Computational Methods for Graph Grammar Analysis

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Introduction

- Graph grammars have a lot of computational power
- They can model chemical reactions
- Graph Grammar Library (Christoph Flamm and Martin Mann)
- Interesting properties: Chemical patterns

Outline

Graphs and Molecules

Undirected graphs, with labels on both nodes and edges.
Molecules: Node labels ≈ atom names, edge labels ≈ bond type

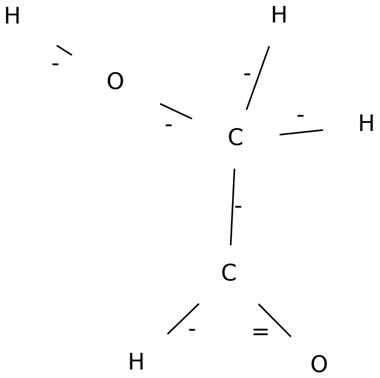

Figure: A labeled undirected graph

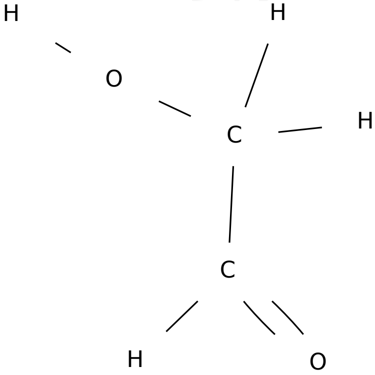

Figure: The same graph drawn like a molecule (glycolaldehyde)

Graph Grammars

- Graph grammar: A set of rules
- Rule: Left side, context, right side (all are subgraphs)
- Reactions as rules: Left ≈ broken bonds, right ≈ formed bonds, context ≈ atoms and unchanged bonds

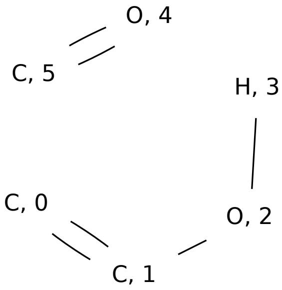

Figure: Aldol addition, left side and context

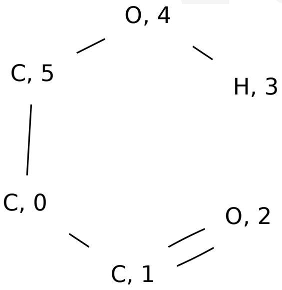

Figure: Aldol addition, right side and context

Graph Grammars

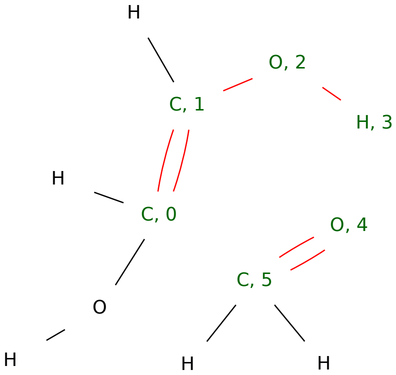

Figure: Addition of formaldehyde, before

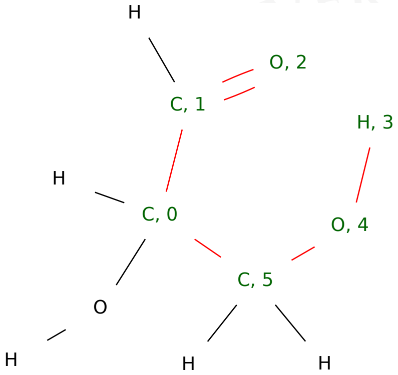

Figure: Addition of formaldehyde, after

Node Constraints

Constraint on the number of neighbours to a given node

Examples:

- At least 2 hydrogen atoms
- Exactly 0 double bounded oxygens
- At least 3 bonds (of any type)
- Exactly 1 neighbouring oxygen

Rules and Graphs for the Formose reaction

Graphs:

- Formaldehyde
- Glycolaldehyde

Rules:

- Keto-enol isomerization
- Reverse keto-enol isomerization
- Aldol-addition
- Reverse Aldol-addition

Derivation Graph

- Input: A set of graphs, a set of rules
- Output: A directed hypergraph, nodes are graphs (molecules), edges are rule applications (reations)
- Example: 2 generations of the formose reaction

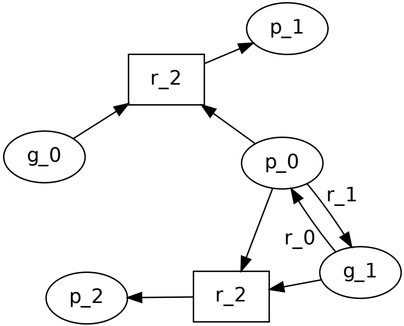

Figure: Hypergraph style

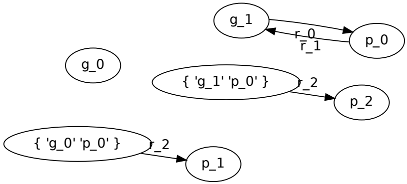

Figure: Normal graph style

Derivation Graph

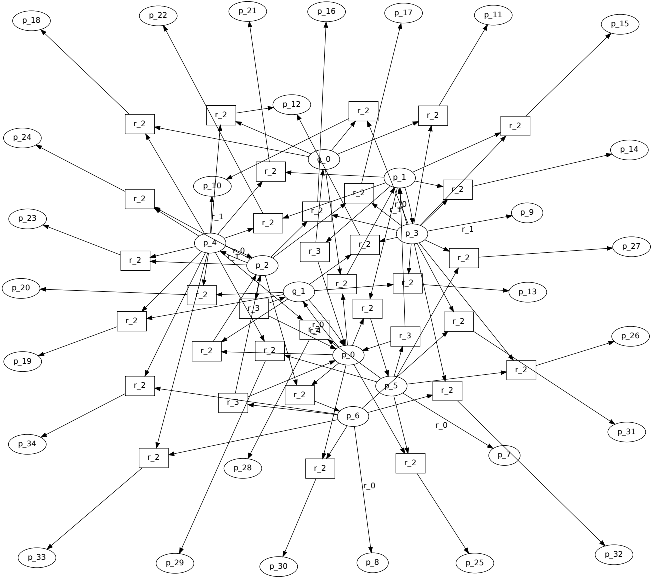

Figure: Formose with 4 generations, hypergraph style

Derivation Graph

Formose with all generations, but ≤ 43 nodes per reaction

External file due to size

Also available at http://imada.sdu.dk/~jla06/formose_large.pdf

Path Analysis

- Idea: Graphs (molecules) on a simple path in a derivation graph might have an interesting relationship
- E.g: Number of occurences of a specific subgraph

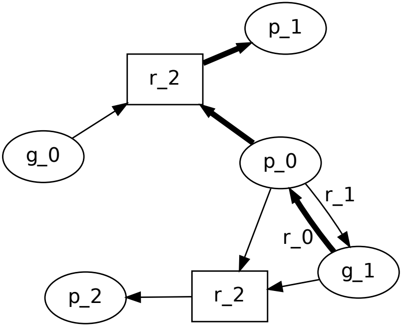

Figure: Formose with 2 generations

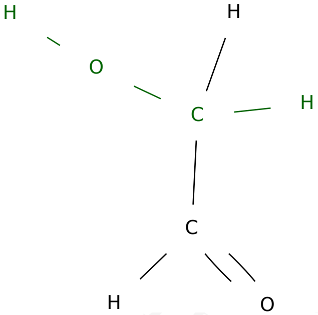

Figure: g_1, 1 match

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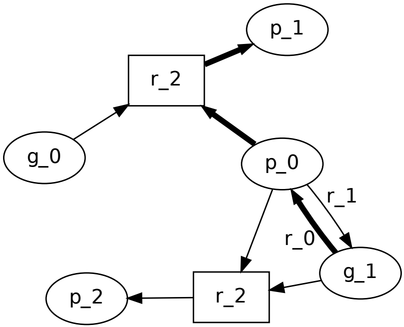

Figure: Formose with 2 generations

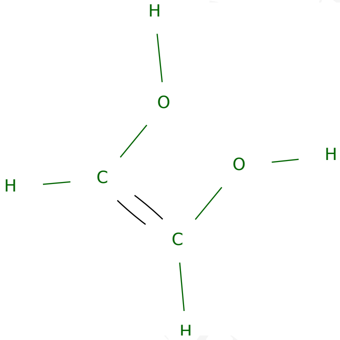

Figure: p_0, 2 matches

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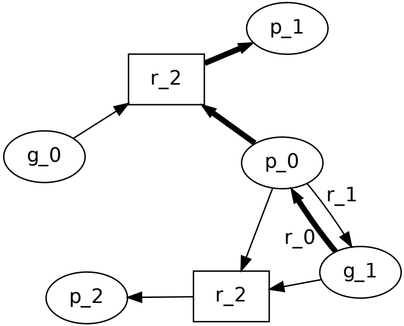


Figure: Formose with 2 generations

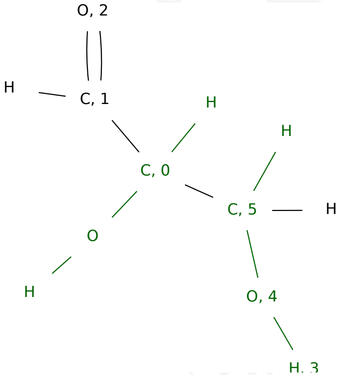


Figure: p_1, 2 matches

Flows on Derivation Graphs

- Idea: Use network flows to model interesting queries to the derivation graph
- Current implementation: Integer Linear Programming
- Example: Can 2 formaldehyde and 1 glycolaldehyde react and become only glycolaldehyde? and how?

IP Formulation

$$\text{minimize} \quad 0 \quad \text{s.t :}$$

$$
\begin{aligned}
x_3 + x_{17} + x_{18} - x_{21} - x_5 - x_{16} - x_{19} &= 0 \qquad g_0 \\
x_{23} + x_1 + x_6 - x_{22} - x_2 - x_8 &= 0 \qquad g_1 \\
x_2 + x_3 + x_6 - x_1 - x_5 - x_8 &= 0 \qquad p_0 \\
x_9 + x_{10} + x_{17} + x_{18} - x_4 - x_{13} - x_{16} - x_{19} &= 0 \qquad p_3 \\
x_{11} + x_{12} - x_7 - x_{14} &= 0 \qquad p_4 \\
x_{14} + x_{15} + x_{16} - x_{12} - x_{18} - x_{20} &= 0 \qquad p_6
\end{aligned}
$$

$$
\begin{aligned}
x_4 + x_5 - x_3 - x_9 &= 0 \quad p_1 & x_i &\geq 0, & \forall i &\in [1;20] \\
x_7 + x_8 - x_6 - x_{11} &= 0 \quad p_2 & x_{21} &= 2 & & g_0 \\
x_{13} - x_{10} &= 0 \quad p_5 & x_{22} &= 1 & & g_1 \\
x_{19} - x_{17} &= 0 \quad p_7 & x_{23} &\geq 0 & & g_1 \\
x_{20} - x_{15} &= 0 \quad p_8 & x_i &\in \mathbb{Z}, & \forall i &\in [1;23]
\end{aligned}
$$

Formose Cycle

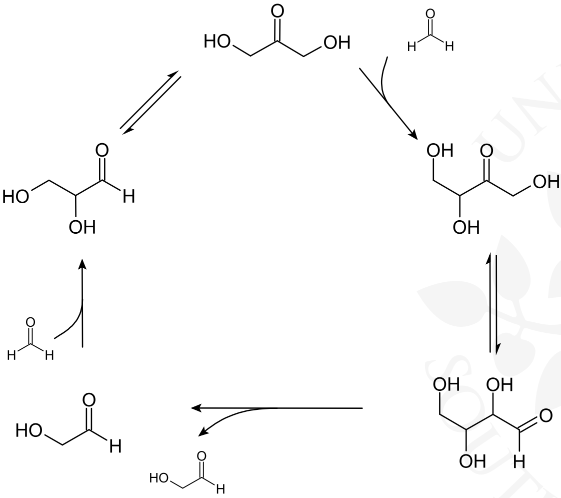
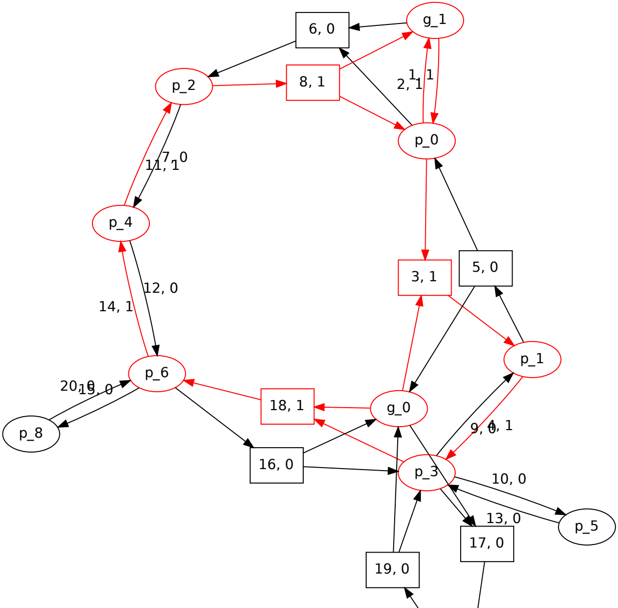


Figure: From http://de.wikipedia.org/wiki/Formose

Flows on Derivation Graphs



Summary

- GGL is used to explore graph grammars
- Derivation Graphs can represent chemical reaction networks
- Path analysis might find interesting properties
- Flows seem to capture the idea of chemical pathways
- A lot of possibilities to explore

Future Work

- Path analysis: Overlap, optimization, relationships
- Flows: More models, extra constraints, enumeration
- Grammars: Pentose-Phosphate Pathway
- ...