Methods for the Randomization of Metabolic Networks

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TBI

Outline

- Main Goal and Model

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- Overall Randomization Scheme

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- Main Goal and Model

- Overall Randomization Scheme

- Methods to create large sample-spaces

The Main Goal

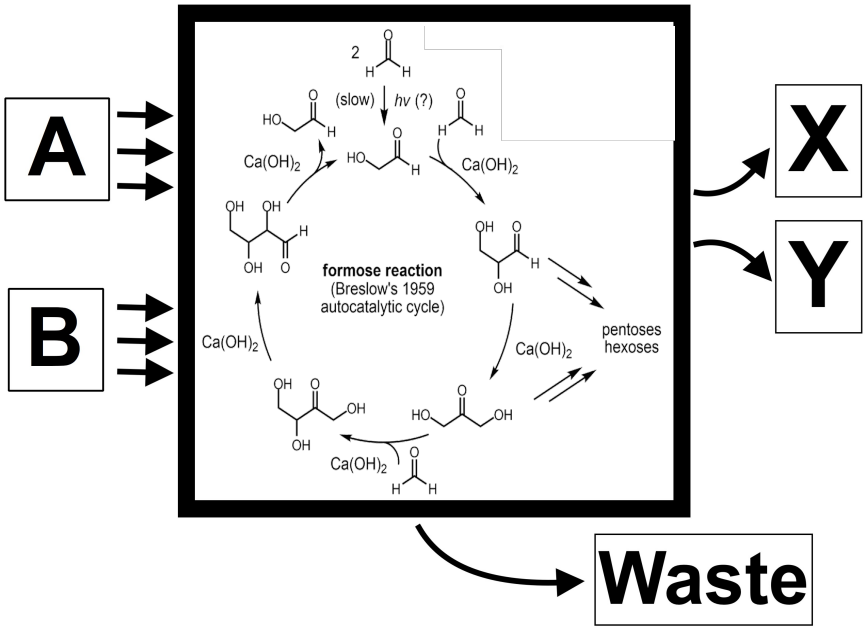
The Creation of randomized CRNs as statistical background models.

Requirements:

1) **Reference Network**

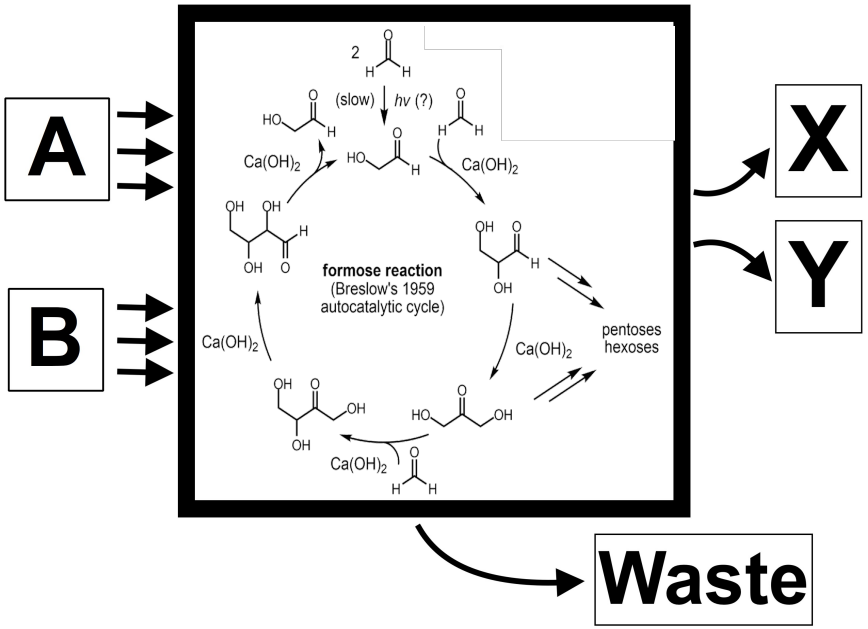
2) Keeping its **function**

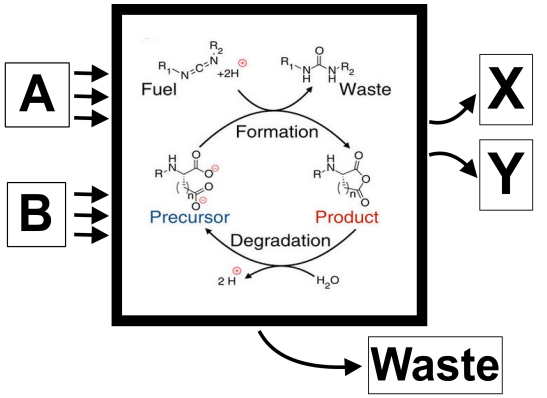
The Main Goal



1) Formose catalytic cycle https://commons.wikimedia.org/wiki/File:Formose.png

The Main Goal





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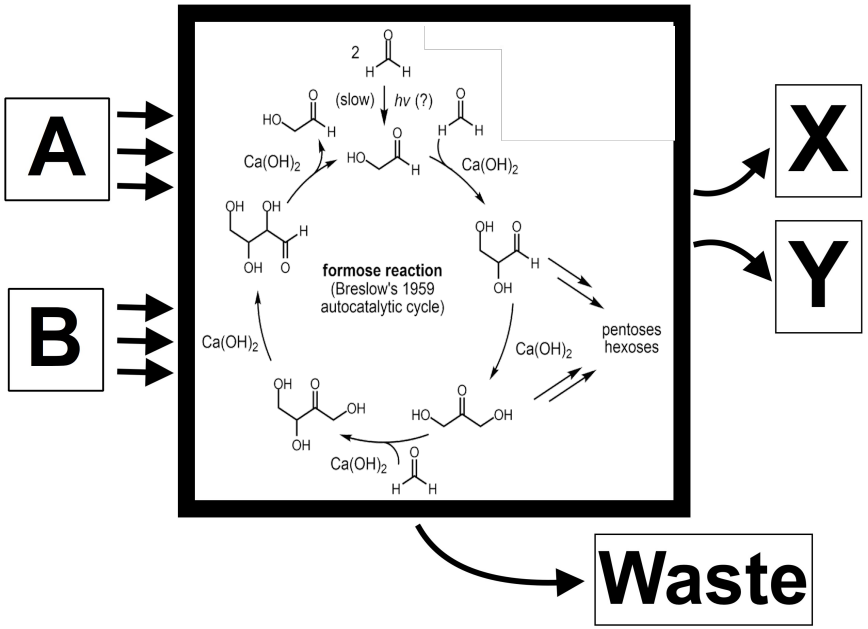
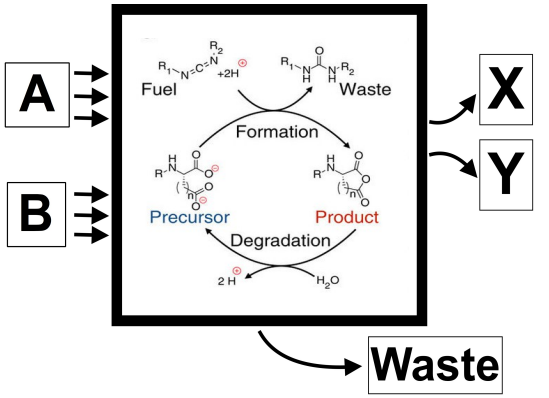
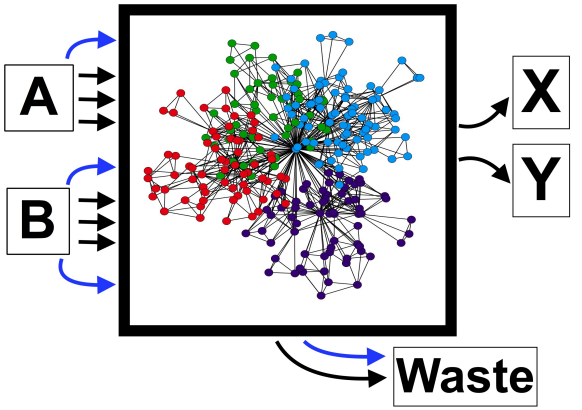
2) Tena-Solsona et.al, *Non-equilibrium dissipative supramolecular materials with a tunable lifetime*

The Main Goal

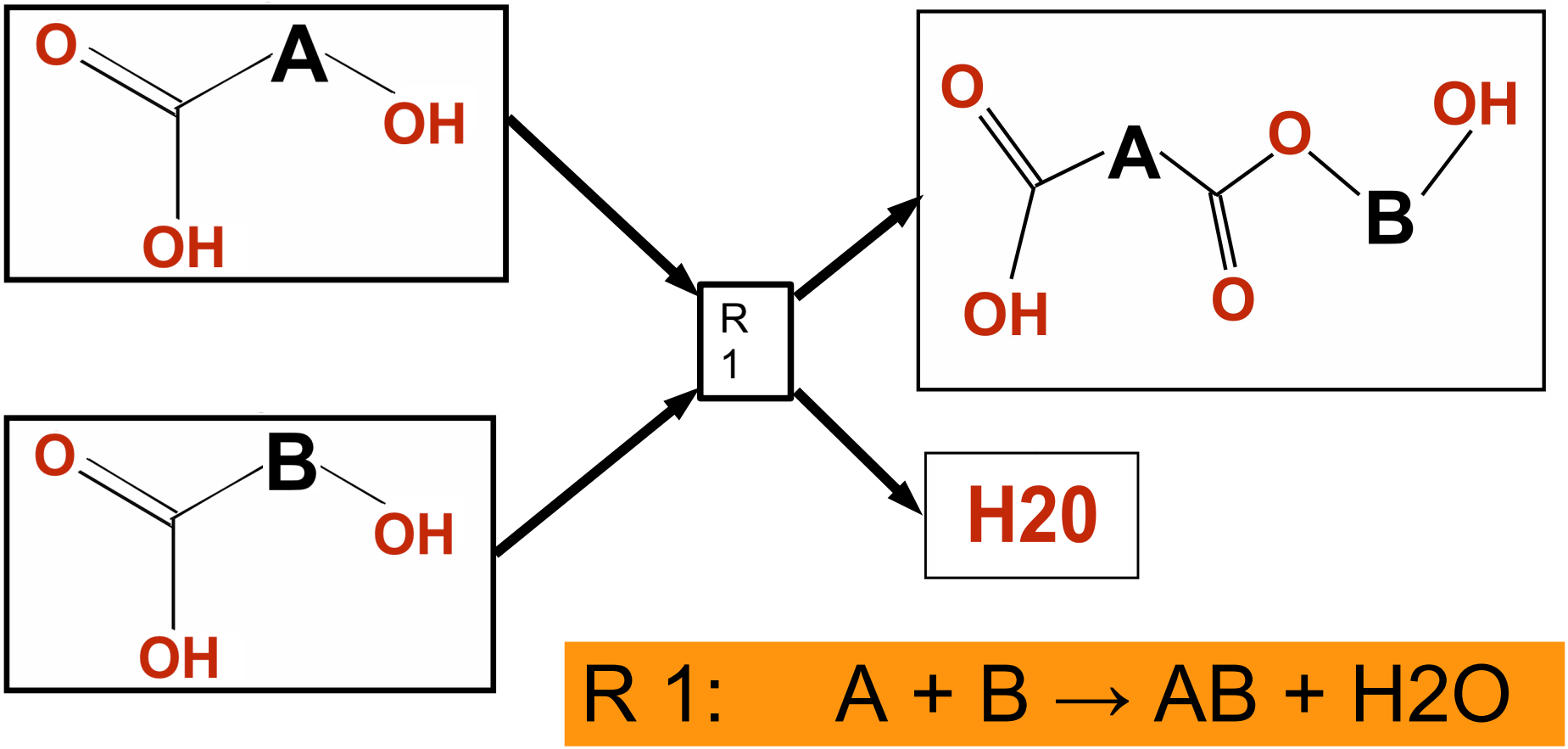






1) Formose catalytic cycle https://commons.wikimedia.org/wiki/File:Formose.png
2) Tena-Solsona et.al, *Non-equilibrium dissipative supramolecular materials with a tunable lifetime*
3) https://www.taylorintime.com/wp-content/uploads/2016/02/Brain-network.png

Molecule- and CRN-model (MØD[1])



R 1: A + B → AB + H2O

[1] Jakob L. Andersen, Christoph Flamm, Daniel Merkle, and Peter F. Stadler: „A software package for chemically inspired graph transformation.“ CoRR, abs/1603.02481, 2016.

Main Problem

- CRNs are heavily constrained

- randomized CRNs should be tailored to the Reference Network

Our Strategy

1) Create a large sample space

from species and reactions of the Reference CRN

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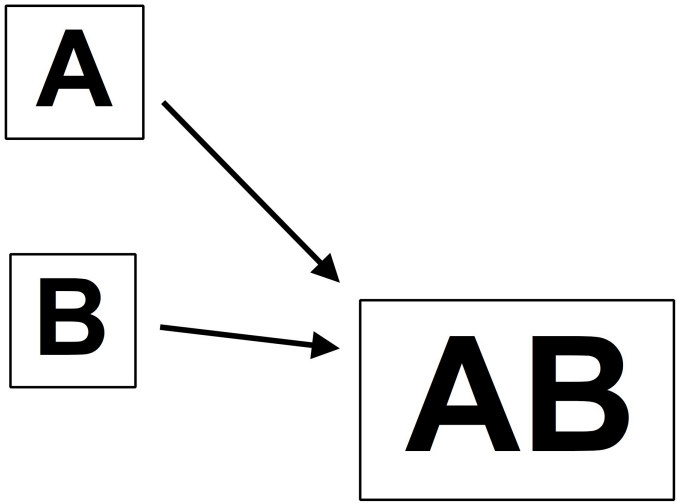
3) Enumerate pathways that

   preserve the reference function

Reaction - Closure



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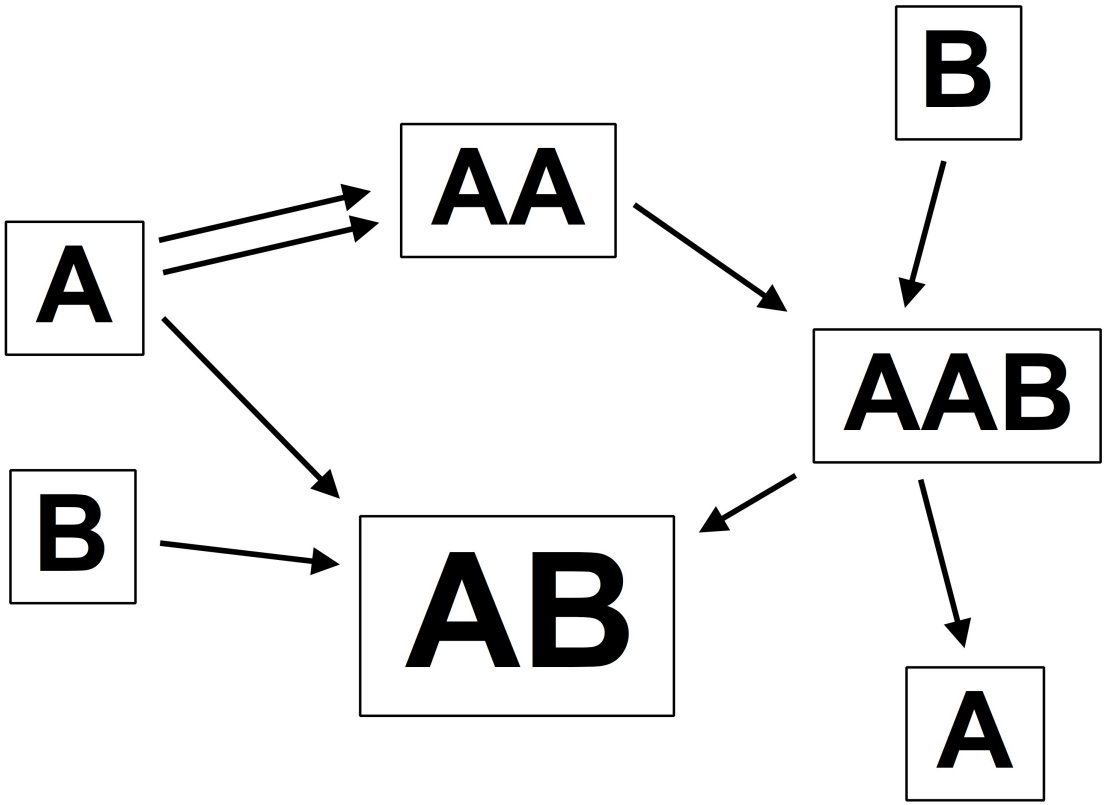

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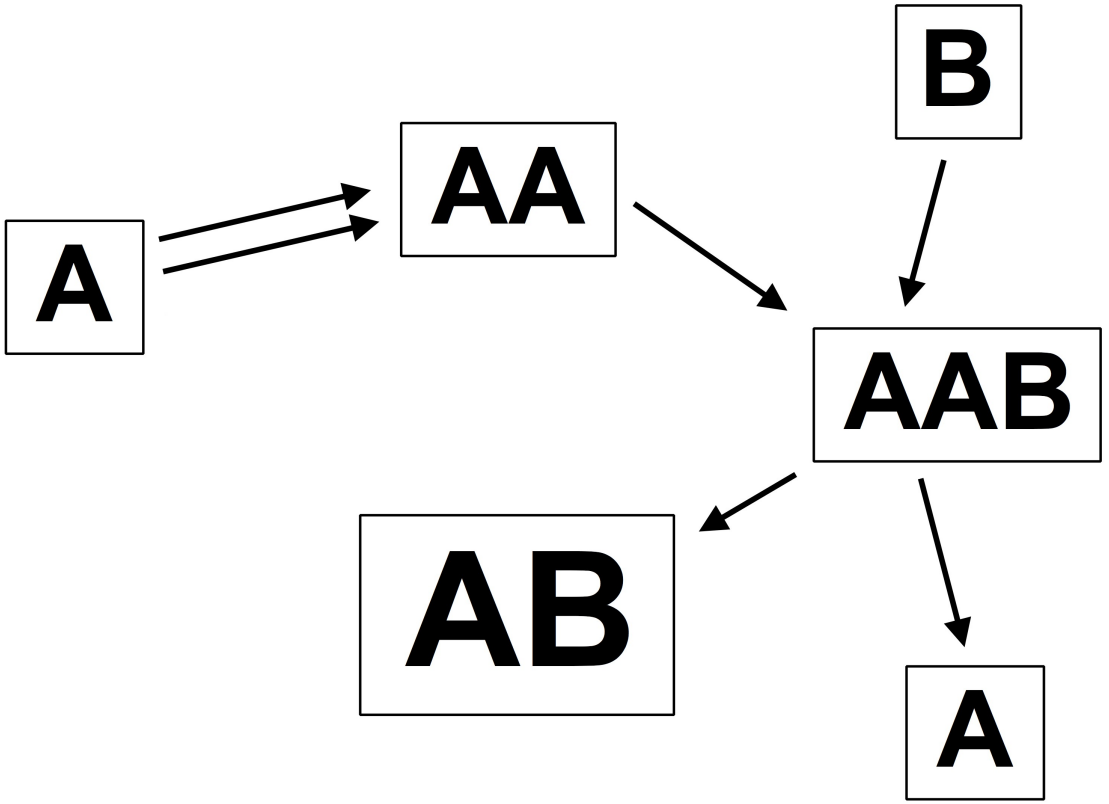
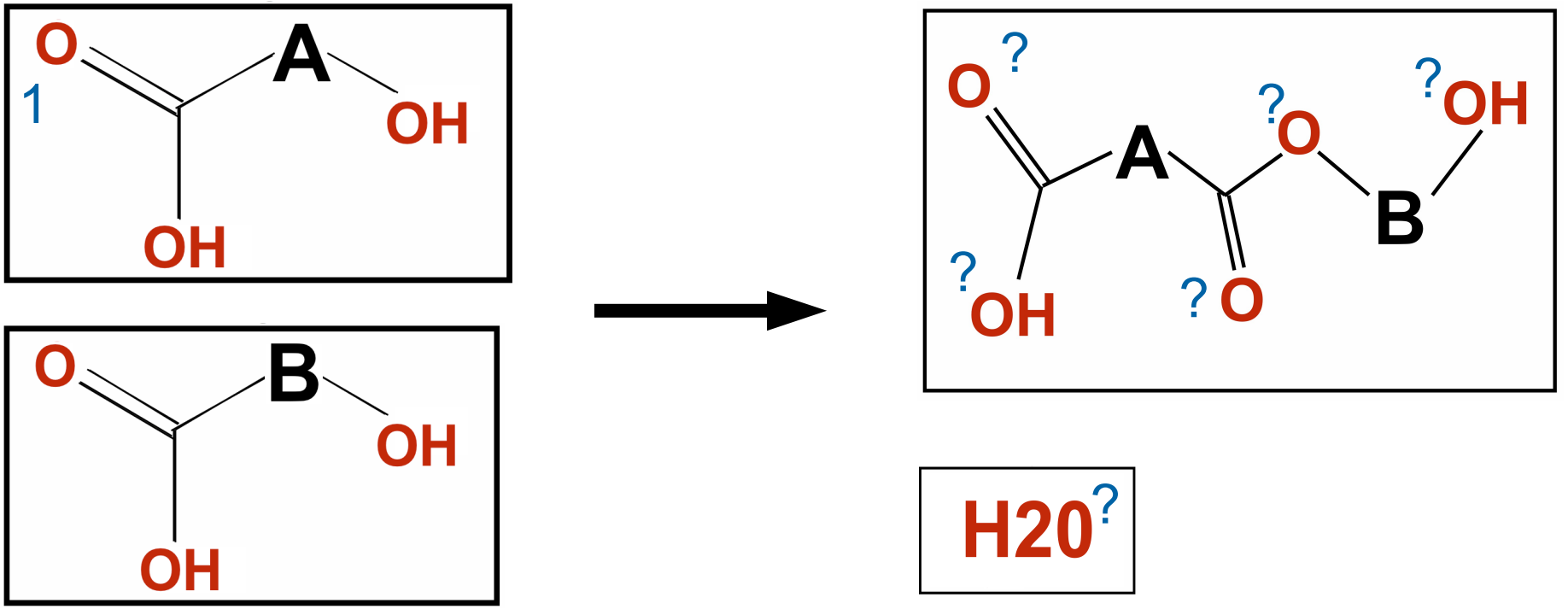


Reaction - Mapping

(atom-atom mapping)



A + B → AB + H2O

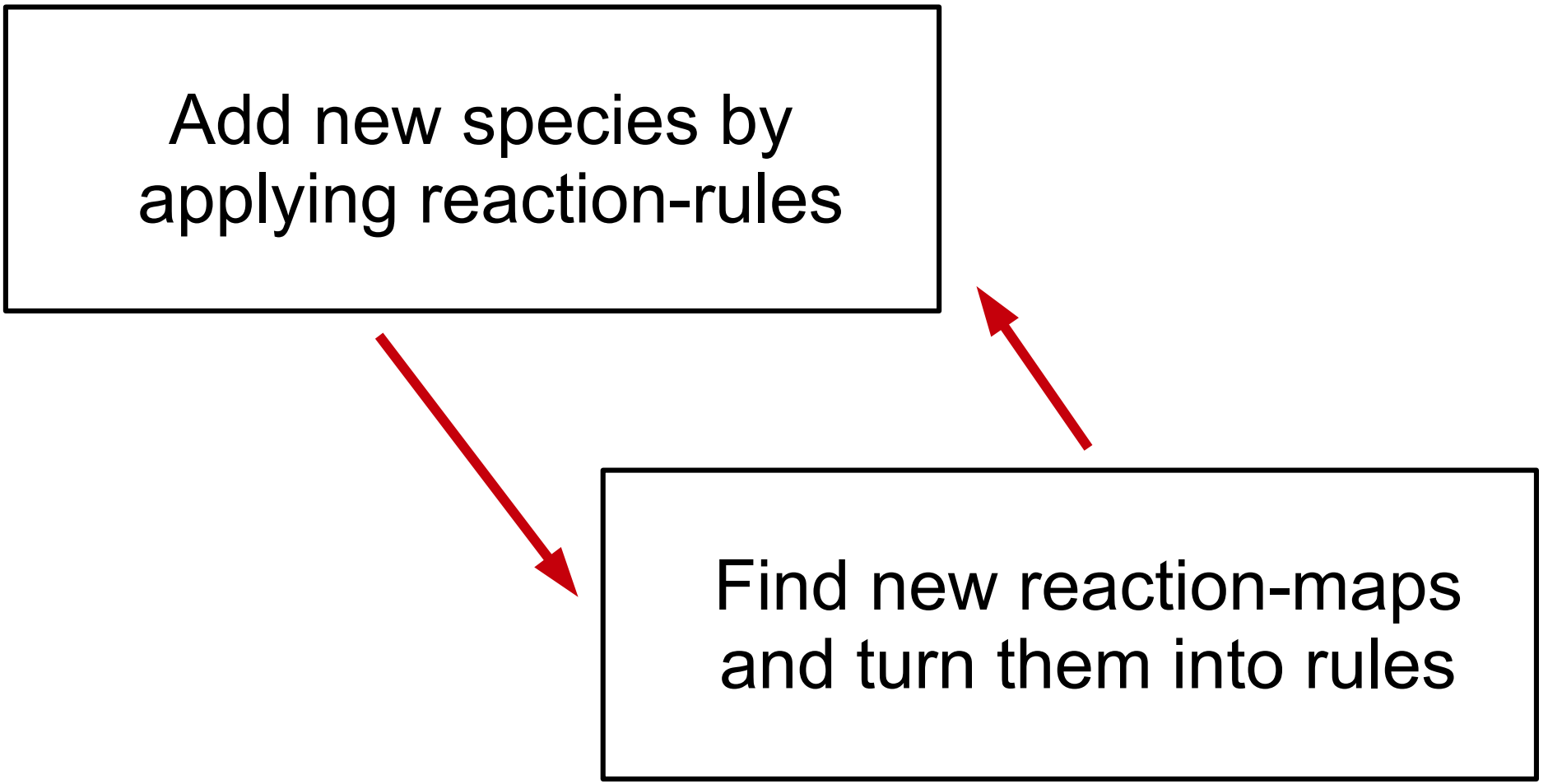
Reaction - Mapping

- Integer Linear Programming (ILP)-based Algorithm (First et al. 1969[1])

- Implementation with MØD in mind: ChemRULER (by B. Thiel)

1)First et al. Stereochemically consistent reaction mapping and identification of multiple reaction mechanisms through integer linear opti- mization. J Chem Inf Model 2012, 52:84–92.

Combined


Add new species by applying reaction-rules
Find new reaction-maps and turn them into rules

And Finally...

My Thanks to the people at the TBI

And a recommendation for

MedØlDatschgerl(MØD[1])

[1] Jakob L. Andersen, Christoph Flamm, Daniel Merkle, and Peter F. Stadler: „A software package for chemically inspired graph transformation.“ CoRR, abs/1603.02481, 2016.

Classification using bisimulation

- A weak Bisimulation-approach to CRN-equivalence using Nuskell[1]

- Equivalence of partitions

1) Stefan Badelt, Seung Woo Shin, Robert F. Johnson, Qing Dong, Chris Thachuk, and Erik Winfree (2017) "A General-Purpose CRN-to-DSD Compiler with Formal Verification, Optimization, and Simulation Capabilities"