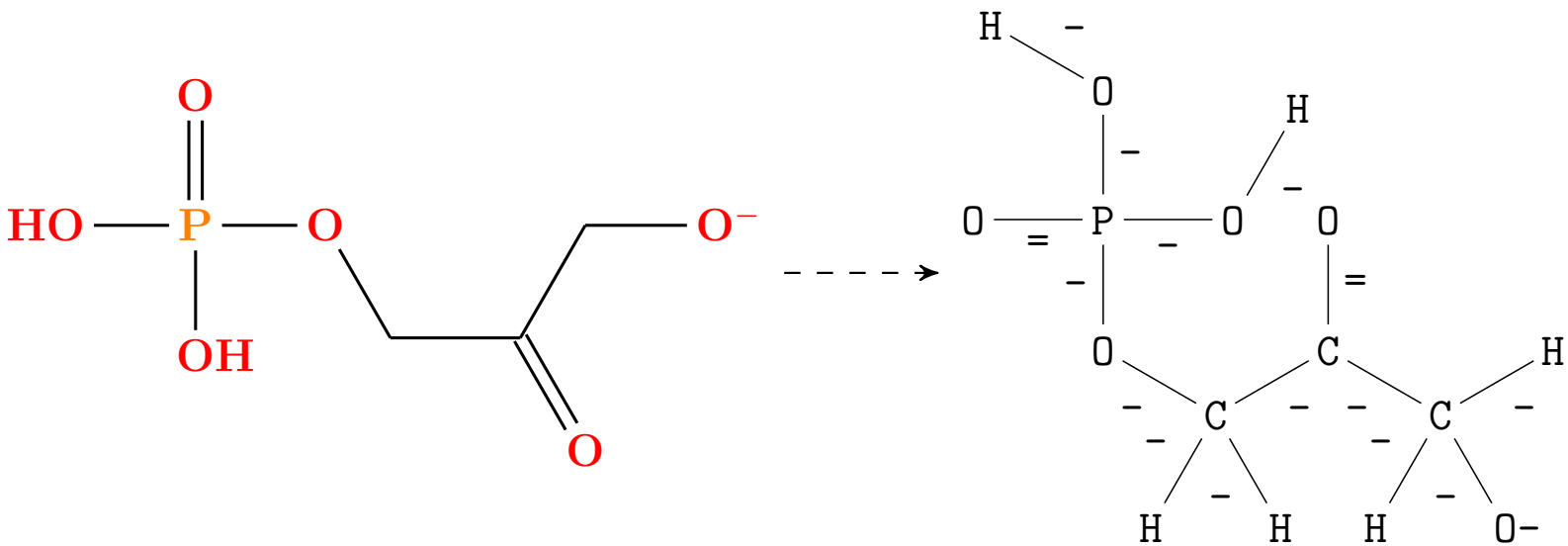
A Software Package for Chemically Inspired Graph Transformation

Algorithmic Cheminformatics - Week 19, 2024

Molecules as Labelled Graphs

- An old idea: [J. J. Sylvester, *Chemistry and Algebra*, Nature 1878]
- Molecule: simple, connected, labelled graph.
- Vertex labels: atom type, charge.
- Edge labels: bond type.



Simple: 2 single bonds is not the same as 1 double bond.
Connected: all atom interactions must be encoded as edges.

Using MØD

- Python script: "`test.py`":

```
myGraph = graphGMLString("""
  graph [
    node [ id 0 label "u" ]
    node [ id 1 label "v" ]
    edge [ source 0 target 1 label "e" ]
  ]""")
myGraph.print()
```

- Run the wrapper script:

```
mod -f test.py
```

enhanced version of

```
python3 test.py
mod_post
```

- Look at the generated "`summary/summary.pdf`".

External Graph Representaion

GML: list of vertices and edges.

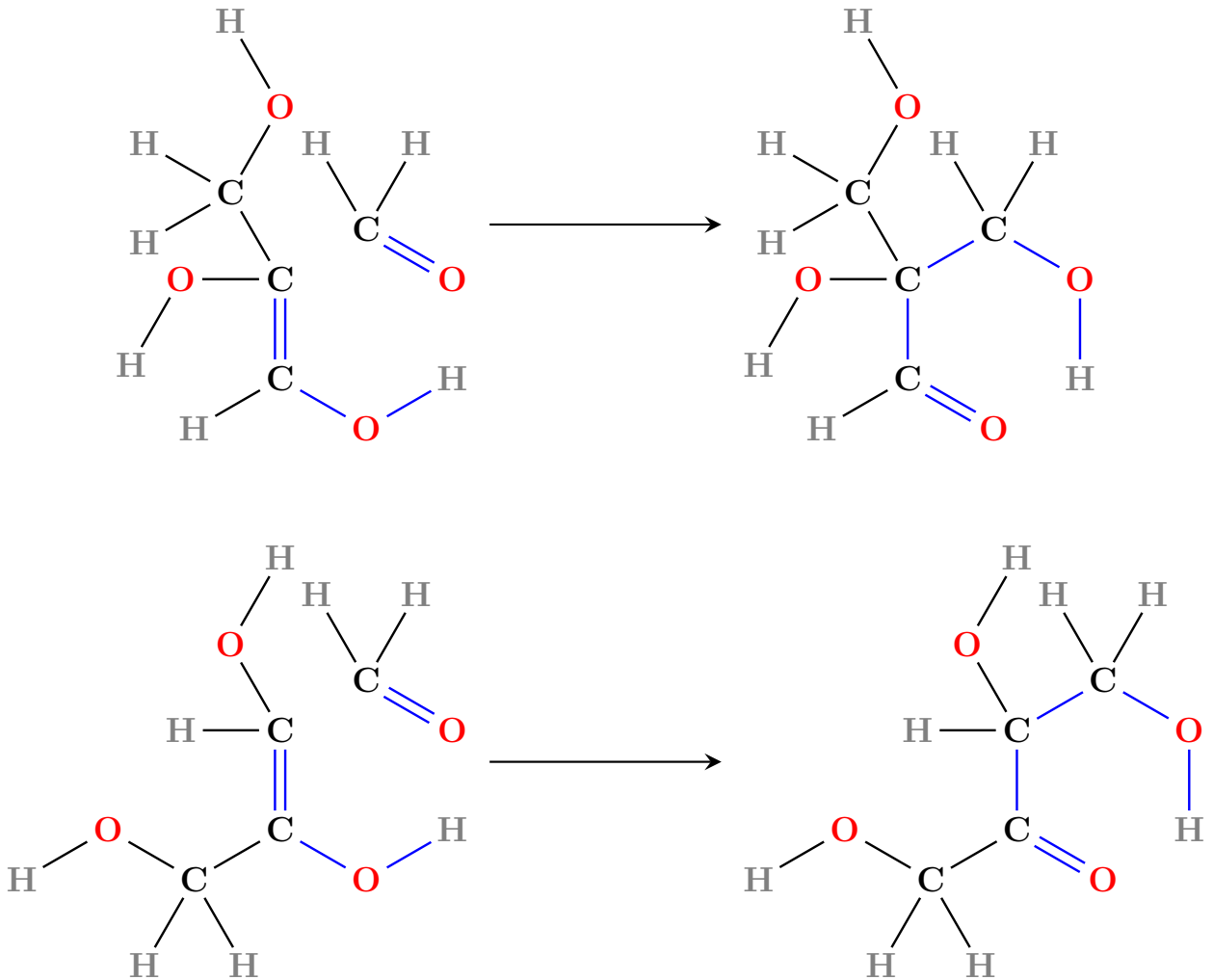
SMILES: Simplified Molecular-Input Line-entry System

- Recording of a depth-first traversal.
- Only for molecules.
- Most hydrogen atoms are implicit.

GraphDFS: similar to SMILES but for general graphs.

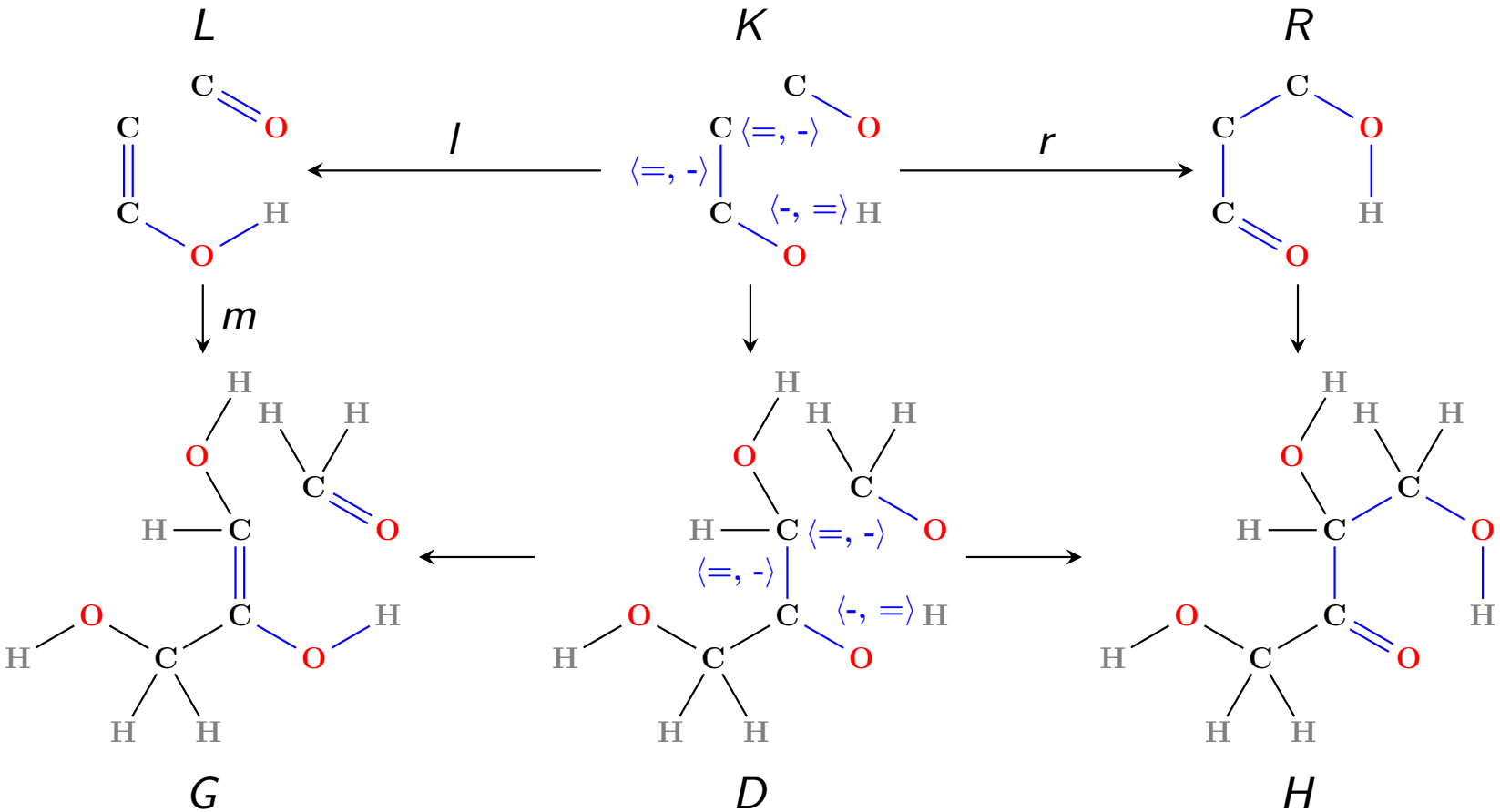
```
ethanol1 = smiles("CCO", name="Ethanol1")
ethanol2 = graphDFS("[C]([H])([H])([H])[C]([H])([H])[O][H]", name="Ethanol2")
ethanol3 = graphDFS("CCO", name="Ethanol3")
ethanol4 = graphGMLString("""graph [
    node [ id 0 label "C" ]   node [ id 1 label "C" ]   node [ id 2 label "O" ]
    node [ id 3 label "H" ]   node [ id 4 label "H" ]   node [ id 5 label "H" ]
    node [ id 6 label "H" ]   node [ id 7 label "H" ]   node [ id 8 label "H" ]
    edge [ source 1 target 0 label "-" ]   edge [ source 2 target 1 label "-" ]
    edge [ source 3 target 0 label "-" ]   edge [ source 4 target 0 label "-" ]
    edge [ source 5 target 0 label "-" ]   edge [ source 6 target 1 label "-" ]
    edge [ source 7 target 1 label "-" ]   edge [ source 8 target 2 label "-" ]
]""", name="Ethanol4")
```

Reactions as Graph Transformations



(Chemical constraint: only bonds and charges may change.)

Reactions as Double Pushout Transformations

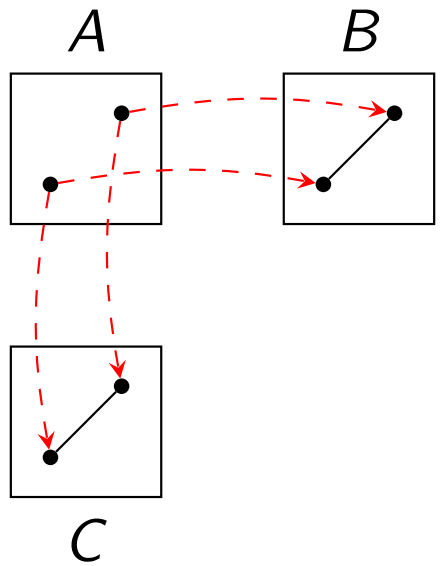


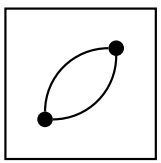
$$p = (L \xleftarrow{l} K \xrightarrow{r} R) \qquad G \overset{p,m}{\Longrightarrow} H$$

Restriction: only injective morphisms.

Pushouts and Simple Graphs

What is the pushout?



 ? No, parallel edges not allowed.

Pushouts and Simple Graphs

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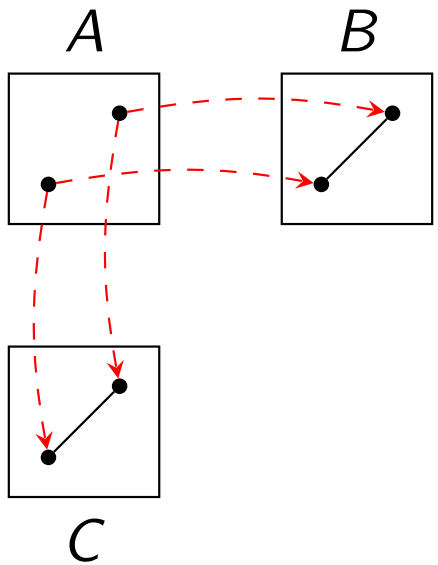
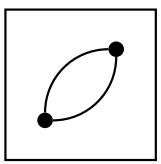
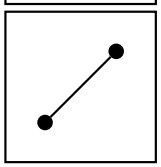


 ? No, parallel edges not allowed.

 ? No, merging of two chemical bonds not meaningful.

Pushouts and Simple Graphs

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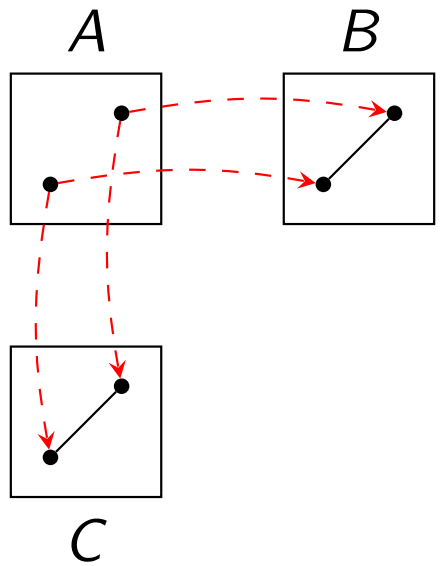
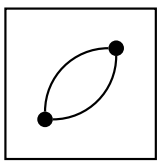
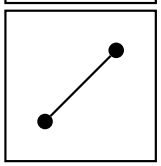


 ? No, parallel edges not allowed.

 ? No, merging of two chemical bonds not meaningful.

The pushout does not exist.

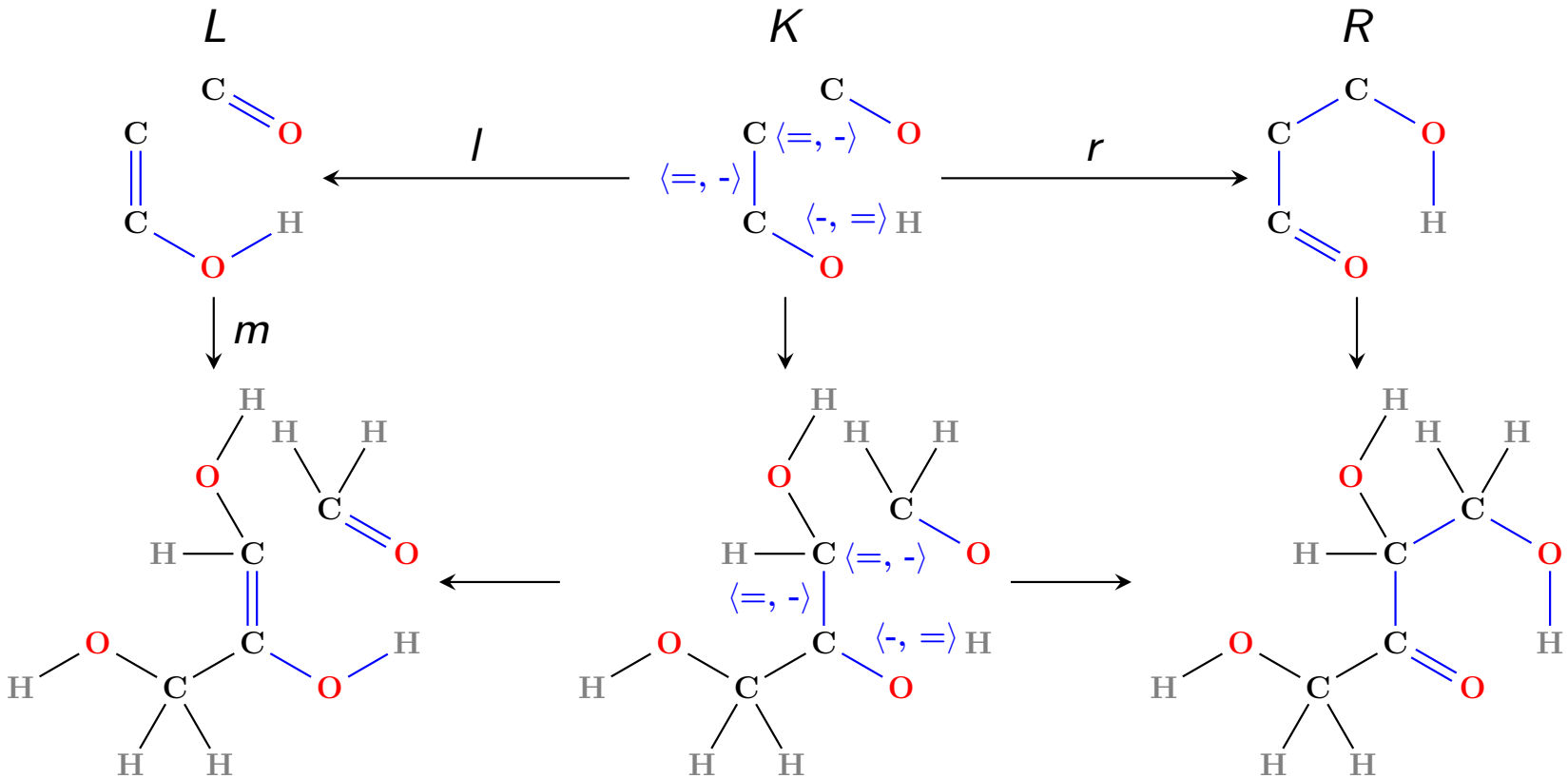
External Rule Representation

```
destroyVertex = ruleGMLString("""rule [
   left [
      node [ id 1 label "A" ]
   ]
]""")
createVertex = ruleGMLString("""rule [
   right [
      node [ id 1 label "A" ]
   ]
]""")
identity = ruleGMLString("""rule [
   context [
      node [ id 1 label "A" ]
   ]
]""")
labelChange = ruleGMLString("""rule [
   left [
      node [ id 1 label "A" ]
      edge [ source 1 target 2 label "A" ]
   ]
   context [
      node [ id 2 label "Q" ]
   ]
   right [
      node [ id 1 label "B" ]
      edge [ source 1 target 2 label "B" ]
   ]
]""")
```

$$L = \text{`left'} \cup \text{`context'} \qquad R = \text{`right'} \cup \text{`context'}$$

$$K = \text{`context'} \cup (\text{`left'} \cap \text{`right'})$$

Transformation of Multisets of Connected Graphs



$$\{\{g_0, g_1\}\} \overset{p,m}{\Longrightarrow} \{\{h_0\}\}$$

In general reactions transform multisets of molecules.

Chemistries as Graph Grammars

A chemistry:

- A set of initial molecules (graphs) $\mathcal{G}$.
- A set of reaction rules (DPO rules) $\mathcal{P}$.

Which molecules (graphs) can be reached?

Which reactions (direct derivations) can happen?

Chemistries as Graph Grammars

A chemistry:

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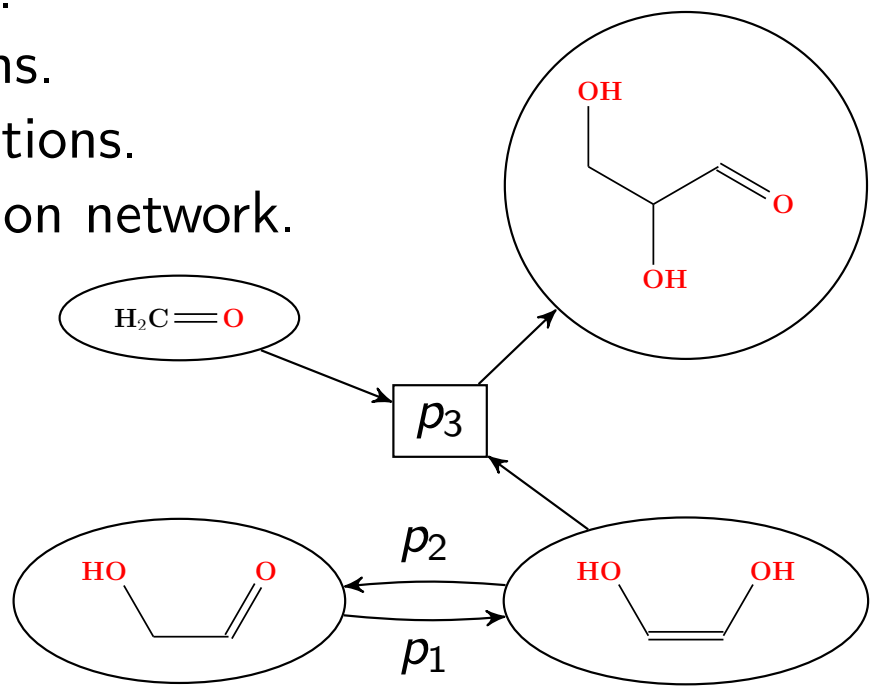
Derivation Graph:

- A directed multi-hypergraph.
- Vertices are connected graphs.
- Hyperedges are direct derivations.
- Can model a chemical reaction network.



Rule Application

Given: a set of graphs $\mathcal{U}$, and a rule $p = (L \leftarrow K \rightarrow R)$.
Brute-force:

1. Enumerate all multisets based on $\mathcal{U}$.
2. Try applying p to each of them.
3. For each successful direct derivation $G \overset{p}{\Rightarrow} H$, split H into connected components.
4. Let $\mathcal{U}' = \mathcal{U} \cup \langle \text{the new graphs} \rangle$.

Strategic Exploration of Graph Languages

An embedded domain-specific programming language.

State: a set of graphs, with a distinguished subset.

Instructions:

- '`addSubset(g)`': add '`g`' to the state.
- '`filterSubset(predicate)`': remove graphs from the state.
- '`p`': apply the rule '`p`', and add the new graphs.
- '`q0 >> q1`': sequence, first do '`q0`' then '`q1`'.
- '`[q0, q1]`': parallel, do '`q0`' and '`q1`' independently.
- '`repeat[k](q)`': sequence '`q`' at most '`k`' times.
- '`repeat(q)`': stop when no new graphs can be found.
- ...

Example:

```
strat = addSubset(inputGraphs) >> repeat(inputRules)
```

Composition of Transformation Rules

Given: rules $p_1 = (L_1 \leftarrow K_1 \rightarrow R_1)$ and $p_2 = (L_2 \leftarrow K_2 \rightarrow R_2)$.

What if R_1 is a supergraph of L_2?

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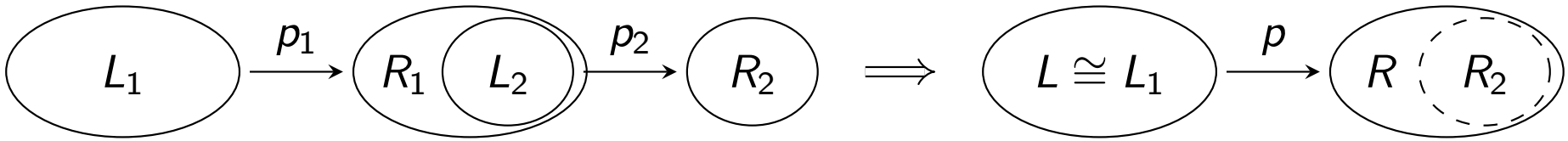

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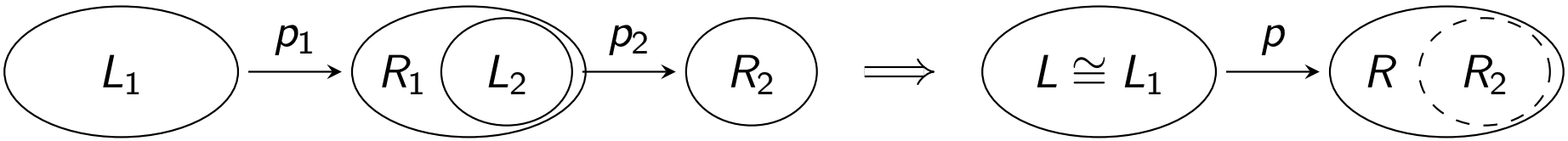
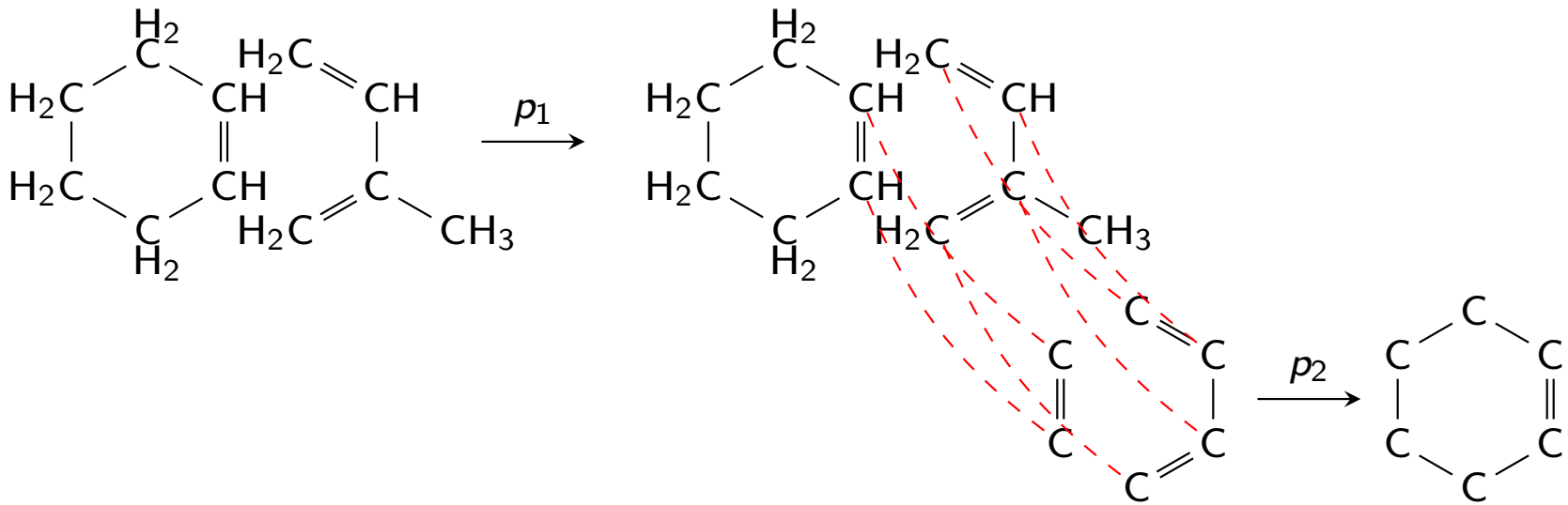
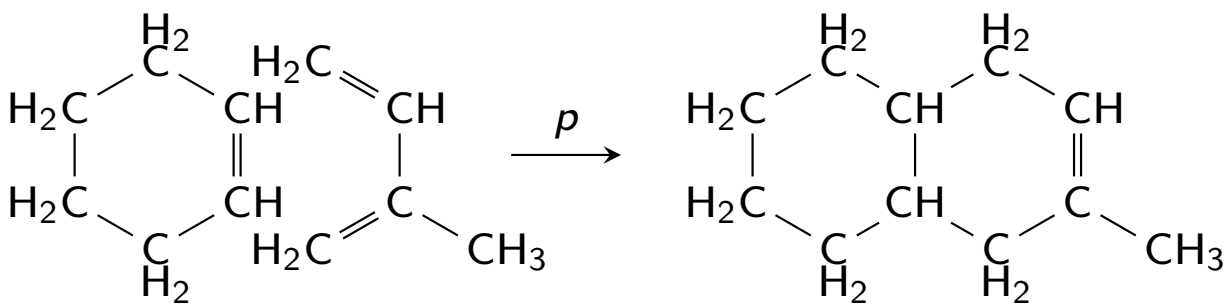
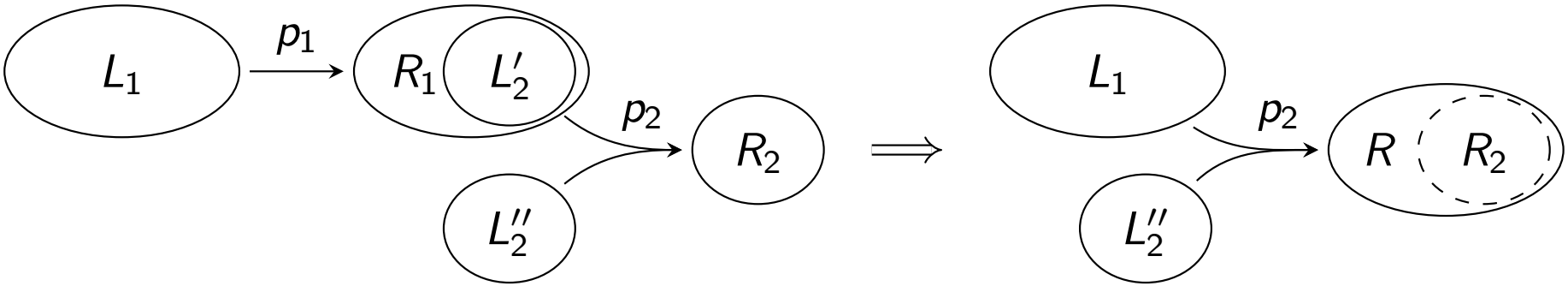
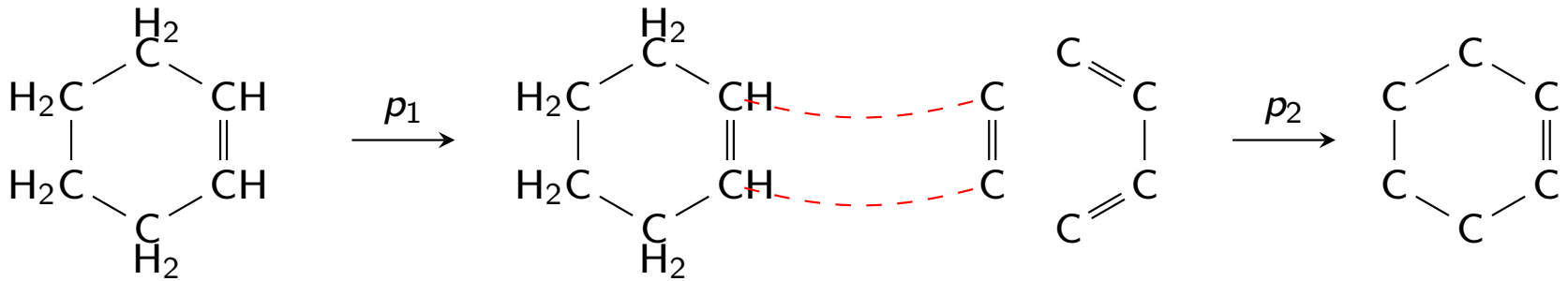


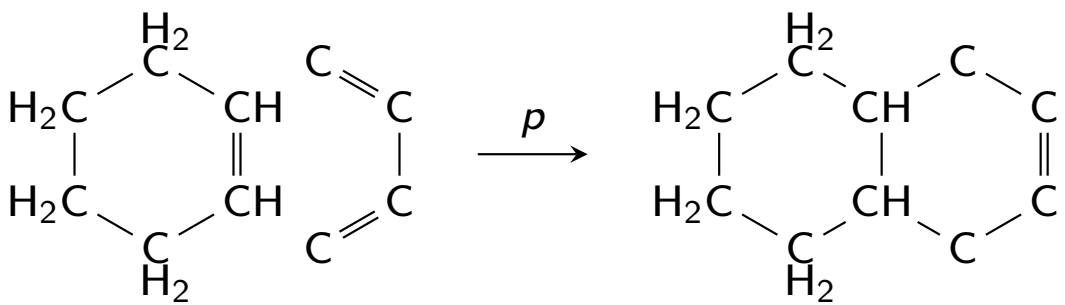




Partial Rule Composition







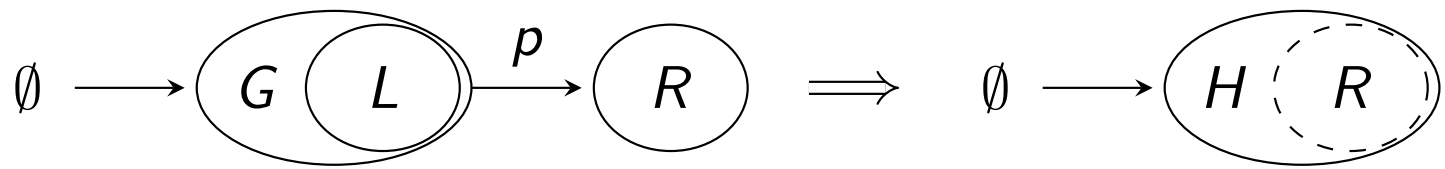
Graphs as Rules

Identity Rule: $(G \leftarrow G \rightarrow G)$
"match G and do nothing"

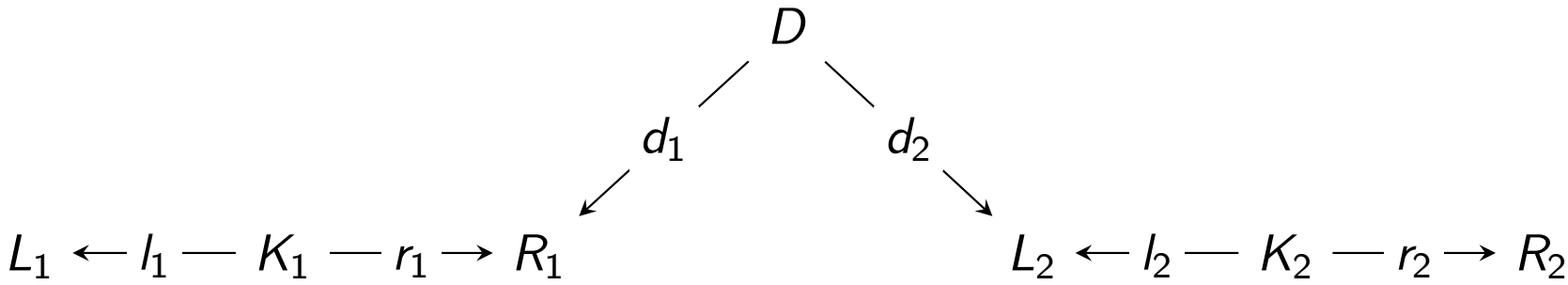
Bind Rule: $(\emptyset \leftarrow \emptyset \rightarrow G)$
"from nothing create G"

Unbind Rule: $(G \leftarrow \emptyset \rightarrow \emptyset)$
"match G and destroy it"

Transformation as Full Composition:
"first create G, then transform with p"

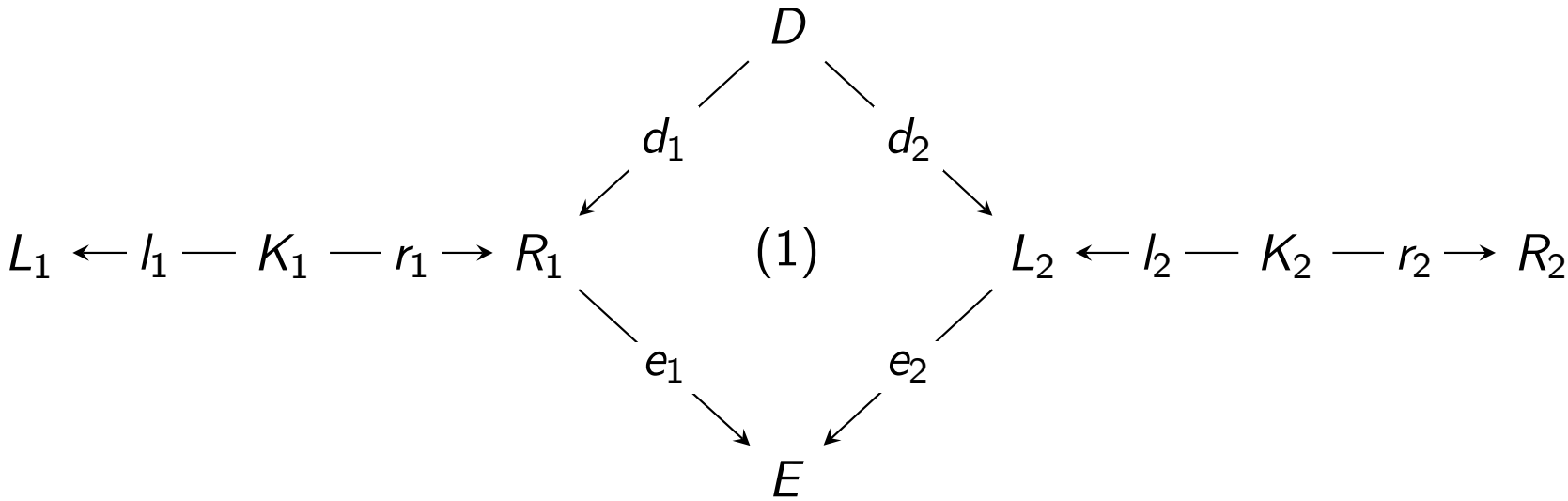


Rule Composition



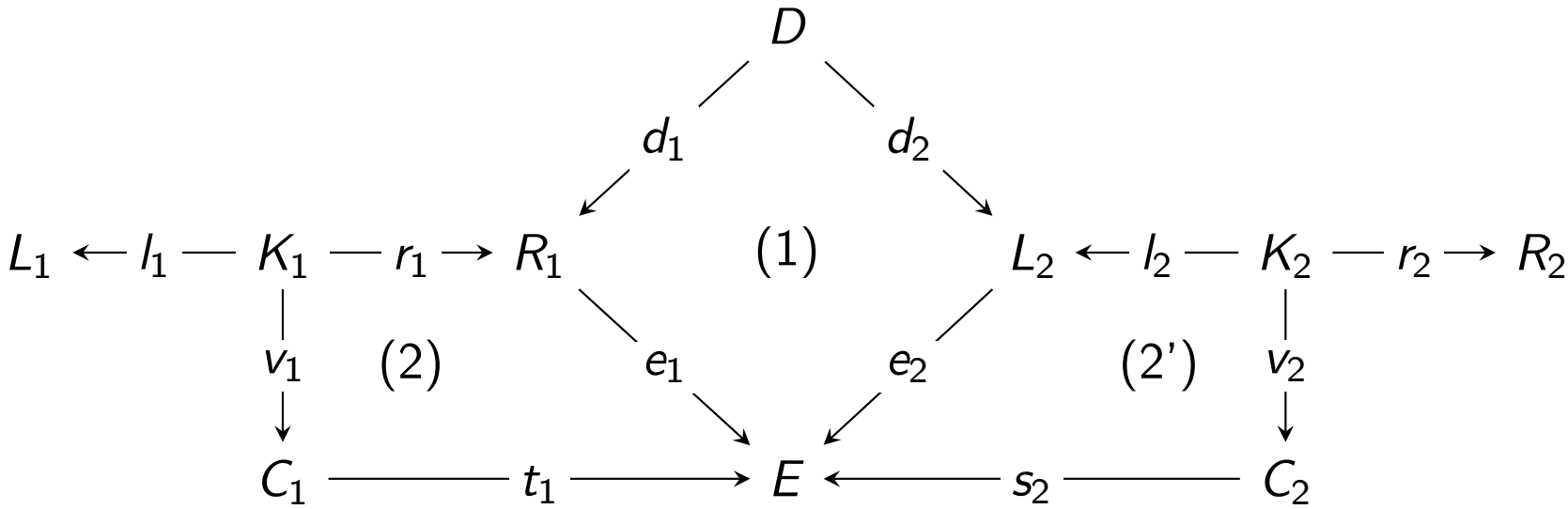
Given: two rules p_1, p_2, and the overlap $R_1 \leftarrow D \rightarrow L_2$.

Rule Composition



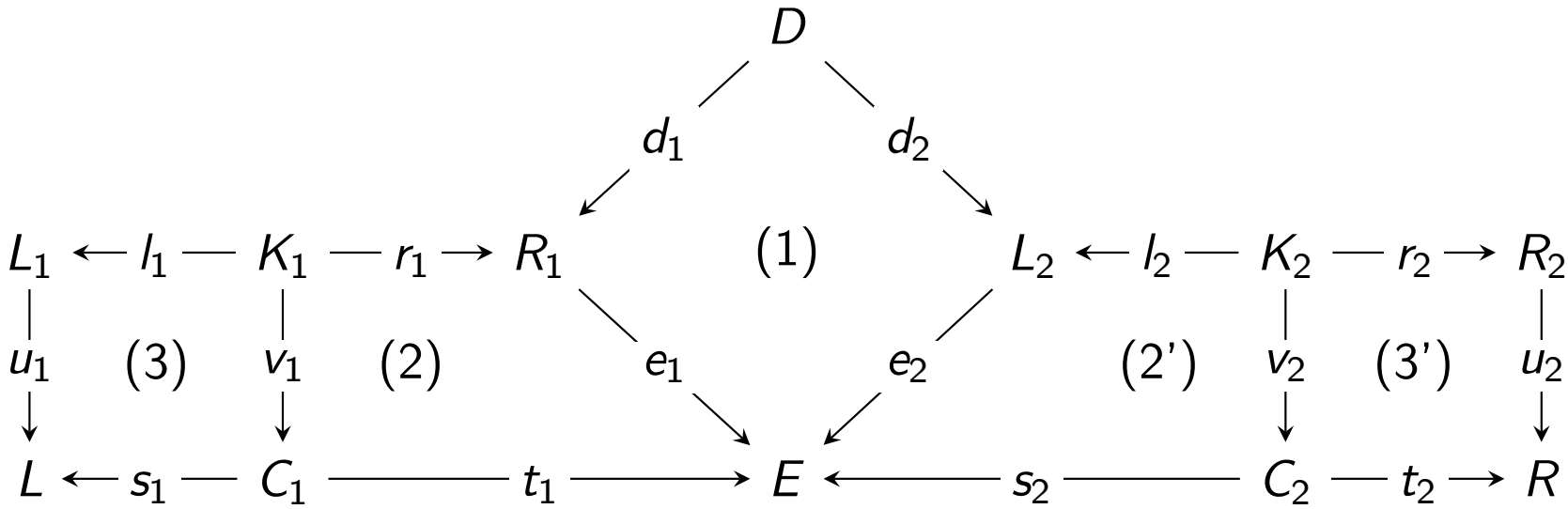
Create E as the pushout object of $R_1 \leftarrow D \rightarrow L_2$.

Rule Composition



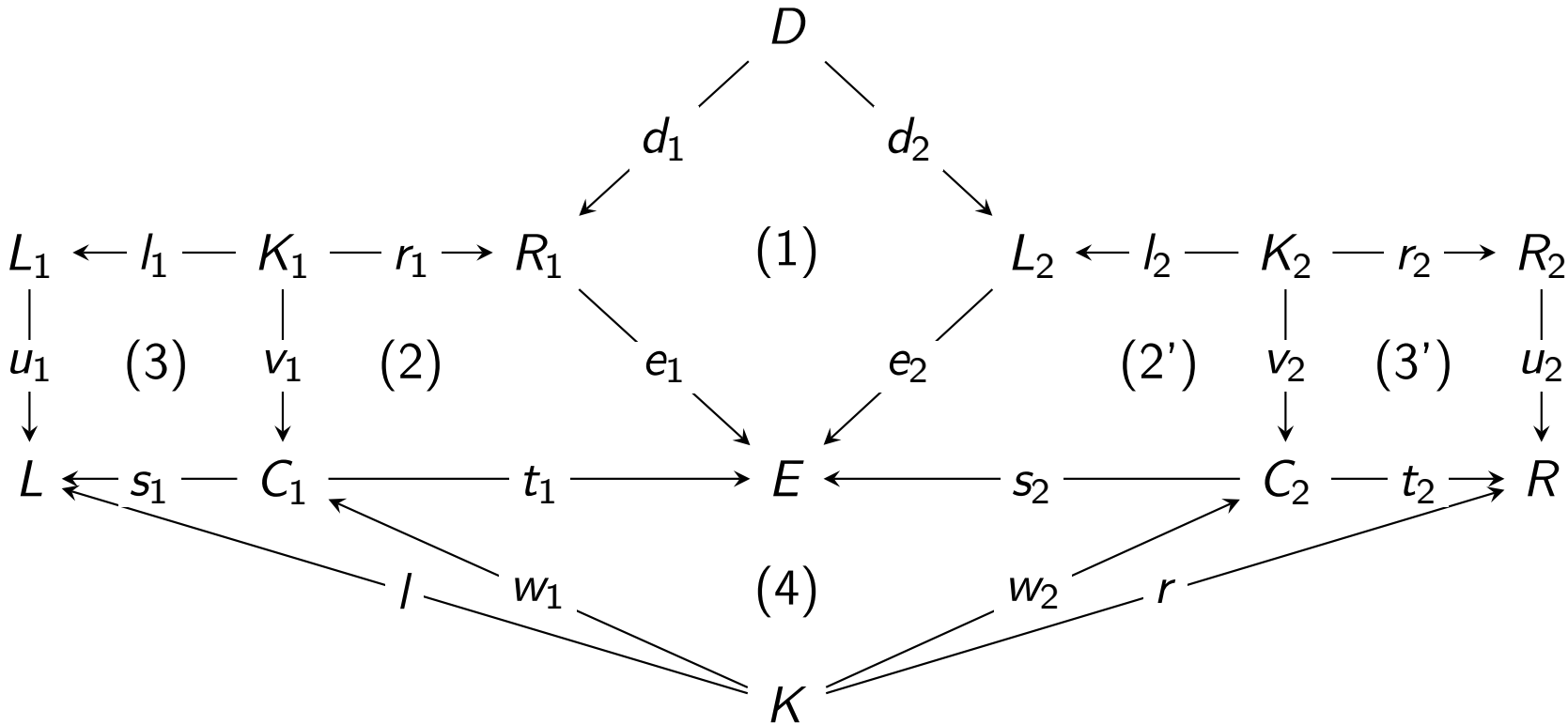
Create C_1 and C_2 as the pushout complement objects of $K_1 \to R_1 \to E$ and $K_2 \to L_2 \to E$.

Rule Composition



Create L and R as pushout objects of $L_1 \leftarrow K_1 \rightarrow C_1$ and $C_2 \leftarrow K_2 \rightarrow R_2$.

Rule Composition



Create K as the pullback object of $C_1 \to E \leftarrow C_2$.

$$(L_1 \leftarrow K_1 \to R_1) \bullet_D (L_2 \leftarrow K_2 \to R_2) = (L \leftarrow K \to R)$$

Classes of Composition

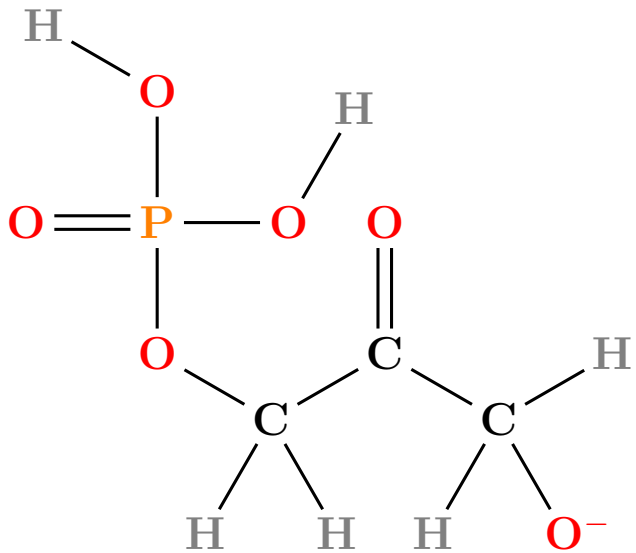
Which $R_1 \leftarrow D \rightarrow L_2$?

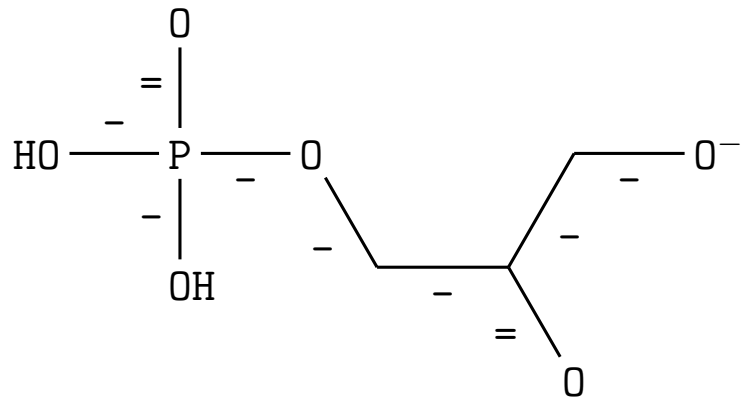
Class	Pseudo Operator, $\langle op \rangle$
$D = \emptyset$	'`*rcParallel*`'
$D = L_2$	'`*rcSuper(allowPartial=False)*`'
$D = L_2', L_2 = \{L_2', L_2''\}$	'`*rcSuper*`'
$D = R_1$	'`*rcSub(allowPartial=False)*`'
$D = R_1', R_1 = \{R_1', R_1''\}$	'`*rcSub*`'
D unrestricted	'`*rcCommon*`'

Another embedded domain-specific language:

$\langle rcExp \rangle$ :: $\langle rcExp \rangle$ $\langle op \rangle$ $\langle rcExp \rangle$
| '`rcBind(`' $\langle graphs \rangle$ '`)`'
| '`rcUnbind(`' $\langle graphs \rangle$ '`)`'
| '`rcId(`' $\langle graphs \rangle$ '`)`'
| $\langle rules \rangle$

LaTeX Package — Graphs





doc.tex:

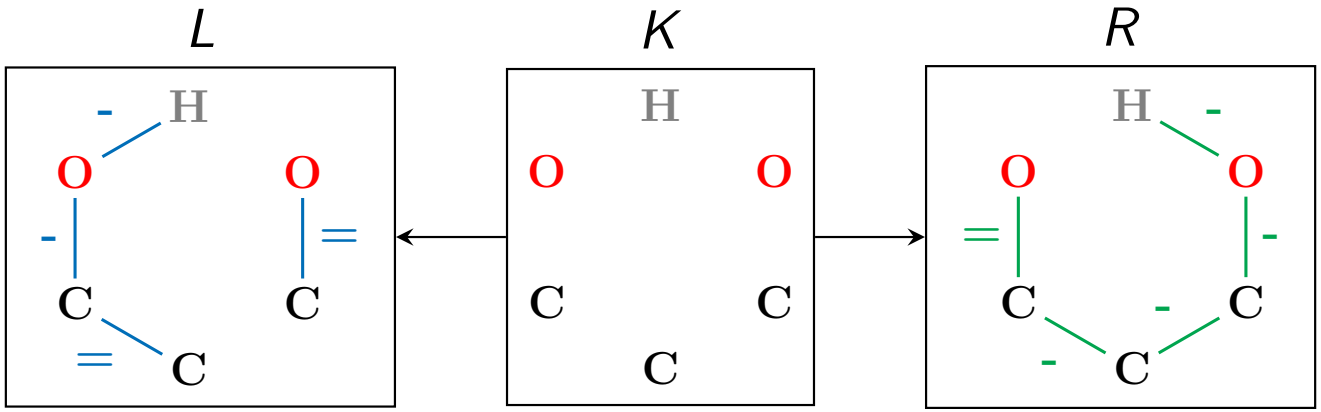
```
\smiles[collapse hydrogens=false, simple carbons=false]
   {O=P(O)(O)OCC(=O)C[O-]}
\smiles[with texttt, edges as bonds=false, with colour=false]
   {O=P(O)(O)OCC(=O)C[O-]}
```

Command line:

```
pdflatex doc.tex; mod -f doc-mod.py; pdflatex doc.tex;
```

(or get a Makefile template with "`mod --get-latex`")

LaTeX Package — Rules



doc.tex

```
\ruleGML[edges as bonds=false]
    {data/aldol_addition_forward.gml}
    {\dpoRule[scale=0.7]}
```

Expands into:

```
\dpoRule[scale=0.7]{fileL.pdf}{fileK.pdf}{fileR.pdf}
```

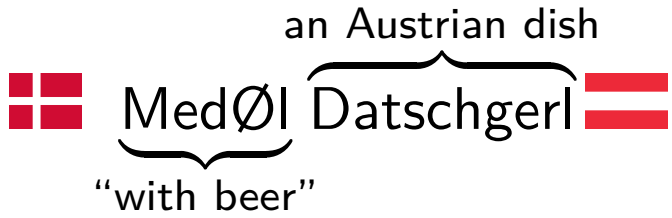
Outlook

Graph Transformation:

- First-order terms as labels (unpublished).
- Attributes for local geometry (in progress).

In General:

- Pathways in reaction networks (submitted).
- Petri-net analysis for reaction networks (in progress).
- Tracing vertices throughout networks/pathways (in progress).


an Austrian dish
MedØl Datschgerl
“with beer”