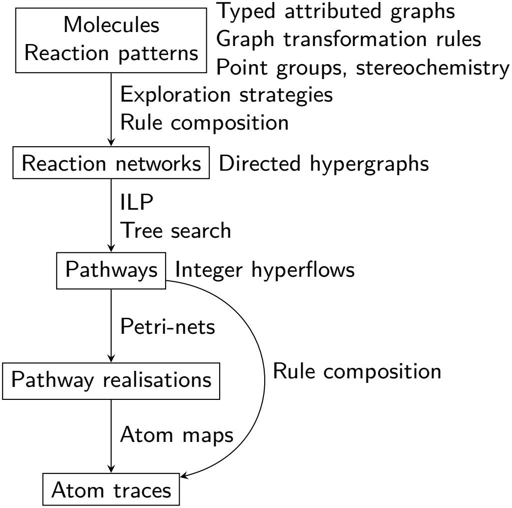


Reactions as graph transformations



MØD Overview

Models, methods, and concepts



Core Graph Algorithms

Monomorphism enum.
Isomorphism
Canonicalization
Automorphism enum.

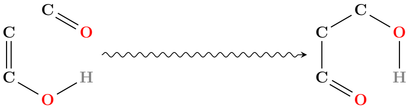
Software

The MØD package:

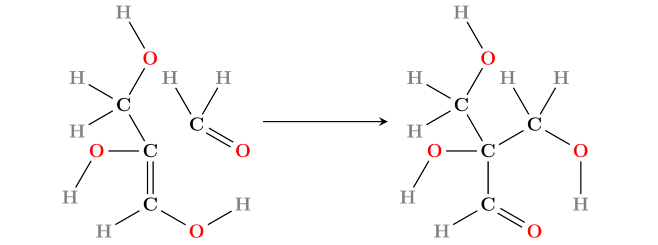
- C++ library
- Python interface
- Figure generation

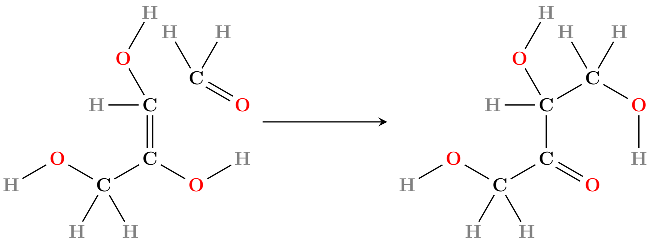
GraphCanon library
PermGroup library

Chemical reaction patterns



Chemical reaction patterns





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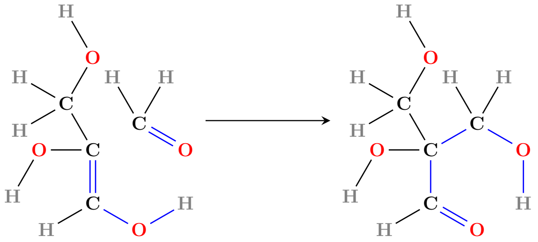
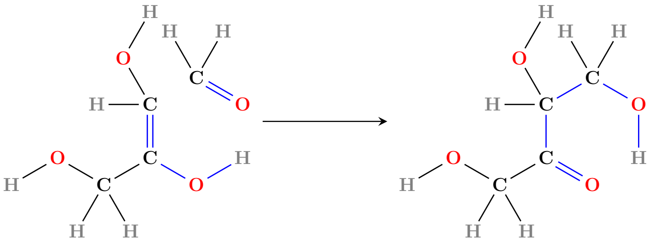
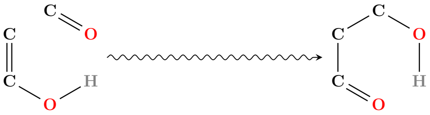
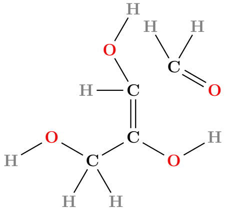




Chemical reaction patterns

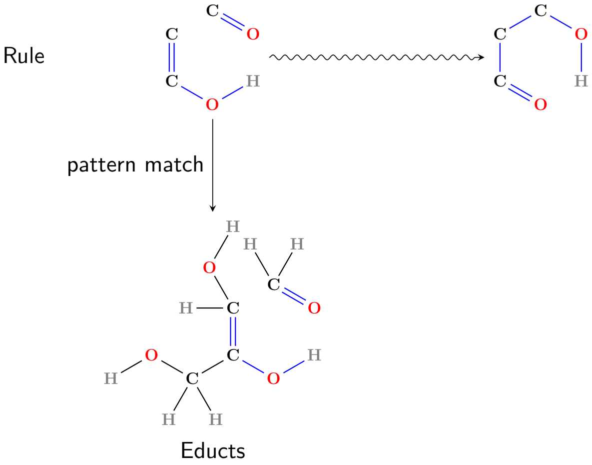
Rule



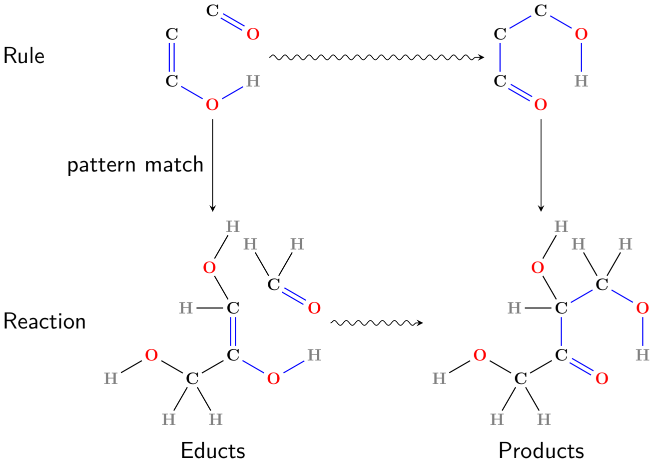


Educts

Chemical reaction patterns



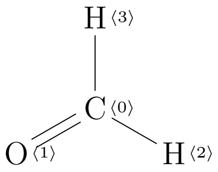
Chemical reaction patterns



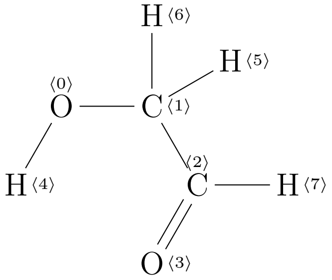
Example: Formose

Molecules

Formaldehyde



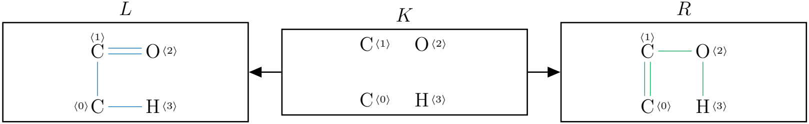
Glycolaldehyde



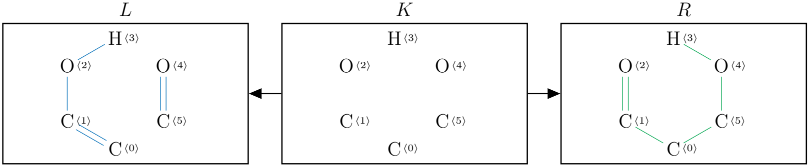
Example: Formose

Rules

Keto-Enol Isomerization

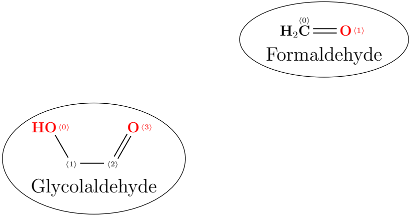


Aldol Addition



Example: Formose

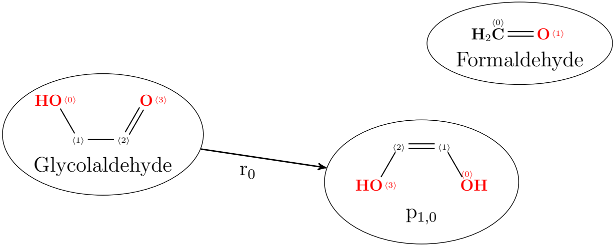
Derivation Graph / Chemical network



Generation 0

Example: Formose

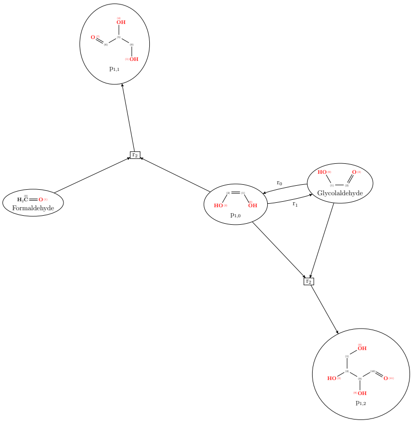
Derivation Graph / Chemical network



Generation 1

Example: Formose

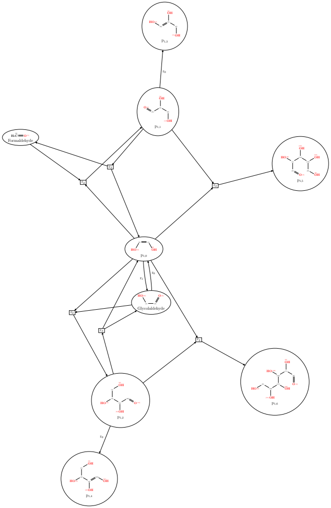
Derivation Graph / Chemical network



Generation 2

Example: Formose

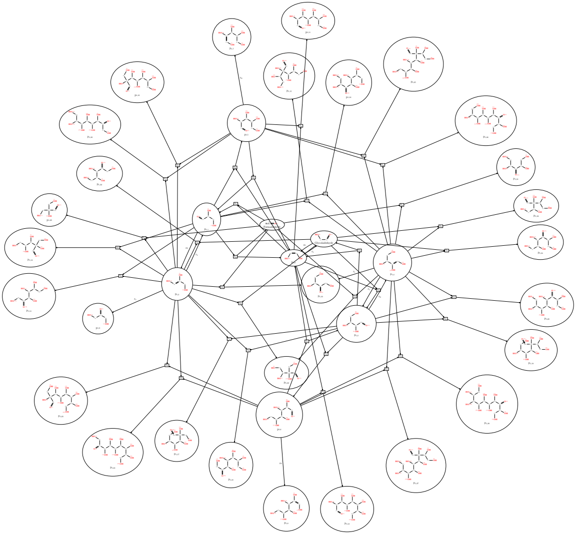
Derivation Graph / Chemical network



Generation 3

Example: Formose

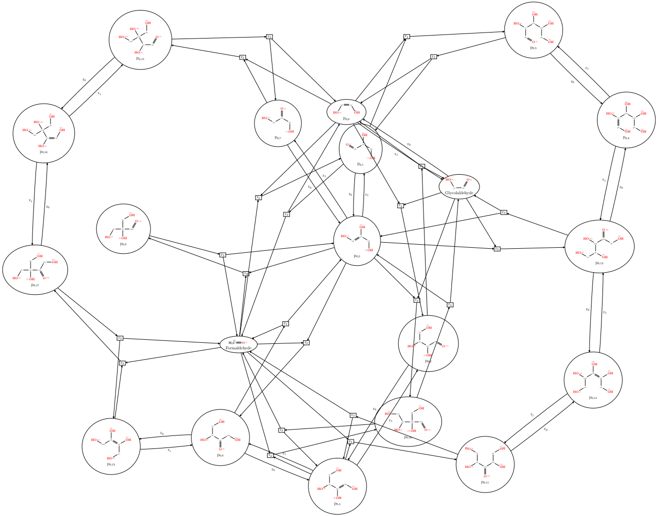
Derivation Graph / Chemical network



Generation 4

Example: Formose

Derivation Graph / Chemical network



Limited to molecules with ≤ 5 carbons

Derivation Graph as Semigroup of Transformations

1. Groups
2. Permutation Groups
3. Construction
4. Semigroups

Group Theory

Group: $(G, \bullet)$

Closure If $g, h \in G$, then $g \bullet h \in G$.

Associativity For all $g, h, k \in G$, then $(g \bullet h) \bullet k = g \bullet (h \bullet k)$.

Identity There exists $e \in G$ s.t. for all $g \in G$, then

$$e \bullet g = g = g \bullet e$$

Inverse For all $g \in G$, there exists $g^{-1} \in G$ s.t.

$$g^{-1} \bullet g = e = g \bullet g^{-1}$$

Group Theory: Example

$$G = \{0, 1, 2, 3\}$$
$$\bullet = \_ + \_ \mod 4$$

Identity: 0

$$0 + 2 = 2$$
$$2 + 0 = 2$$

Group Theory: Example

$$G = \{0, 1, 2, 3\}$$
$$\bullet = \_ + \_ \mod 4$$

Inverse: $-x$

$$1 + (-1) = 1 + 3 = 4 \mod 4 = 0$$

Group Theory: Example

$$G = \{0, 1, 2, 3\}$$
$$\bullet = \_ + \_ \mod 4$$

Closure

$$1 + 1 = 2$$
$$2 + 3 = 5 \mod 4 = 1$$

Group Theory: Example

$$G = \{0, 1, 2, 3\}$$
$$\bullet = \_ + \_ \mod 4$$

Generators

$$G = \langle 1 \rangle = \langle 1, 2 \rangle$$

Permutation Groups

Points

$\Omega = \{0, 1, 2, \ldots, n\}$

Permutation

$\sigma \colon \Omega \to \Omega$

Permutation Groups

Permutation

$\sigma\colon \Omega \to \Omega$

Ex:

$$\begin{aligned} \sigma\colon 5 &\mapsto 7 \\ 7 &\mapsto 5 \\ 11 &\mapsto 42 \\ 42 &\mapsto 10 \\ 10 &\mapsto 11 \end{aligned}$$

(rest unchanged)

Permutation Groups

Permutation

$\sigma\colon \Omega \to \Omega$

Ex:

$$\begin{aligned}\sigma\colon 5 &\mapsto 7\\ 7 &\mapsto 5\\ 11 &\mapsto 42\\ 42 &\mapsto 10\\ 10 &\mapsto 11\end{aligned}$$

(rest unchanged)

Cyclic notation

$$\sigma = (5\ 7)(11\ 42\ 10)$$

Cool Tools from Group Theory

- Orbit
- Schreier-Sims algorithm
- ...

Cool Tools from Group Theory

- Orbit

$$G = \left\langle \underbrace{(1\ 2)(3\ 4)}_{g_1}, \underbrace{(2\ 5)}_{g_2} \right\rangle$$

$$\begin{aligned} \mathrm{Orbit}_G(\omega) &= \{g(\omega) \mid g \in G\} \\ \mathrm{Orbit}_G(1) &= \{\mathrm{id}(1), g_1(1), g_2(1), (g_1 \circ g_2)(1)\} \\ &= \{1, 2, 5\} \end{aligned}$$

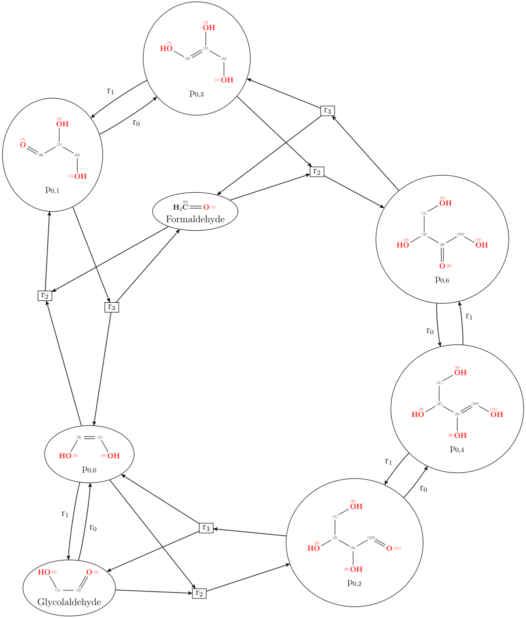
Can be done on pairs too.

- Schreier-Sims algorithm

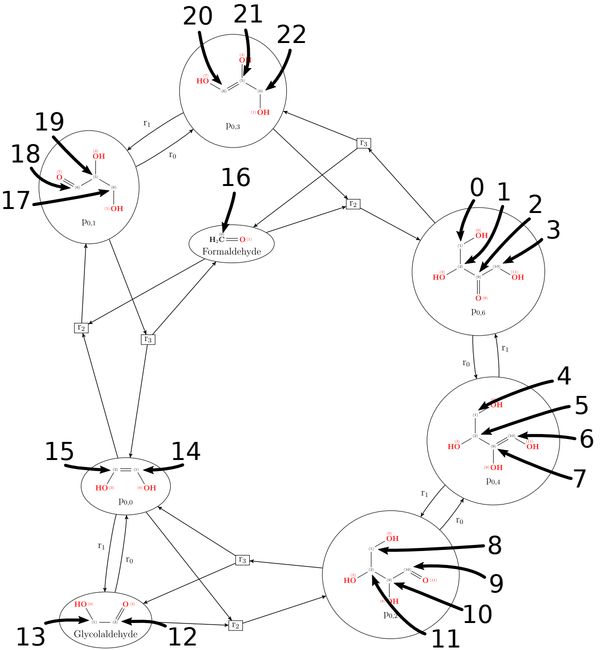
Cool Tools from Group Theory

- Orbit
- Schreier-Sims algorithm
  - Membership testing in poly time
  - Element decomposition

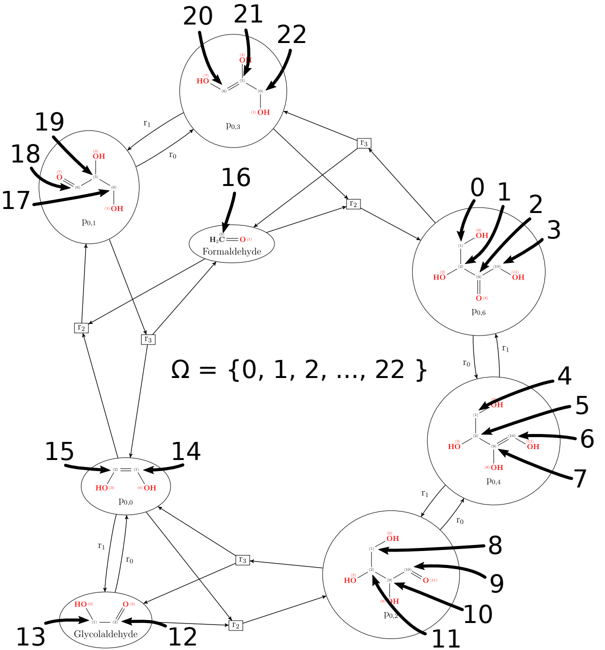
Permutation Group of Derivation Graph



Permutation Group of Derivation Graph

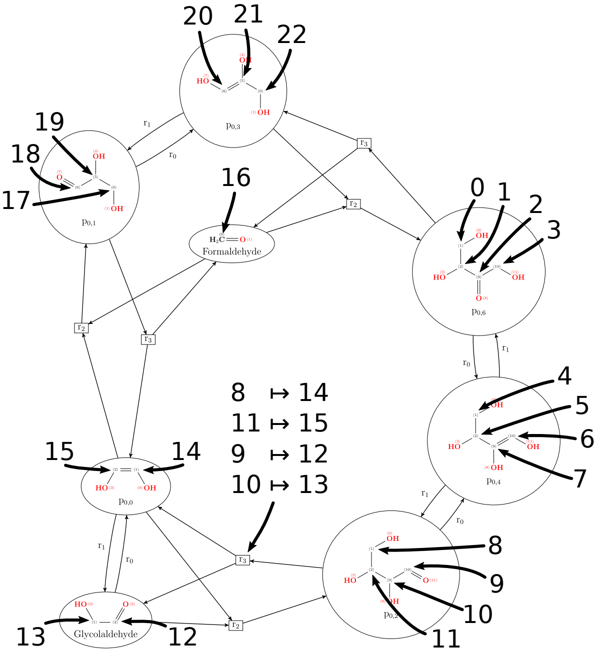


Permutation Group of Derivation Graph



$\Omega = \{0, 1, 2, ..., 22\}$

Permutation Group of Derivation Graph



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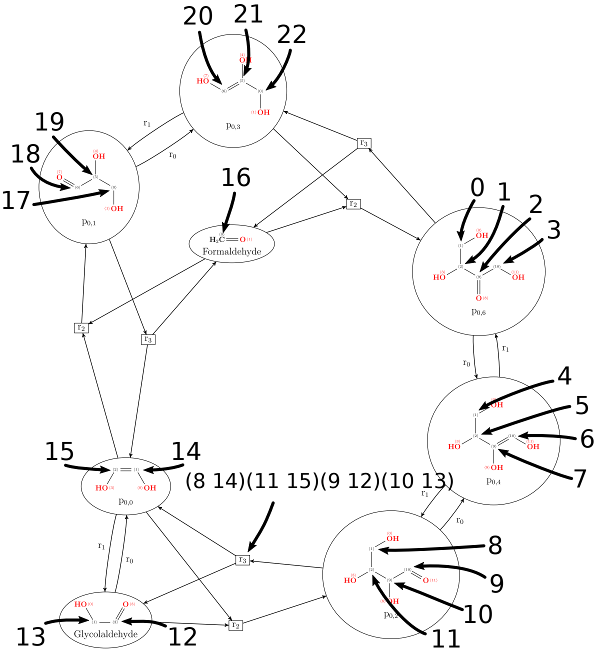

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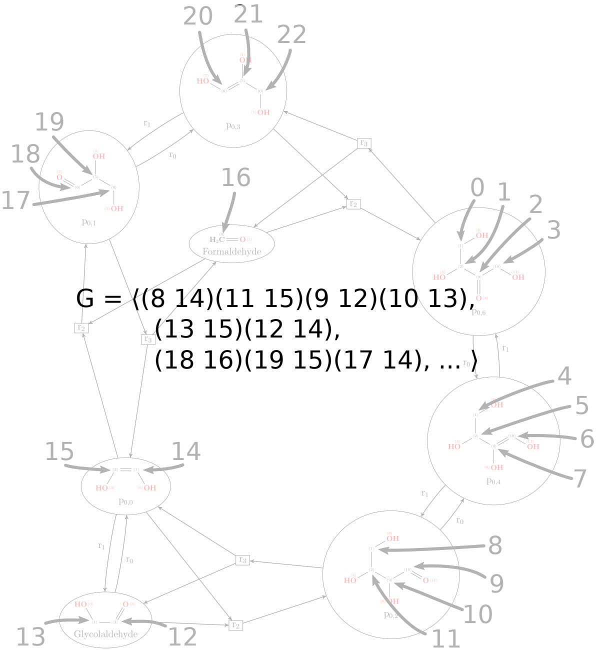
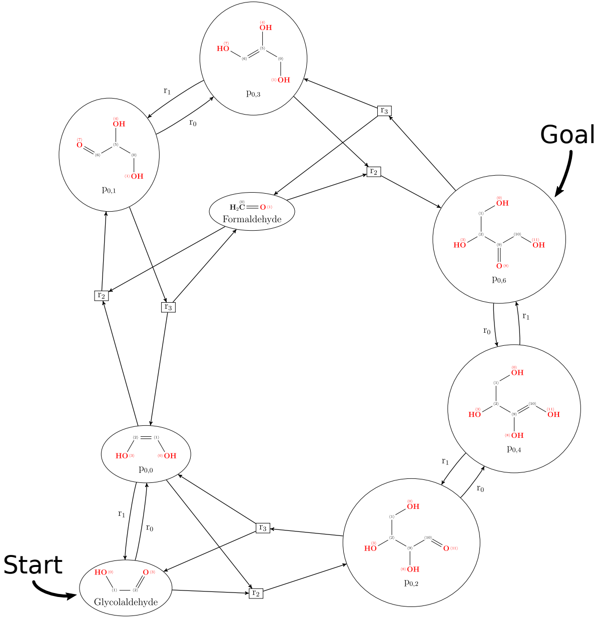


$$G = \langle (8\ 14)(11\ 15)(9\ 12)(10\ 13),\ (13\ 15)(12\ 14),\ (18\ 16)(19\ 15)(17\ 14), \ldots \rangle$$

Permutation Group of Derivation Graph



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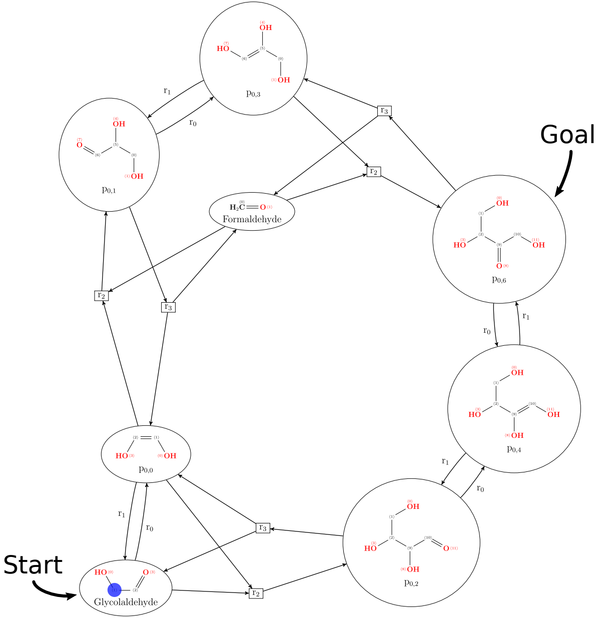

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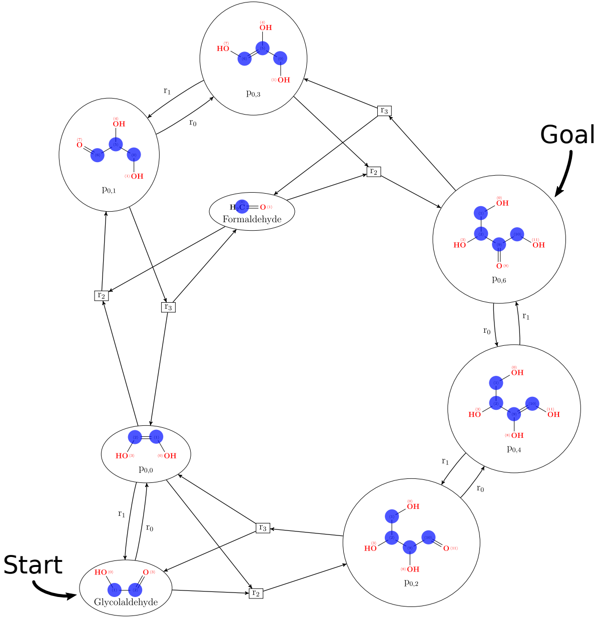

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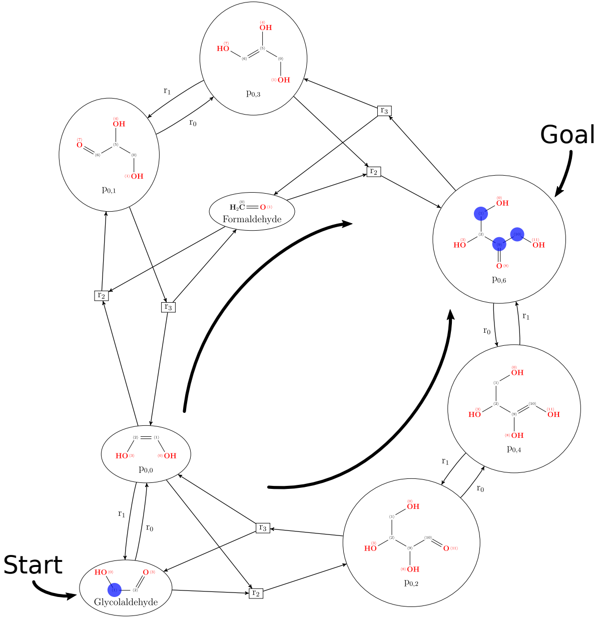

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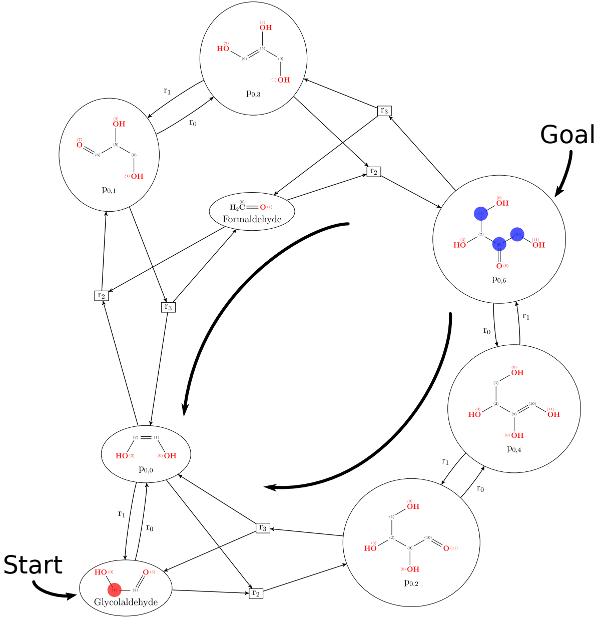
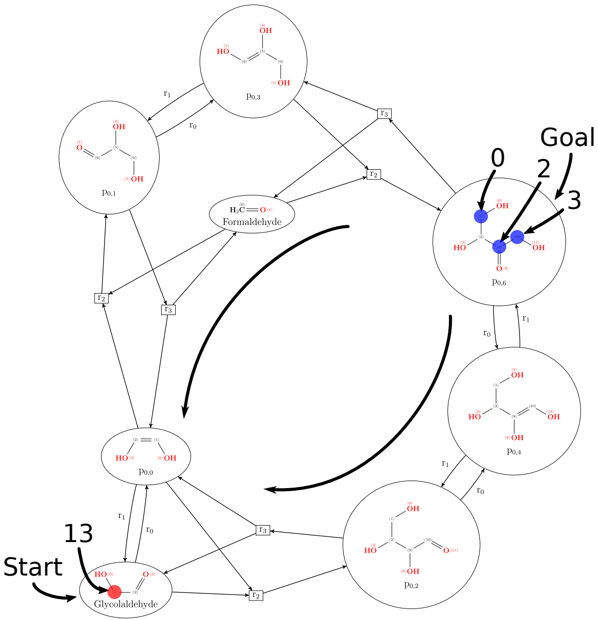


Permutation Group of Derivation Graph



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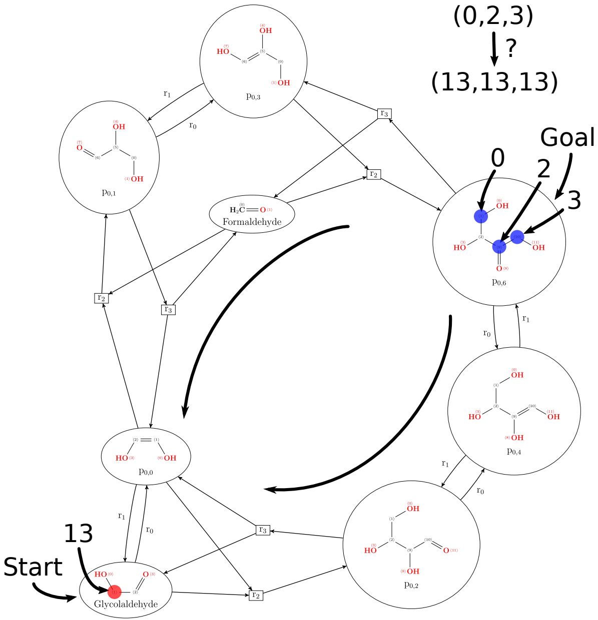

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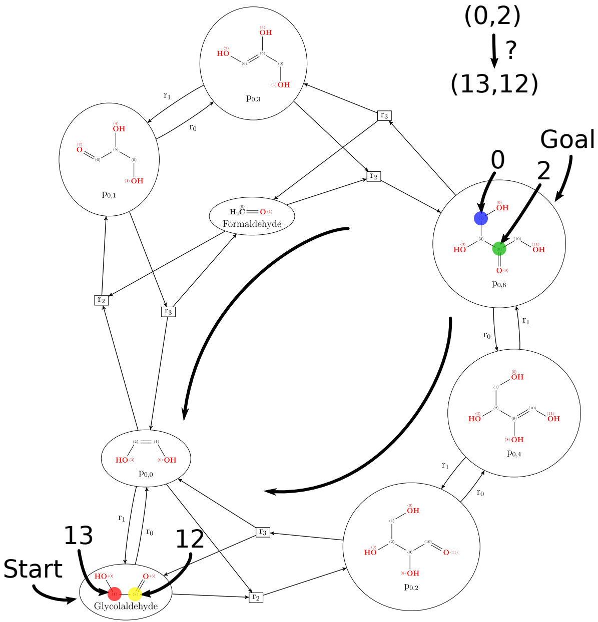

Semigroups

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~~**Inverse** For all $g \in G$, there exists $g^{-1} \in G$ s.t.~~

$$\sout{g^{-1} \bullet g = e = g \bullet g^{-1}}$$

Semigroup Tools

- Orbit calculation: ✓
- Schreier-Sims: ✓

Demo

Current Work

- Further development of MØD.
- Python implementation of semigroup construction.
- Ability to trace atoms of specific markings via orbits.

Use Cases

- Glycolysis: ED & EMP Pathways
- TCA
- PPP
- Formose
- Polyketides
- ...

Future Work

- Assist in isotope labelling experiments (automated)
- Constraint-based membership testing
- Dynamic simulation w. ODEs

Questions?