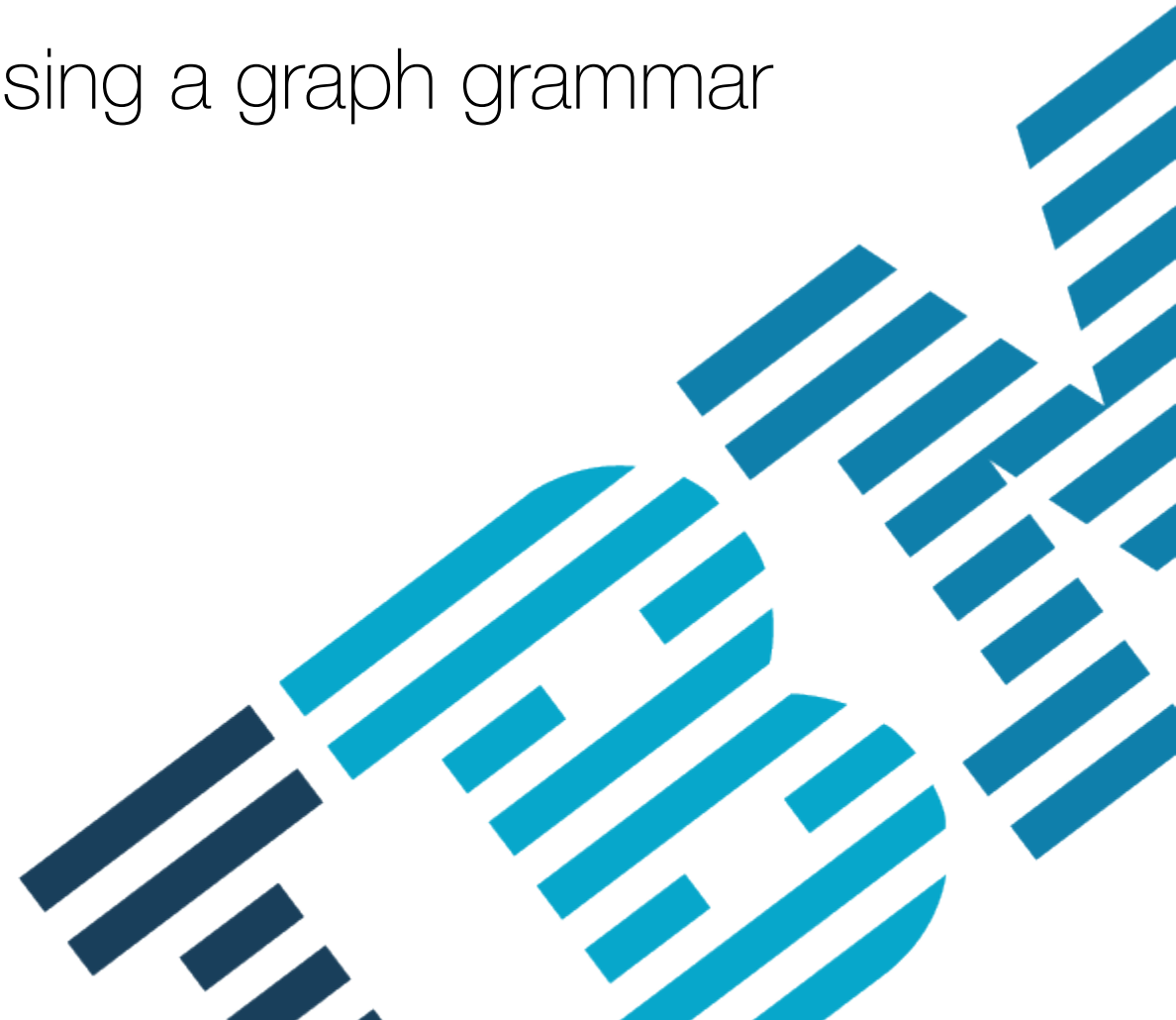
Graph generation using a graph grammar

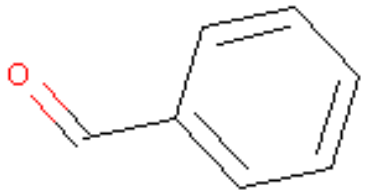
Hiroshi Kajino

IBM Research - Tokyo



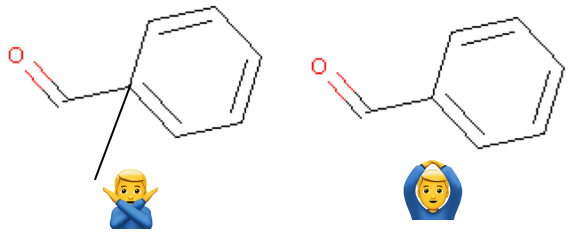
I will talk about an application of formal language to a graph generation problem

- Formal language
  - Context-free grammar
  - Hyperedge replacement grammar (HRG)
  - HRG inference algorithm
- Application to molecular graph generation
  - Molecular hypergraph grammar (a special case of HRG)
  - MHG inference algorithm
  - Combination with VAE



A molecular graph should satisfy some constraints to be valid

- Learning a generative model of a molecular graph
  - **Input:** set of molecular graphs $G = \{g_1, g_2, \ldots, g_N\}$
  - **Output:** probability distribution $p(g)$ such that $g_n \sim p$
- Hard vs. soft constraints on $p(g)$'s support
  - **Hard constraint:** valence condition
    - ∃ rule-based classifier that judges this constraint
  - **Soft constraint:** stability
    - ∄ rule-based classifier, in general



Formal language can help

A formal language defines a set of strings with certain properties; an associated grammar tells us how to generate them

- Formal language

  Typically defined as a set of strings

  – **Language** point of view

  = a set of strings with certain properties

  (= a subset of all possible strings)

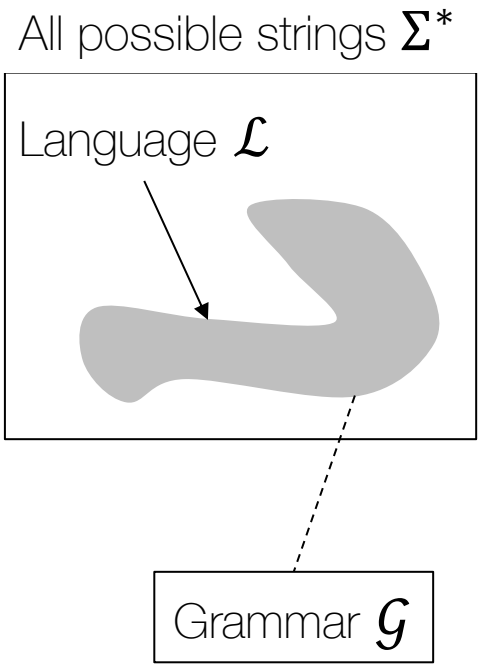
$$\mathcal{L} = \{a^n b^n : n \geq 1\} \subset \{a, b\}^* = \Sigma^*$$

  – **Generative** point of view

  A grammar is often associated with a language

  = how to generate strings in $\mathcal{L}$

$$\mathcal{G} = (\{S\}, \{a, b\}, S, \{S \to ab, S \to aSb\})$$



A formal language defines a set of graphs satisfying hard constraints; an associated grammar tells us how to generate them

- Formal language

  Typically defined as a set of graphs

  – Language point of view

  = a set of graphs satisfying the hard constraints

  (= a subset of all possible graphs)

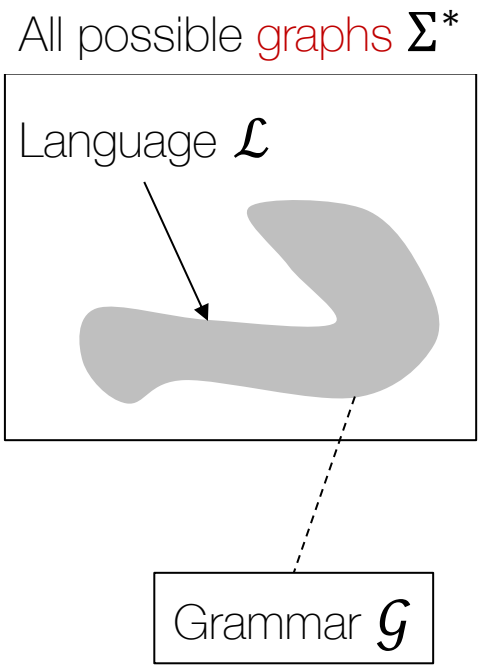
$$\mathcal{L} = \left\{ \begin{matrix} \text{Molecules satisfying} \\ \text{the valence conditions} \end{matrix} \right\} \subset \{\text{All possible graphs}\}$$

  – Generative point of view

  A grammar is often associated with a language

  = how to generate graphs in $\mathcal{L}$

  ???



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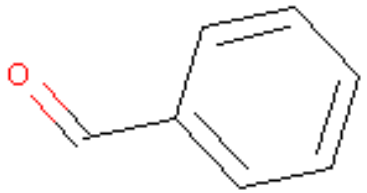

CFG generates a string by repeatedly applying a production rule to a non-terminal, until there exists no non-terminal

- Context-free grammar $G = (V, \Sigma, R, S)$
  - V: set of non-terminals
  - Σ: set of terminals
  - R: set of production rules
  - $S \in V$: the start symbol

- Example
  - $V = \{S\}$
  - $\Sigma = \{a, b\}$
  - $R = \{S \rightarrow ab,\ S \rightarrow aSb\}$
  - S

$$S$$

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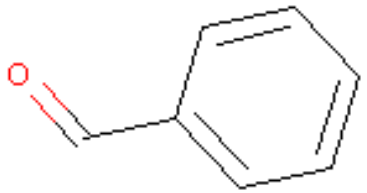
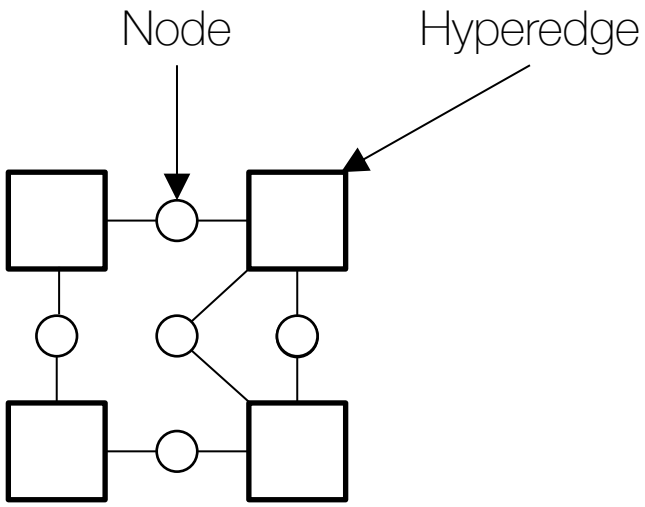


Hypergraph is a generalization of a graph

- Hypergraph $H = (V, E)$ consists of…
  - Node $v \in V$
  - Hyperedge $e \in E \subseteq 2^{|V|}$: Connect an arbitrary number of nodes

    cf, An edge in a graph connects exactly two nodes



HRG generates a hypergraph by repeatedly replacing non-terminal hyperedges with hypergraphs

- Hyperedge replacement grammar (HRG) $\mathcal{G} = (V, \Sigma, R, S)$
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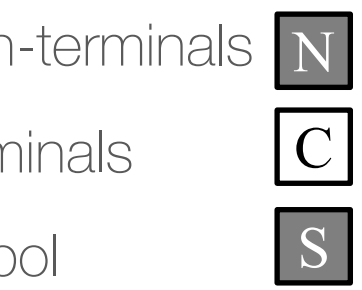
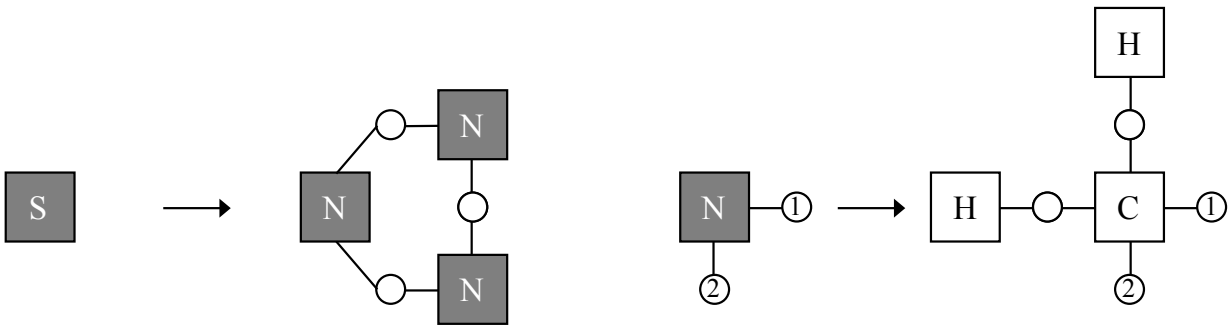


Labels on hyperedges

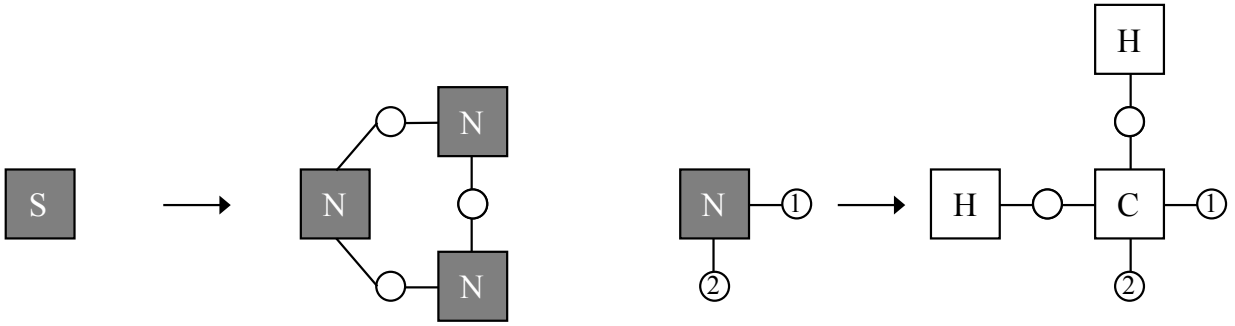
A rule replaces a non-terminal hyperedge with a hypergraph



[Feder, 71], [Pavlidis+, 72]

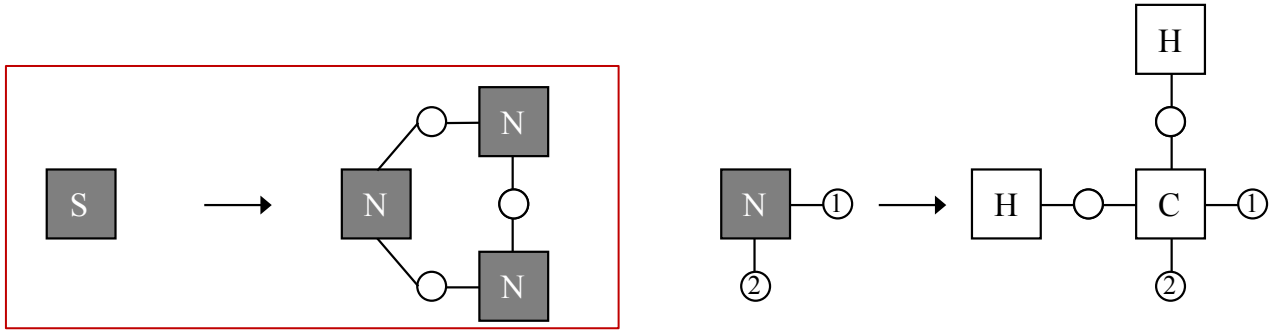
Start from start symbol $\mathbf{S}$

Production rules P

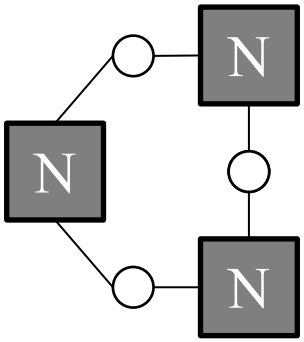


The left rule is applicable

Production rules P



We obtain a hypergraph with three non-terminals



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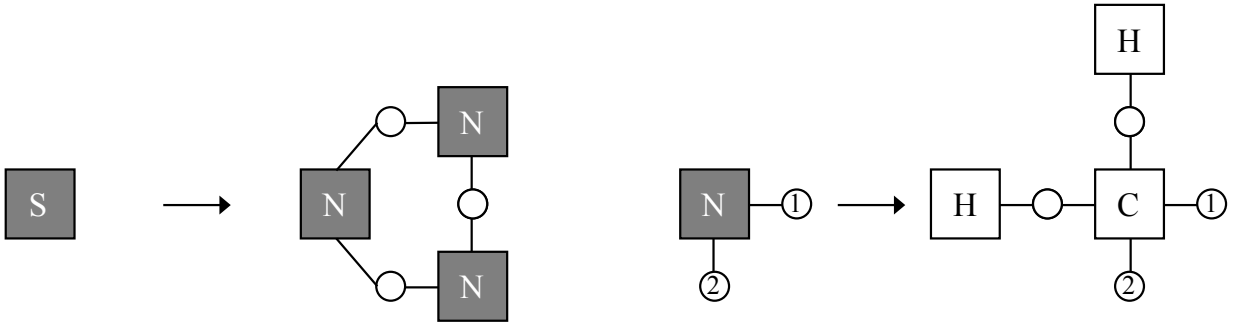
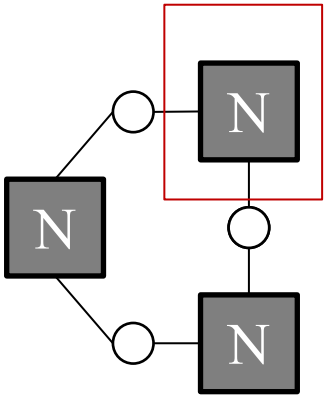


Apply the right rule to one of the non-terminals



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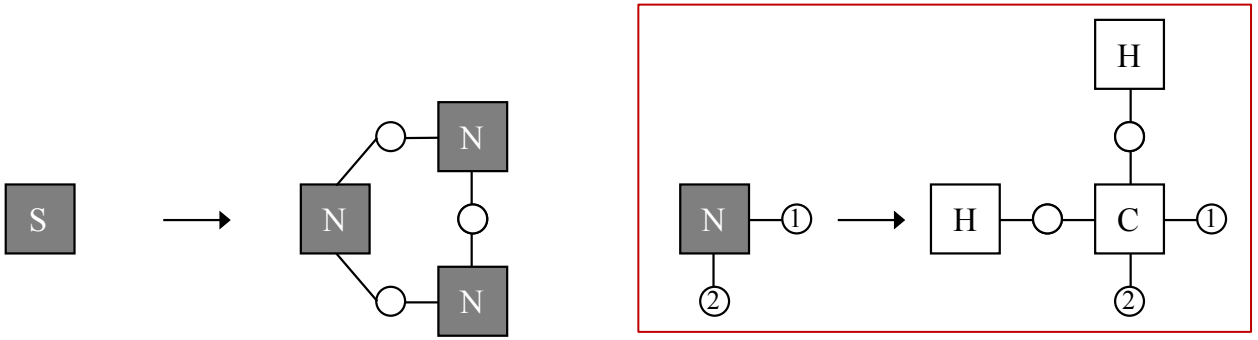
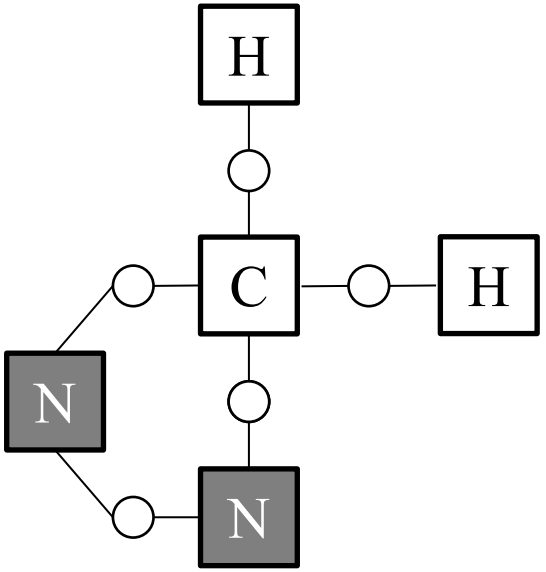


Two non-terminals remain



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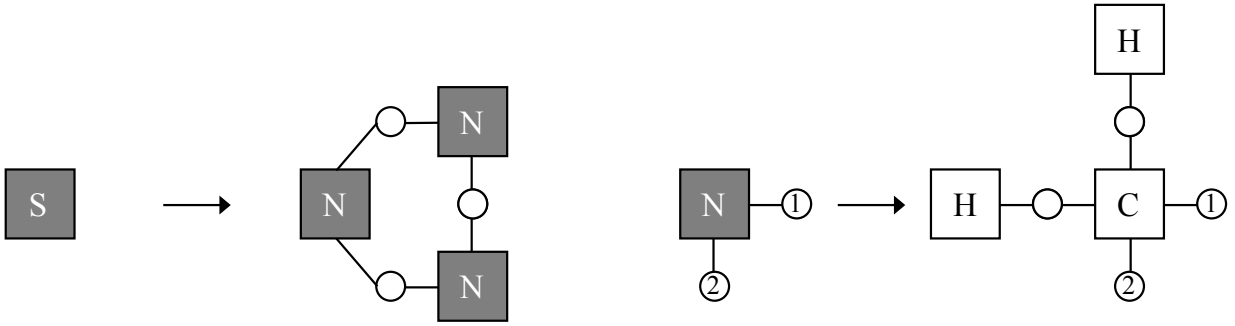
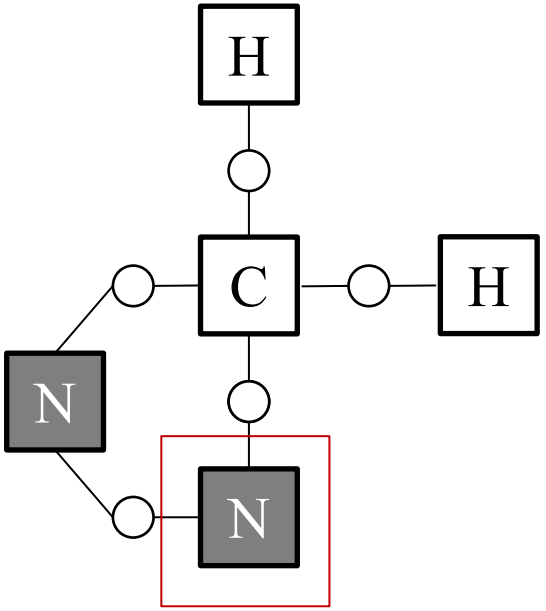


Repeat the procedure until there is no non-terminal



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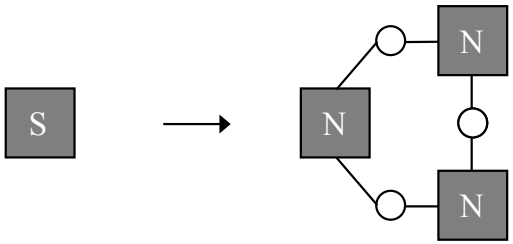

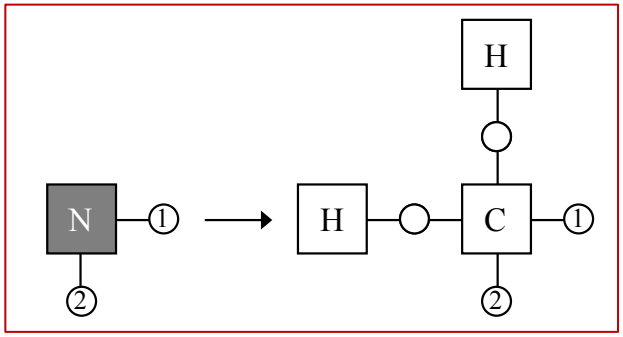

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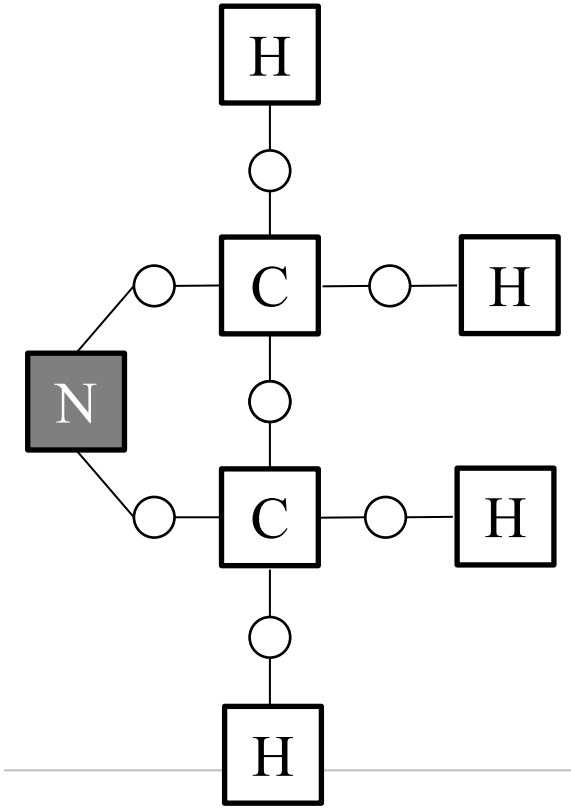

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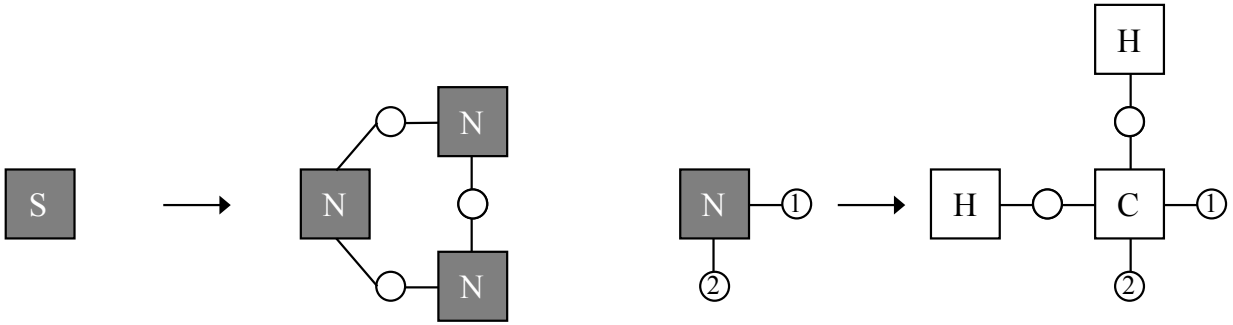

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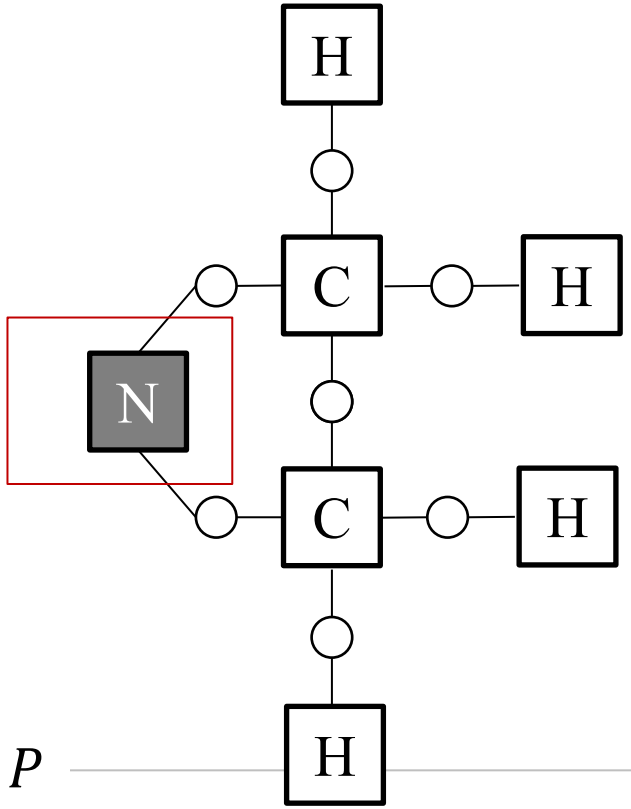

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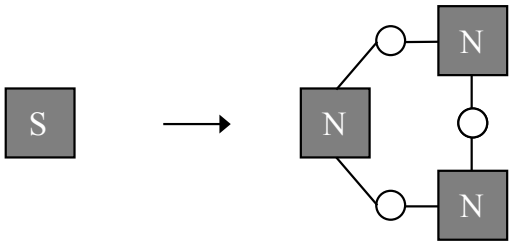
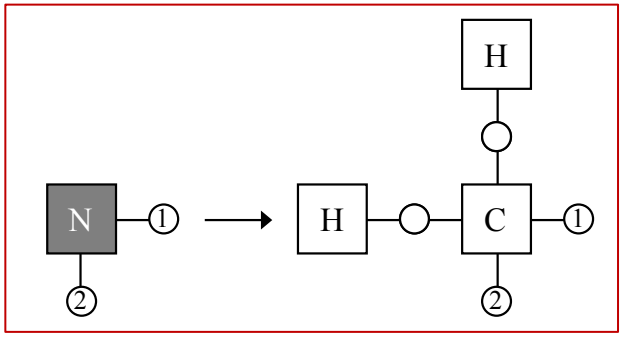
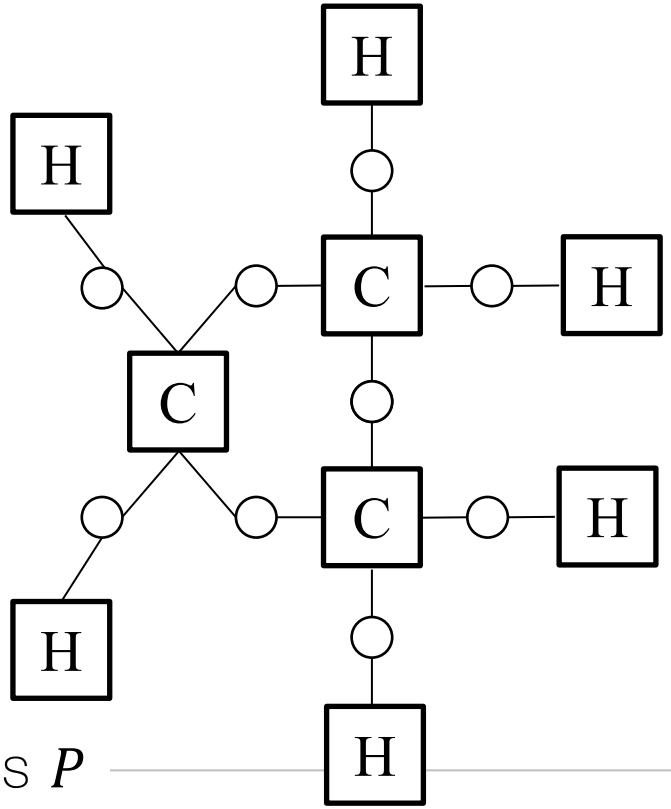




Graph generation halts when there is no non-terminal



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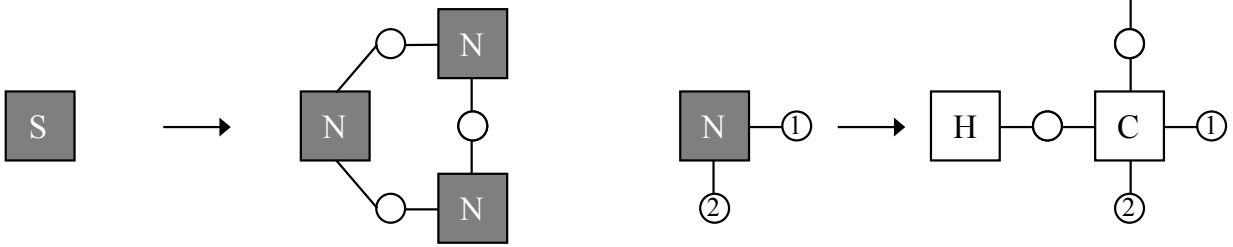

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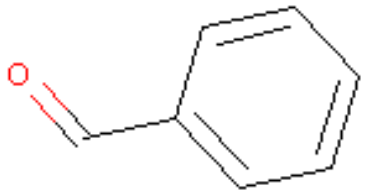


HRG inference algorithm outputs HRG that can reconstruct the input

- HRG inference algorithm [Aguiñaga+, 16]
  - **Input:** Set of hypergraphs $\mathcal{H}$
  - **Output:** HRG such that $\mathcal{H} \subseteq \mathcal{L}(\mathrm{HRG})$

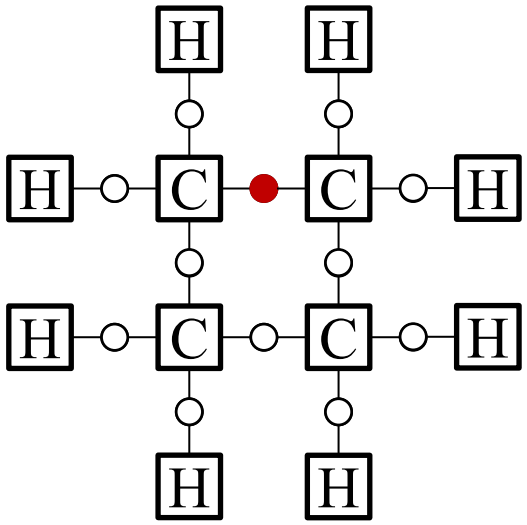
    Minimum requirement of the grammar's expressiveness
  - **Idea:** Infer production rules necessary to obtain each hypergraph

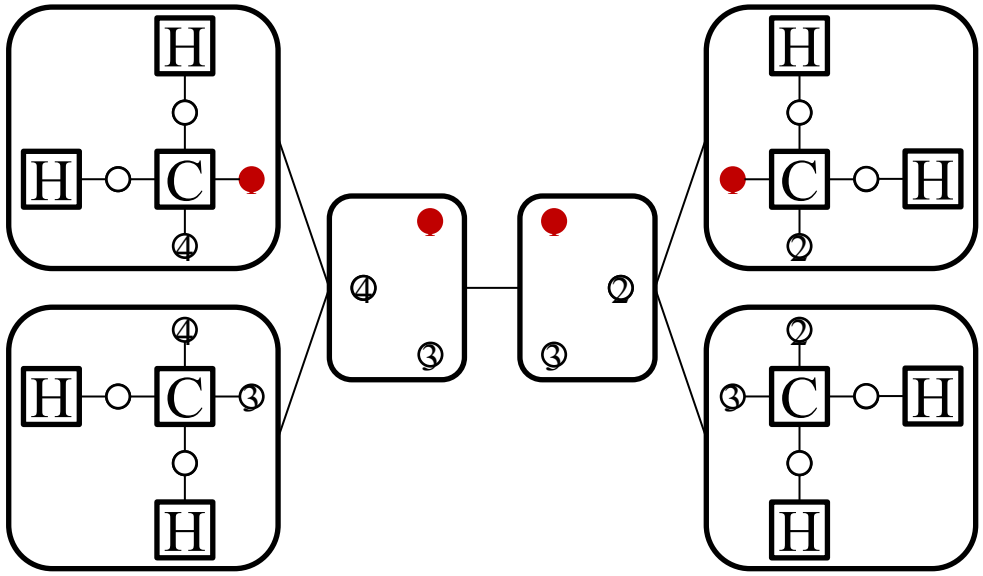
    Decompose each hypergraph into a set of production rules

Language of the grammar

Tree decomposition discovers a tree-like structure in a graph

- Tree decomposition
  - All the nodes and edges must be included in the tree
  - For each node, the tree nodes that contain it must be connected

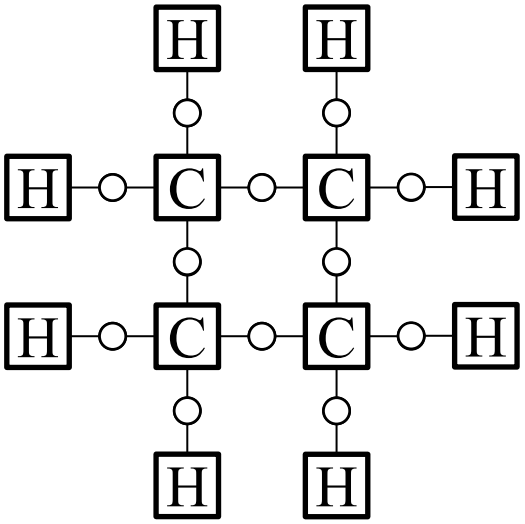


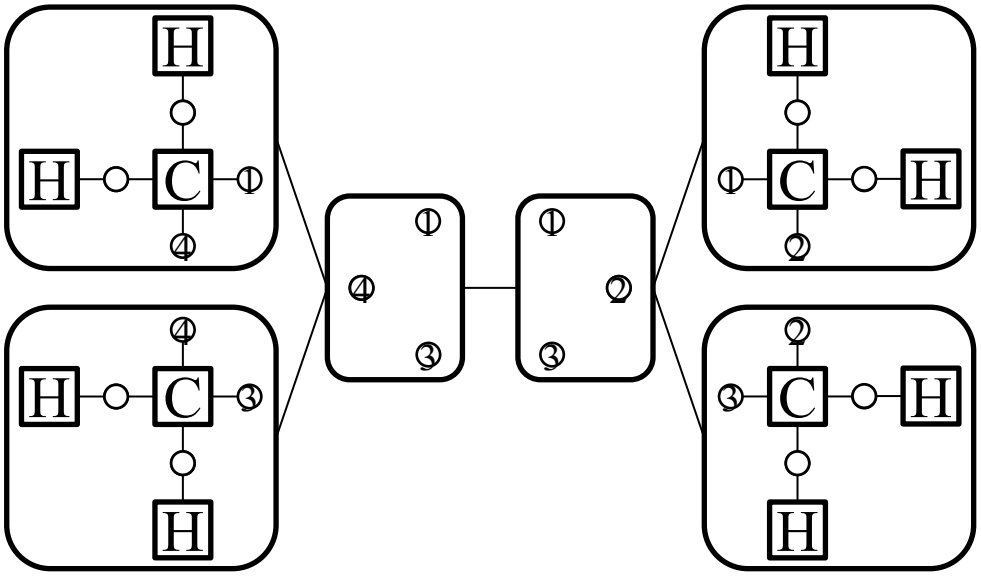


* Digits represent the node correspondence

Tree decomposition and (a syntax tree of) HRG are equivalent

- Relationship between tree decomposition and HRG
  1. Connecting hypergraphs in tree recovers the original hypergraph
  2. Connection ⇔ Hyperedge replacement





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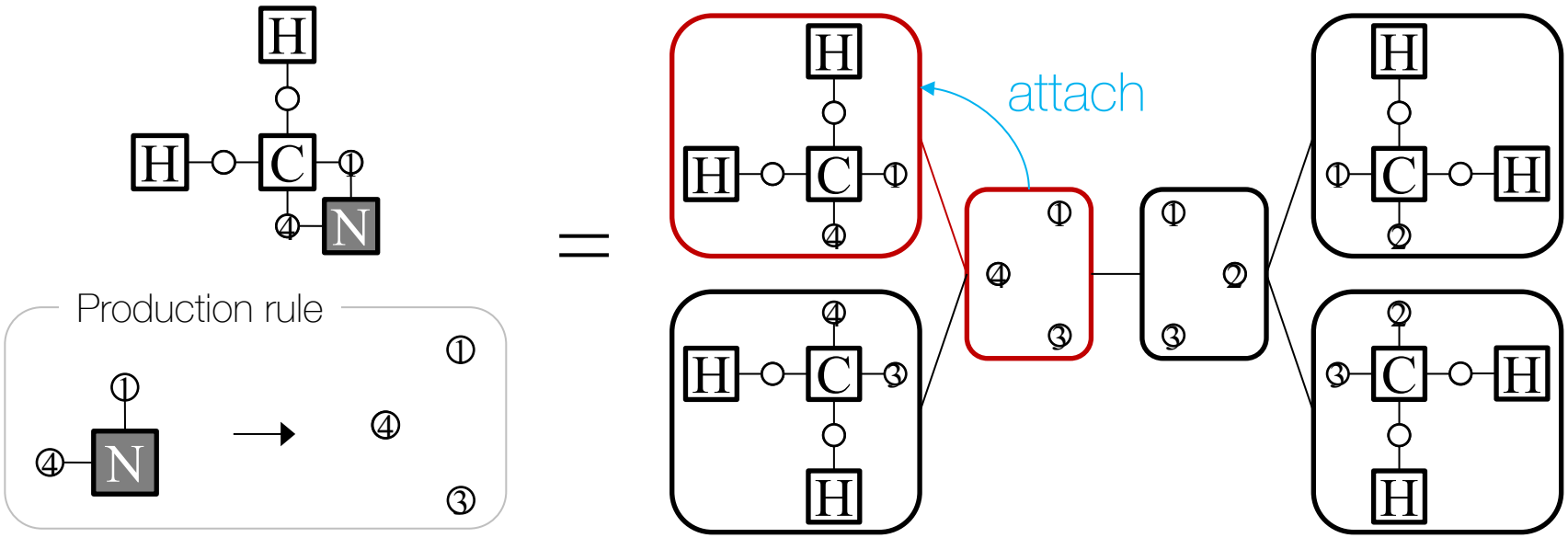

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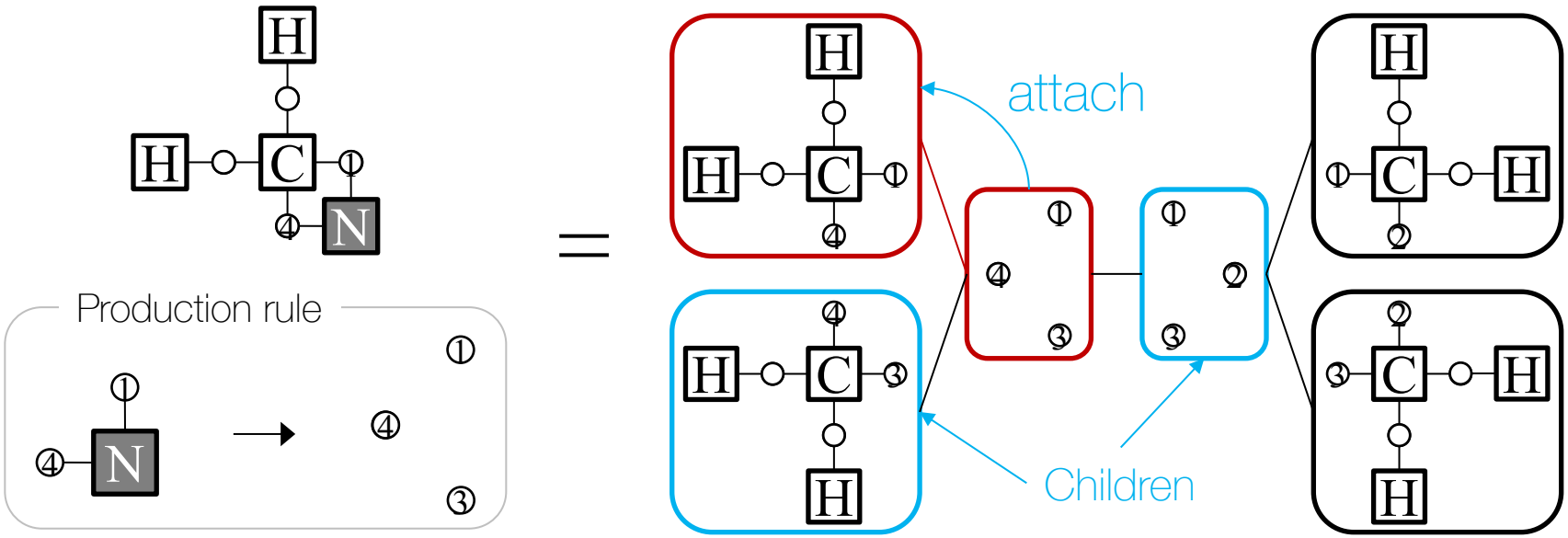

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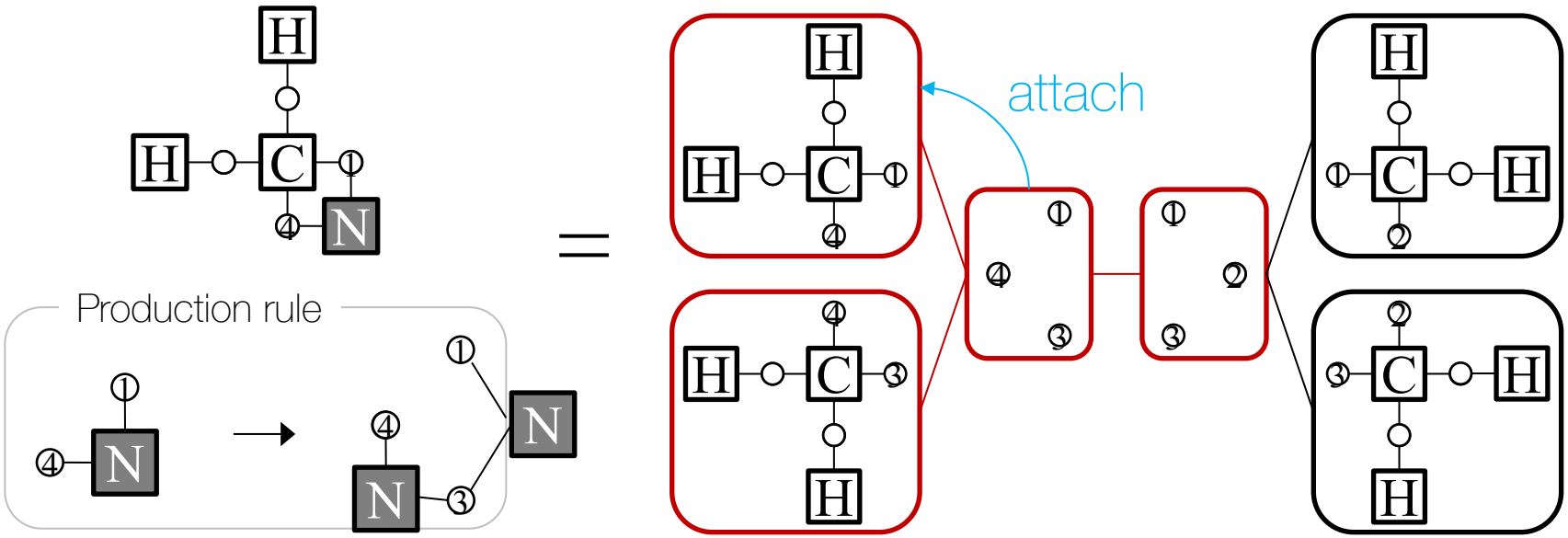

HRG can be inferred from tree decompositions of input hypergraphs.

- HRG inference algorithm [Aguiñaga+, 16]
  - –Algorithm:

1. Compute tree decompositions of input hypergraphs
2. Extract production rules
3. Compose HRG by taking their union

  - –Expressiveness: $\mathcal{H} \subseteq \mathcal{L}(\mathrm{HRG})$

    The resultant HRG can generate all input hypergraphs.

    (∵ clear from its algorithm)

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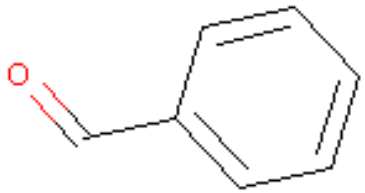
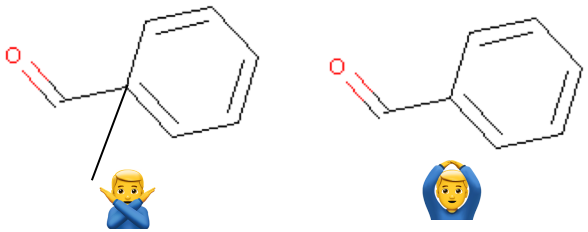


We want a graph grammar that guarantees hard constraints

- Objective

  Construct a graph grammar that *never* violates the valence condition



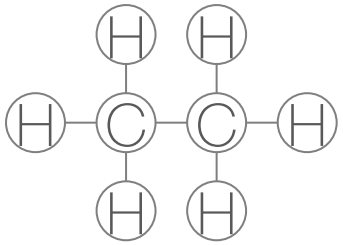
- **Application:** Generative model of a molecule
  - Grammar-based generation guarantees the valence condition
  - Probabilistic model could learn soft constraints

A simple application to molecular graphs doesn't work

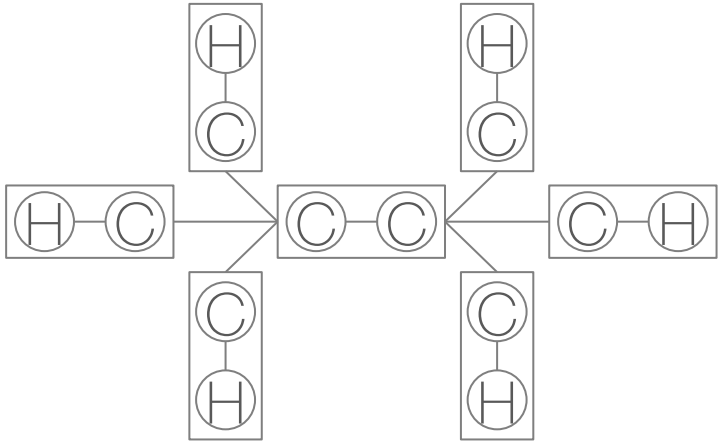
- A simple application to molecular graphs
  - **Input:** Molecular graphs
  - **Issue:** Valence conditions can be violated

This rule increases the degree of carbon

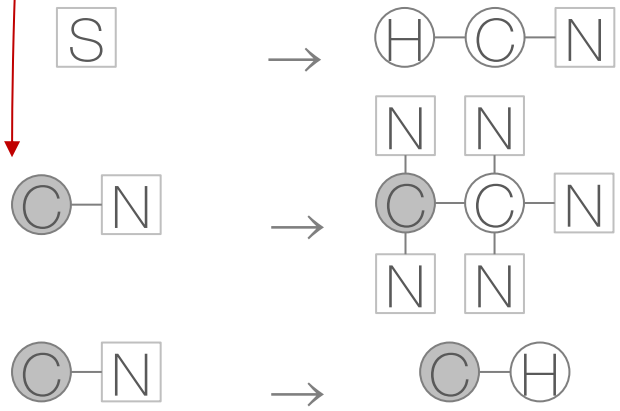
Input



Tree decomposition

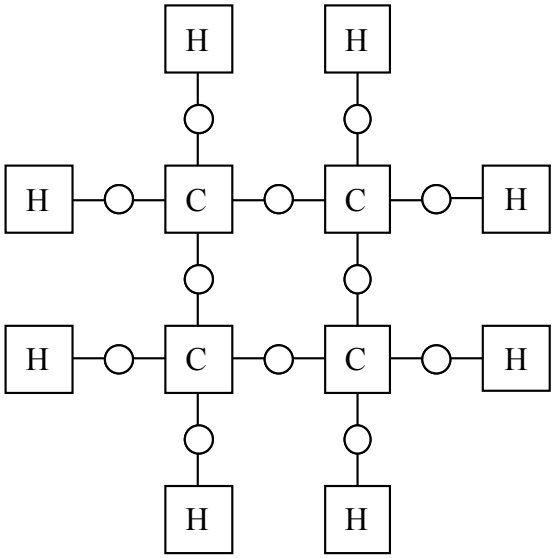


Extracted rules



Our idea is to use a hypergraph representation of a molecule

- Conserved quantity
  - –HRG: # of nodes in a hyperedge
  - –Our grammar: # of bonds connected to each atom (valence)
  - ∴ Atom should be modeled as a hyperedge
- Molecular hypergraph
  - – Atom = hyperedge
  - – Bond = node

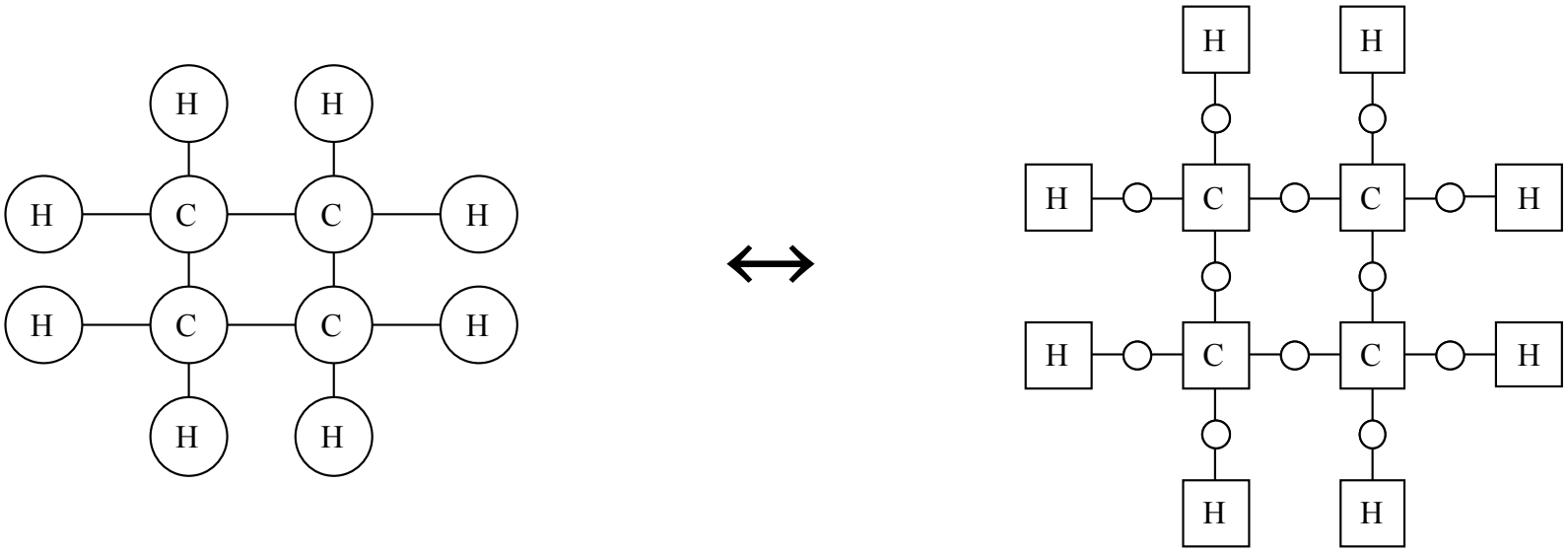


A language for molecular hypergraphs consists of two properties

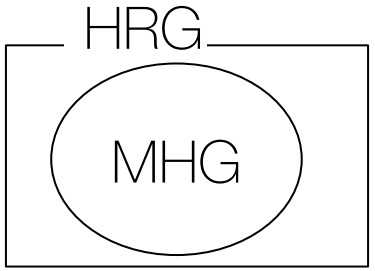
- Molecular hypergraph as a language

  A set of hypergraphs with the following properties:

  1. Each node has degree 2 (=2-regular)
  2. Label on a hyperedge determines # of nodes it has (= valence)

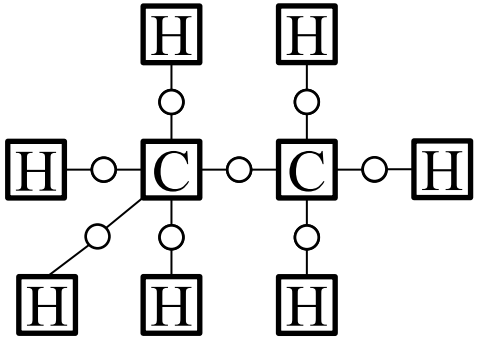


MHG, a grammar for the language, is defined as a subclass of HRG



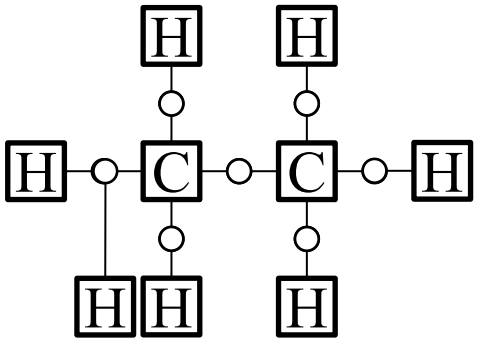
- Molecular Hypergraph Grammar (MHG)
  - **Definition:** HRG that generates molecular hypergraphs only
  - **Counterexamples:**

Valence 😡



This can be avoided by learning HRG from data [Aguiñaga+, 16]

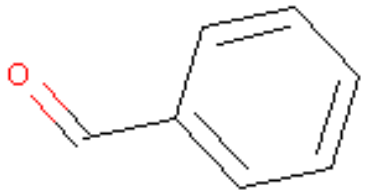
2-regularity 😡



Use an irredundant tree decomposition (our contribution)

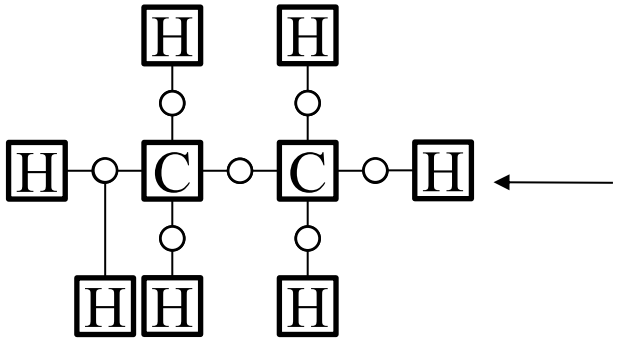
I will talk about an application of formal language to a graph generation problem

- Formal language
  - ~~Context-free grammar~~
  - ~~Hyperedge replacement grammar (HRG)~~
  - ~~HRG inference algorithm~~
- Application to molecular graph generation
  - ~~Molecular hypergraph grammar (a special case of HRG)~~
  - MHG inference algorithm
  - Combination with VAE



A naive application of the existing algorithm doesn't work

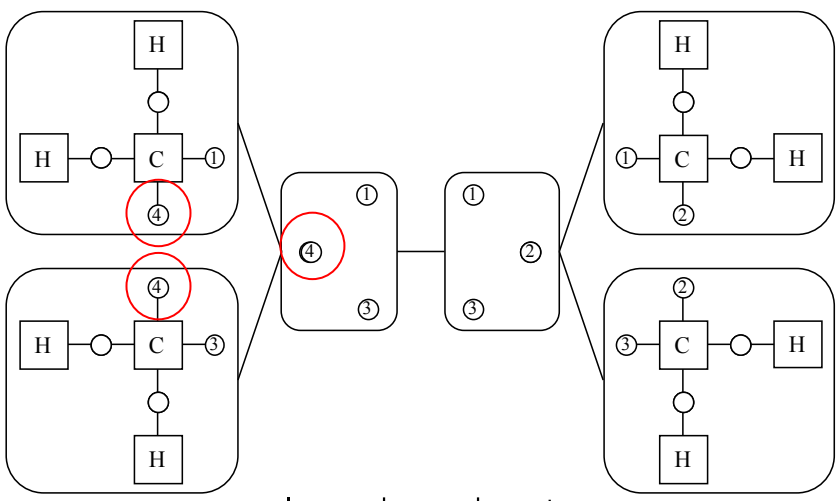
- Naive application of the HRG inference algorithm [Aguiñaga+, 16]
  - **Input:** Set of hypergraphs
  - **Output:** HRG w/ the following properties:
    - All the input hypergraphs are in the language 😀
    - Guarantee the valence conditions 😀
    - No guarantee on 2-regularity 😭



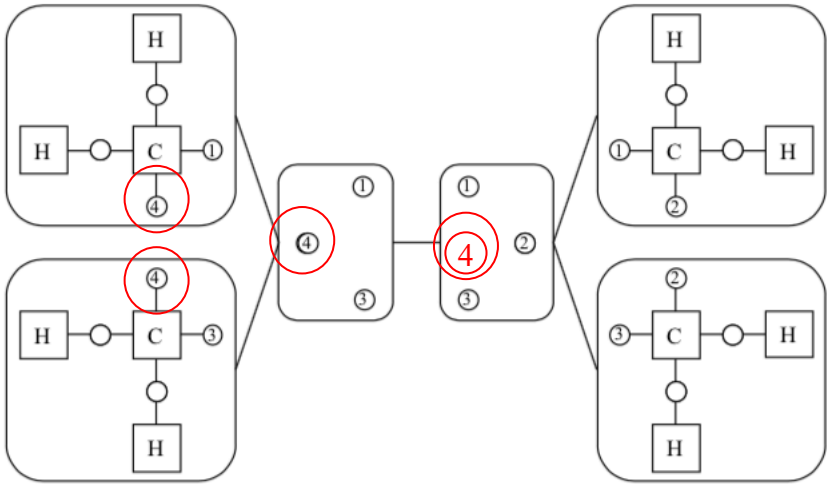
This cannot be transformed into a molecular graph

Irredundant tree decomposition is a key to guarantee 2-regularity

- Irredundant tree decomposition
  - The connected subgraph induced by a node must be a path
  - Any tree decomposition can be made irredundant in poly-time



Irredundant



Redundant

MHG inference algorithm is different from the existing one by two steps

- MHG Inference algorithm [Kajino, 19]
  - **Input:** Set of molecular graphs
  - **Output:** MHG w/ the following properties:
    - All the input hypergraphs are in the language 😀
    - Guarantee the valence conditions 😀
    - Guarantee 2-regularity 🥳

Thanks to HRG

Our contribution

1. Convert molecular graphs into molecular hypergraphs
2. Compute tree decompositions of molecular hypergraphs
3. Convert each tree decomposition to be irredundant
4. Extract production rules
5. Compose MHG by taking their union

I will talk about an application of formal language to a graph generation problem

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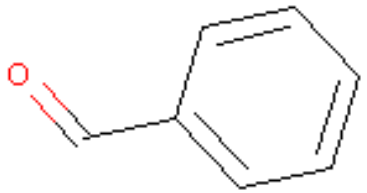
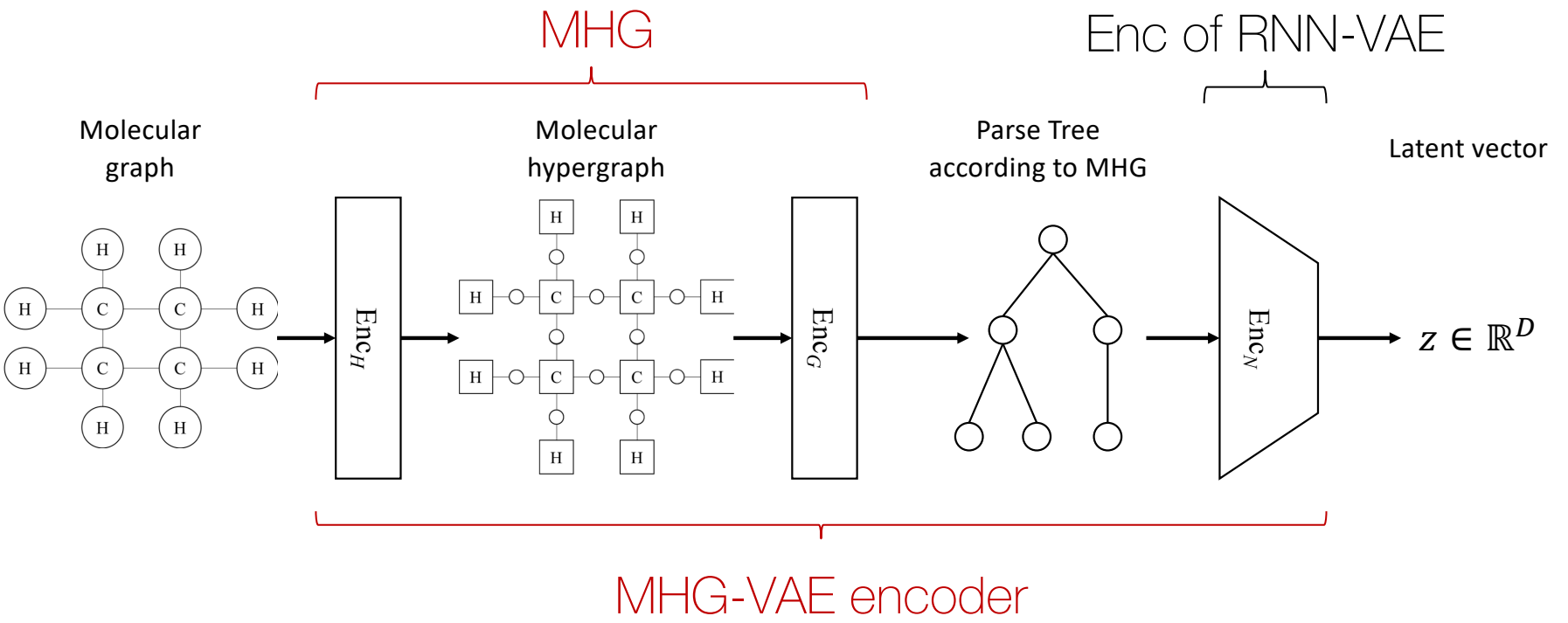


We obtain (Enc, Dec) between molecule and latent vector by combining MHG and RNN-VAE

- MHG-VAE: (Enc, Dec) between molecule & latent vector



First, we learn (Enc, Dec) between a molecule and its vector representation using MHG-VAE

- Global molecular optimization [Gómez-Bombarelli+, 16]
  - **Find:** Molecule that maximizes the target
  - **Method:** VAE+BO
    1. Obtain MHG from the input molecules
    2. Train RNN-VAE on syntax trees
    3. Obtain vector representations $\{\boldsymbol{z_n} \in \mathbb{R}^D\}_{n=1}^N$

       Some of which have target values $\{y_n \in \mathbb{R}\}$
    4. BO gives us candidates $\{\boldsymbol{z}_m \in \mathbb{R}^D\}_{m=1}^M$ that may maxim
    5. Decode them to obtain molecules $\{G_m\}_{m=1}^M$

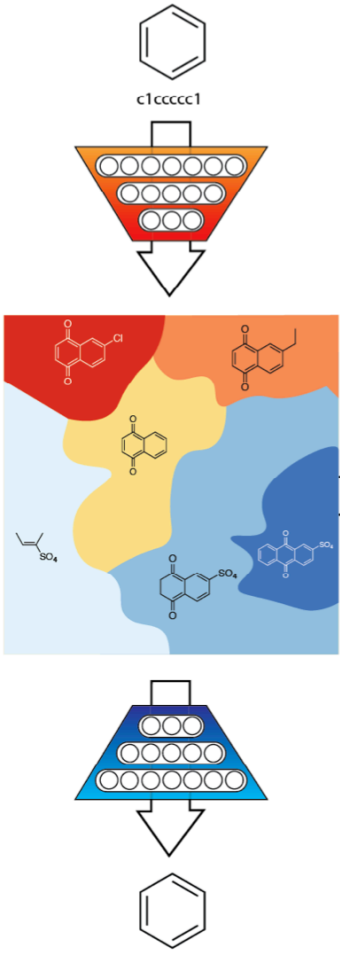


 Image from [Gómez-Bombarelli+, 16]

Given vector representations and their target values, we use BO to obtain a vector that optimizes the target

- Global molecular optimization [Gómez-Bombare[illegible]]
  - –Find: Molecule that maximizes the target
  - –Method: VAE+BO
    1. Obtain MHG from the input molecules
    2. Train RNN-VAE on syntax trees
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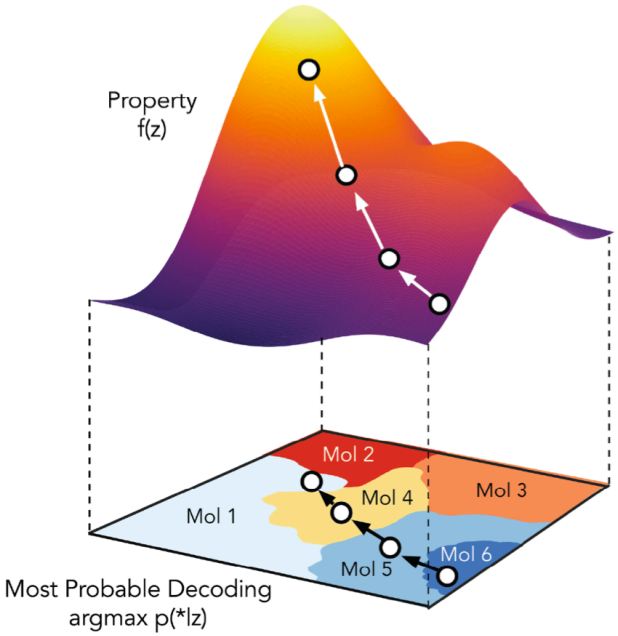

 Image from [Gómez-Bombarelli+, 16]

We evaluate the benefit of our grammar-based representation, compared with existing ones

- Empirical study
  - –**Purpose:** How much does our representation facilitate VAE training?
  - –**Baselines:**
    - {C,G,SD}VAE use SMILES (text repr.)
    - JT-VAE assembles molecular components

      It requires NNs other than VAE for scoring
  - –**Tasks:**
    - VAE reconstruction
    - Valid prior ratio
    - Global molecular optimization

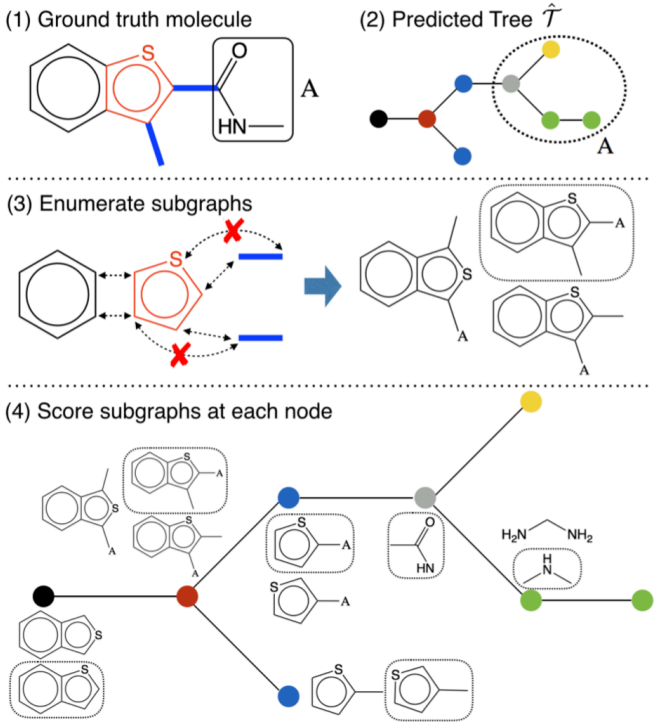

Image from [Jin+, 18]

Our grammar-based representation achieves better scores.
This result empirically supports the effectiveness of our approach.

- Result

Method	% Reconst.	Valid prior	Maximizing $f(m)$ 1st	2nd	3rd	50th	Top 50 Avg.
CVAE	44.6%	0.7%	1.98	1.42	1.19	–	–
GVAE	53.7%	7.2%	2.94	2.89	2.80	–	–
SD-VAE	76.2%	43.5%	4.04	3.50	2.96	–	–
JT-VAE	76.7%	100%	5.30	4.93	4.49	3.48	3.93
GCPN	–	–	7.98	7.85	7.80	–	–
Ours	94.8%	100%	5.56	5.40	5.34	4.12	4.49

$$f(m) = \widehat{\mathrm{logP}}(m) - \widehat{\mathrm{SA}}(m) - \widehat{\mathrm{cycle}}(m)$$

Penalty to a ring larger than six

Synthetic accessibility score

Water solubility

A graph grammar can be a building block for a graph generative model

- Classify constraints into hard ones and soft ones

  ML for the soft ones, rules for the hard ones

- Define a language by encoding hard constraints

  E.g., valence conditions

- Design a grammar for the language

  Sometime, w/ an inference algorithm

Code is now public on Github

https://github.com/ibm-research-tokyo/graph_grammar

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