May 9, 2025

Advancements in Biotransformation Pathway Prediction

Enhancements, Datasets, and Novel Functionalities in enviPath

Jörg Simon Wicker

enviPath / School of Computer Science – University of Auckland

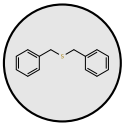
enviPath

UNIVERSITY OF AUCKLAND
Waipapa Taumata Rau
NEW ZEALAND

SCIENCE

Biodegradation Pathway Prediction

Biodegradation Pathways



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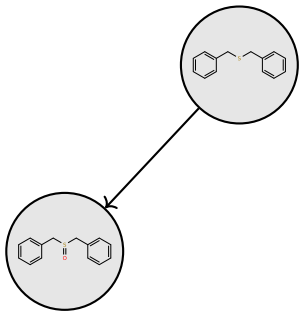

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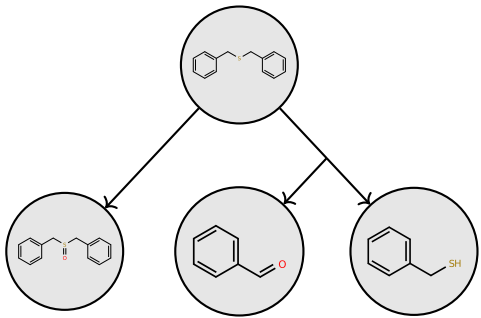

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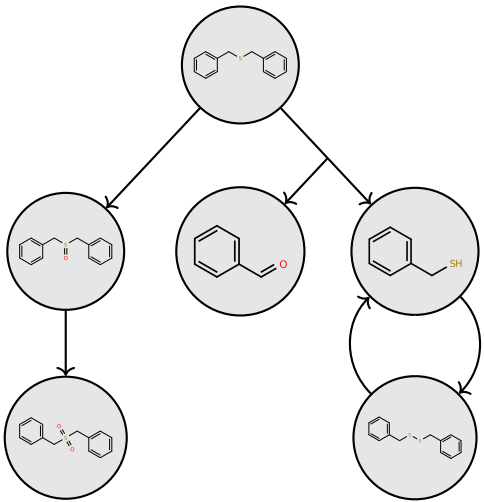

Rule-Based Biodegradation Pathway Prediction

- Rule-based systems predict degradation products using transformation rules
  - Generalizations and abstractions of observed reactions
  - If rule matches certain functional groups on left-hand side, transformation of structure according to right-hand side

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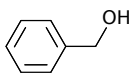
Benzyl Alcohol



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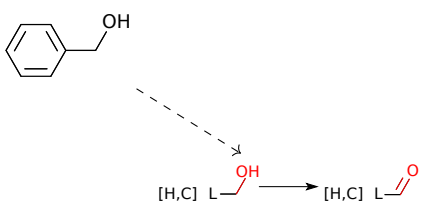

Primary Alcohol → Aldehyde

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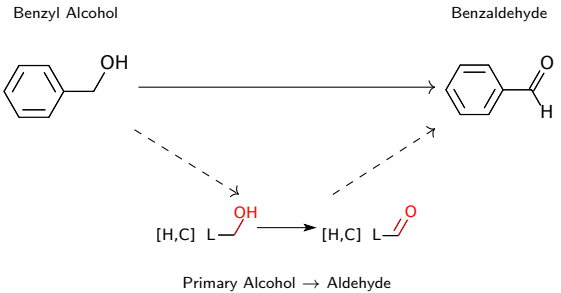

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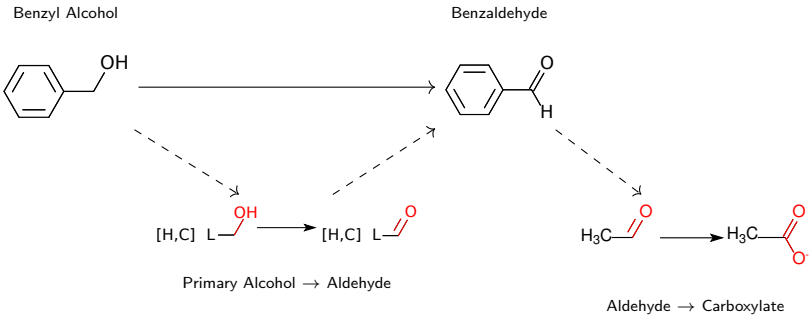

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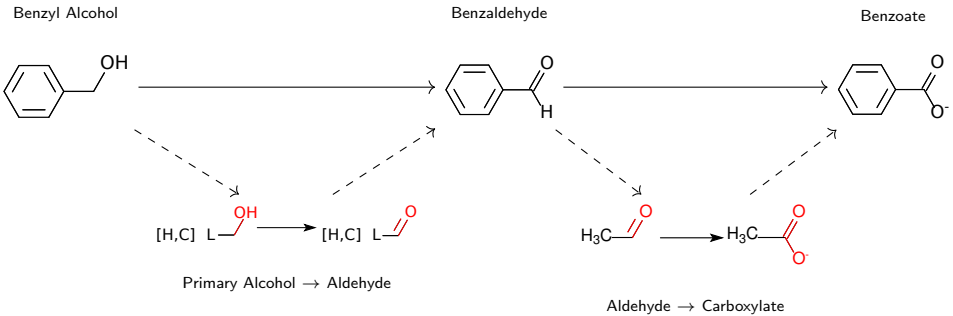
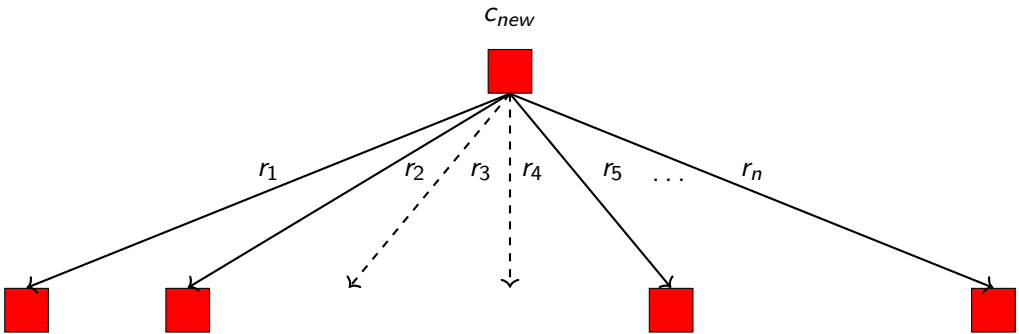


Machine Learning to Limit Combinatorial Explosion



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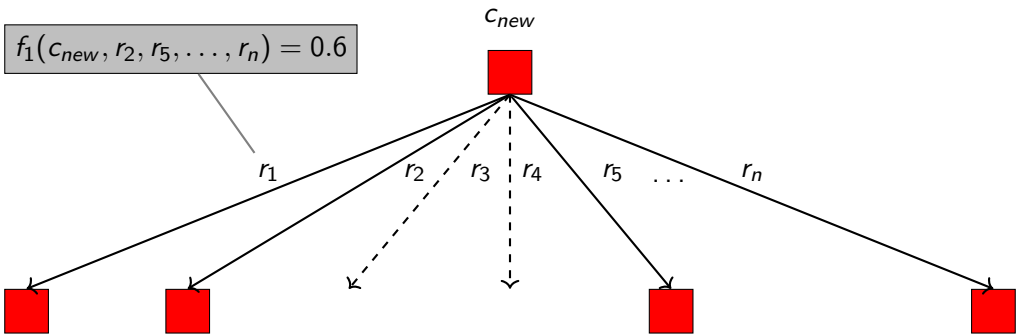

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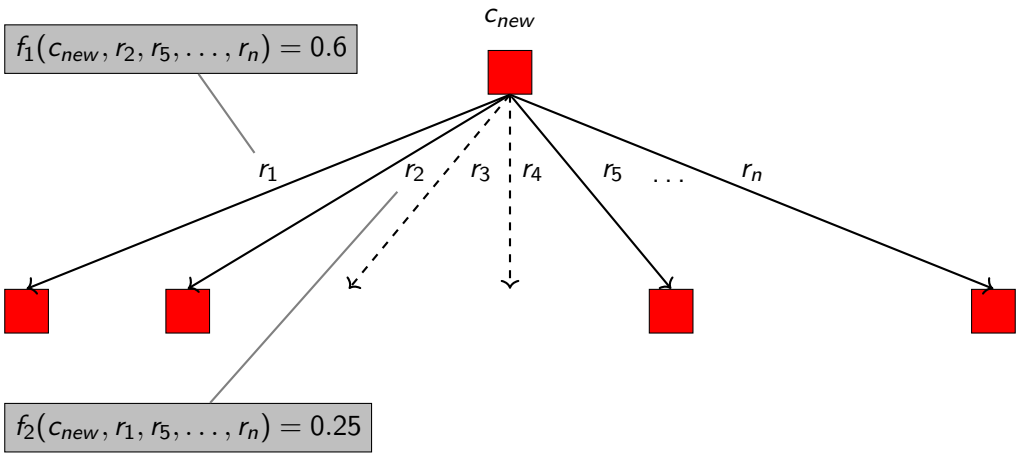

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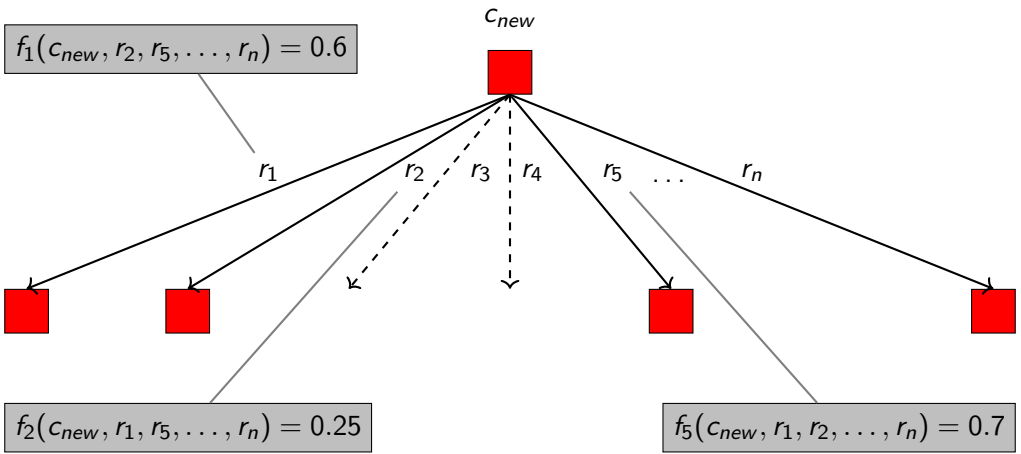

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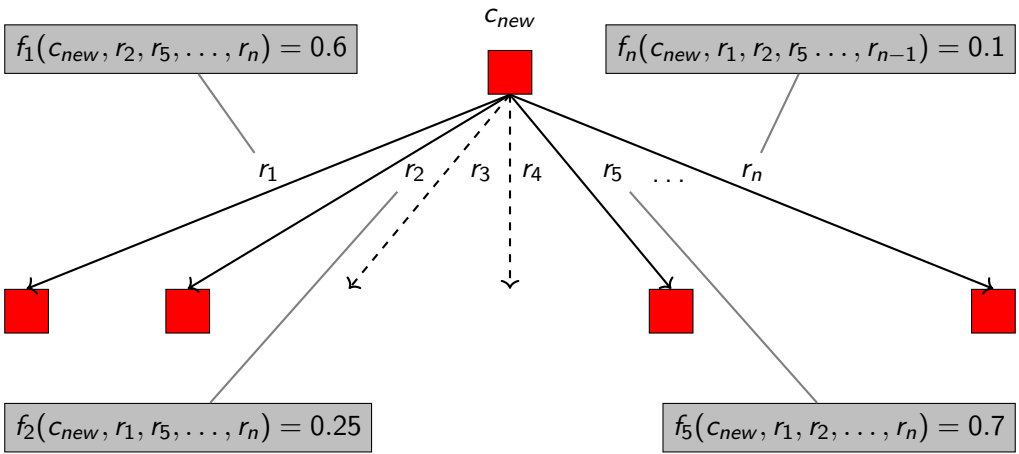
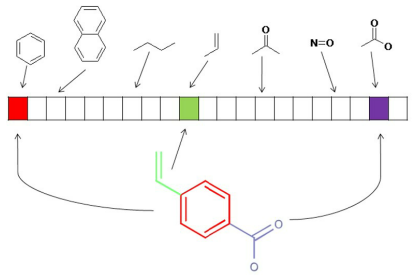


Structural Features – Fingerprints

- Machine Learning algorithms work with tabular data



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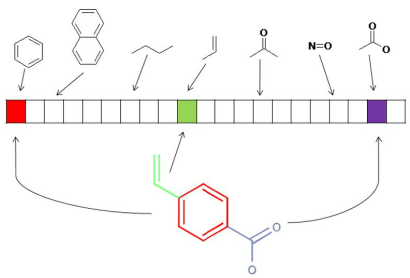

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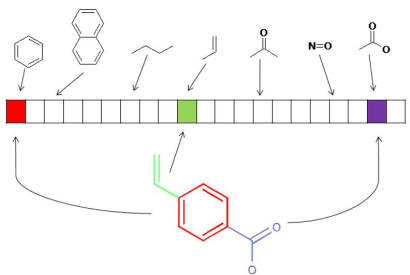

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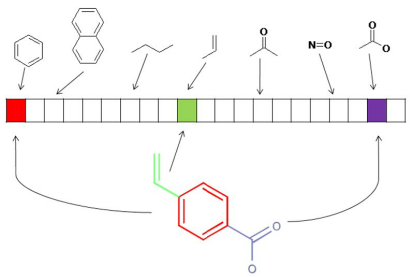

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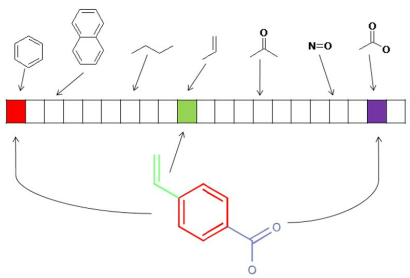

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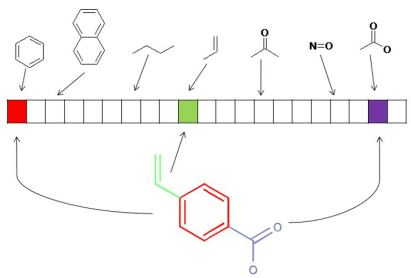

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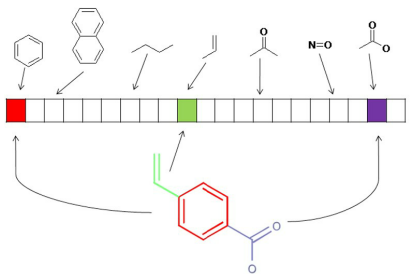
- Lately a lot of approaches to generate embeddings using deep learning
  - Stepišnik *et al.*, *A comprehensive comparison of molecular feature representations for use in predictive modeling*, (2021) gives an overview
- Simple approaches (e.g. pre-defined substructures) perform similarly well to more complicated approaches



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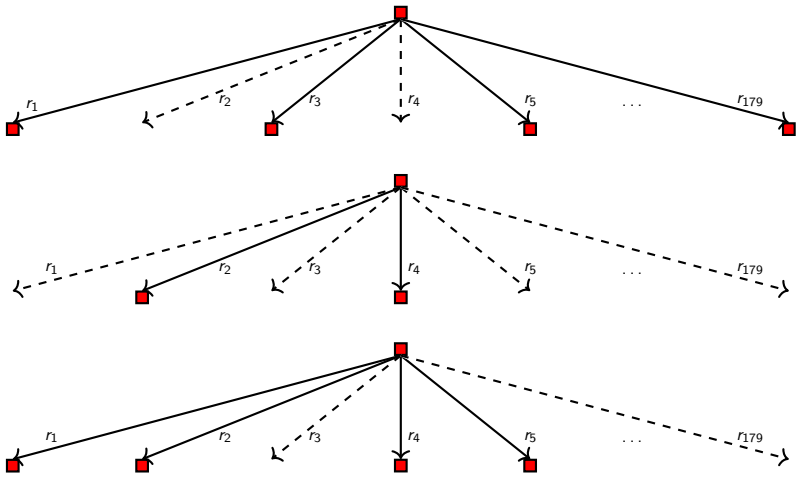

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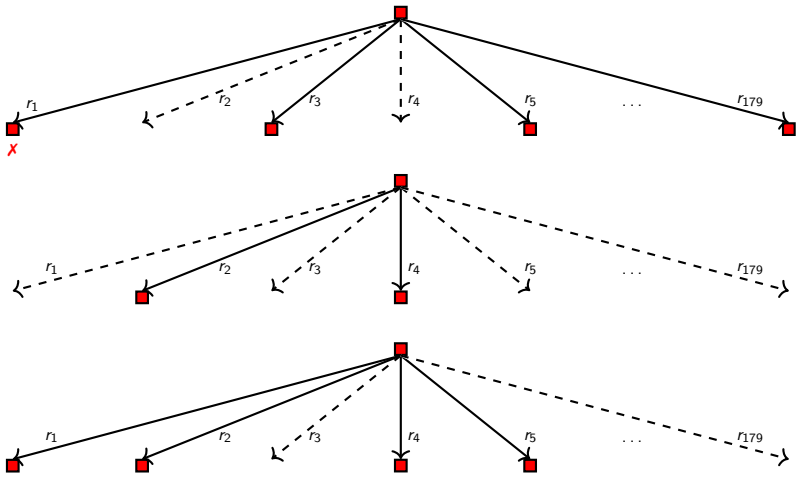

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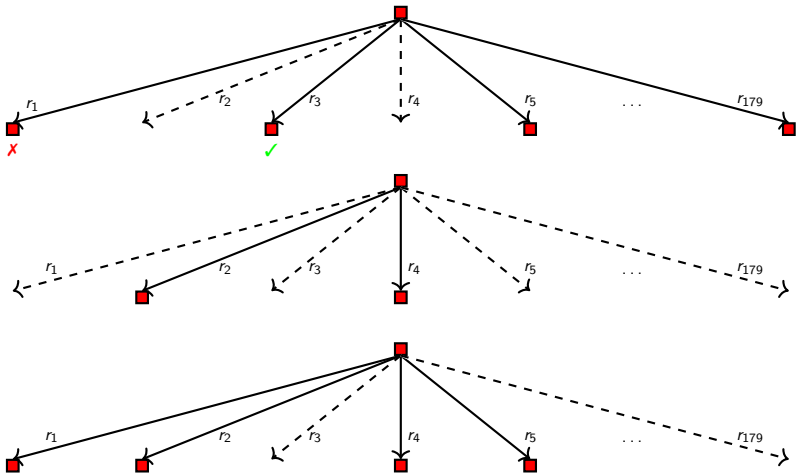

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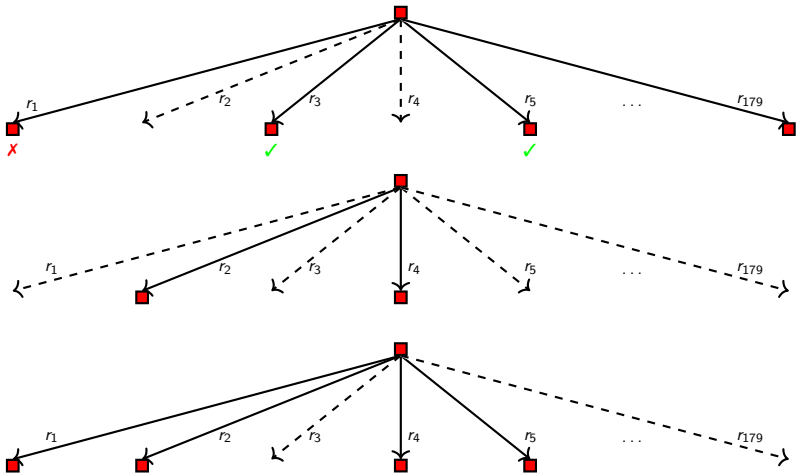

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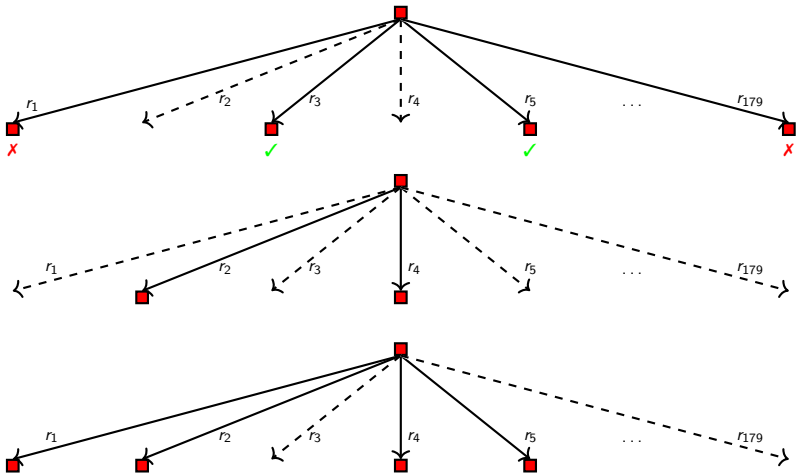

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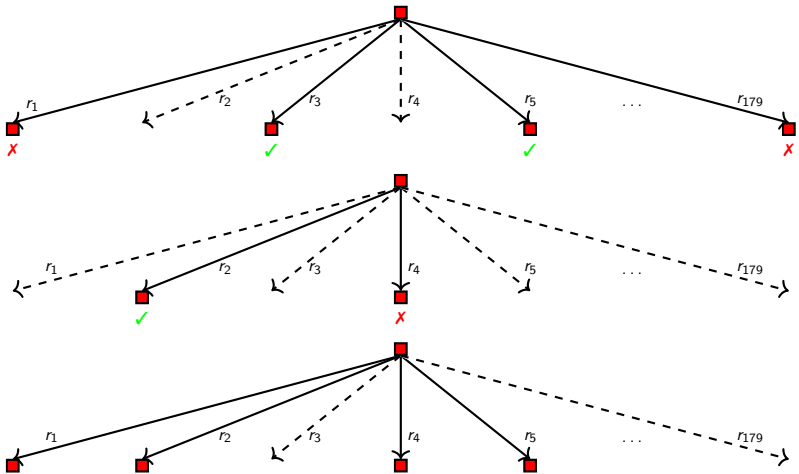

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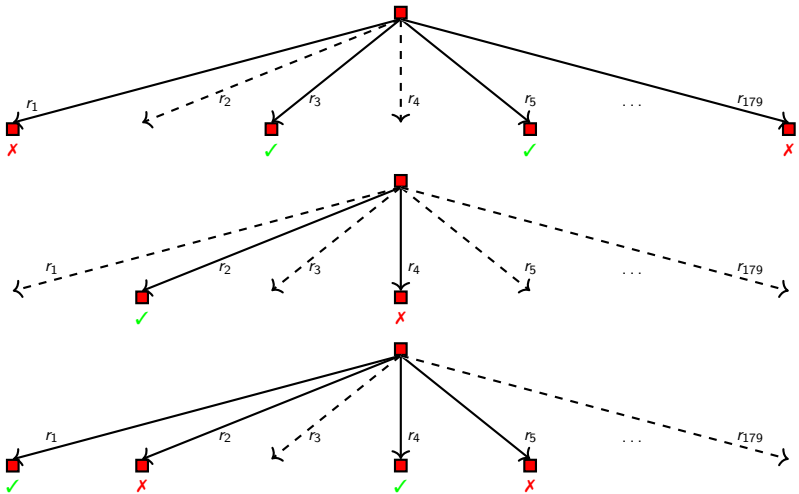
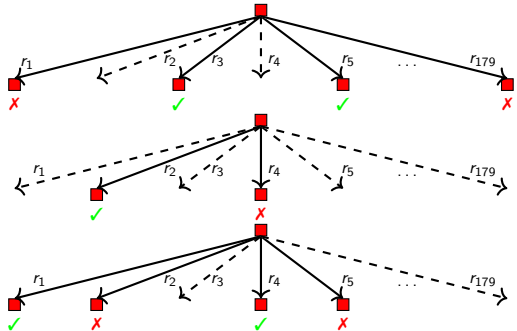


Generation of Training Sets



	s_1	...	s_{547}	r_2	r_3	r_4	r_5	...	r_{179}	$y = r_1$
c_1	+1	...	0	0	+1	0	+1	...	+1	0
c_3	+1	...	+1	+1	0	+1	+1	...	0	+1
...	...	...	...	...	...	...	...	...	...	...
c_{718}	0	...	0	+1	0	0	+1	...	0	0

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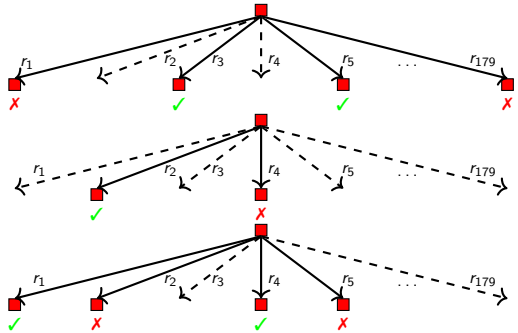


	s_1	...	s_{547}	r_1	r_3	r_4	r_5	...	r_{179}	$y = r_2$
c_2	0	...	+1	0	0	+1	0	...	0	+1
c_3	+1	...	+1	+1	0	+1	+1	...	0	0
...	...	...	...	...	...	...	...	...	...	...
c_{718}	0	...	0	+1	0	0	+1	...	0	+1

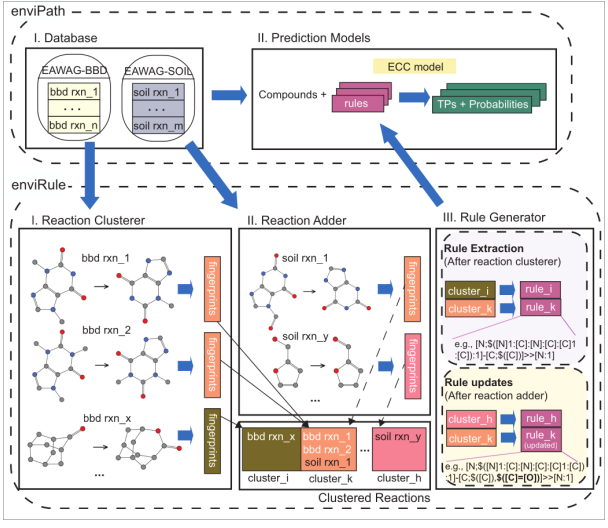
Biodegradation – Multi-Label Perspective

- Learning task is a multi-label problem
- Transformation to multi-label data set using pseudo-label

	correctly triggered	incorrectly triggered	not triggered
label 1 (λ_i) / correctly triggered	1	0	?
label 2 (λ'_i) / known product	1	0	0
feature (r_i) / triggered	1	1	0

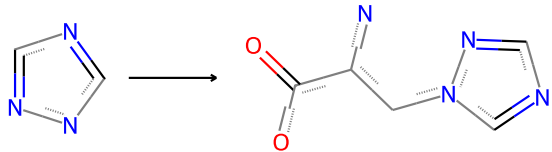
	s_1	...	s_{547}	r_1	...	r_{179}	λ'_1	...	λ'_{179}	λ_1	...	λ_{179}
c_1	+1	...	0	1	...	0	1	...	0	1	...	?
c_2	+1	...	+1	1	...	0	0	...	0	0	...	?
c_3	0	...	+1	1	...	1	0	...	1	0	...	1
...	...	...	...	...	...	...	...	...	...	...	...	...
c_{718}	0	...	0	0	...	1	0	...	0	?	...	0

Learning new Rules from Data



enviFormer – Biodegradation Prediction as Sequence-to-Sequence Task

- Compounds and reactions can be represented as Strings (SMILES and SMIRKS)



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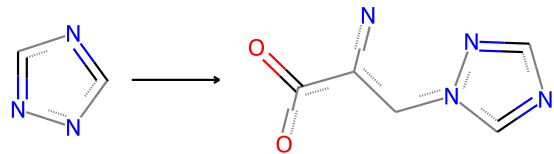
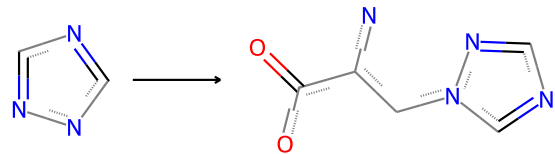


C1=NC=NN1 >> C(C(C(=O)O)N)N1C=NC=N1

enviFormer – Biodegradation Prediction as Sequence-to-Sequence Task

- Compounds and reactions can be represented as Strings (SMILES and SMIRKS)
- This makes the prediction task very similar to the learning task of LLMs such as GPT
  - Given an input sequence (question / compound), predict the most likely output sequence (answer / compound)



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2	CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)C	C
3	CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)	C

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CCC(O)CO.CCC1CO1>>CCC(O)COC	C
CCC(O)CO.CCC1CO1>>CCC(O)CO	C
CCC(O)CO.CCC1CO1>>CCC(O)C	O
CCC(O)CO.CCC1CO1>>CCC(O)	C
CCC(O)CO.CCC1CO1>>CCC(O)	

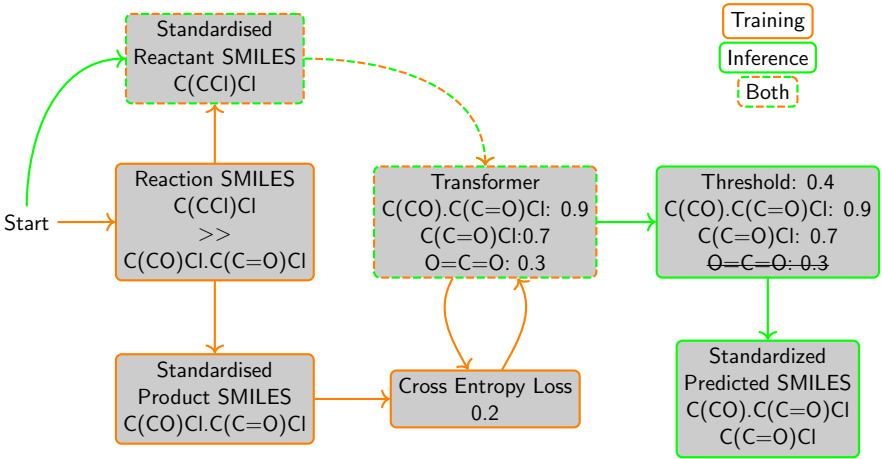
enviFormer – Training Set

features	class
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)CC	
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)C	C
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)	C
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)	
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O	
CCC(O)CO.CCC1CO1>>CCC(O)COCC (	
CCC(O)CO.CCC1CO1>>CCC(O)COC	C
CCC(O)CO.CCC1CO1>>CCC(O)CO	C
CCC(O)CO.CCC1CO1>>CCC(O)C	O
CCC(O)CO.CCC1CO1>>CCC(O)	C
CCC(O)CO.CCC1CO1>>CCC(O)	
CCC(O)CO.CCC1CO1>>CCC(O	

enviFormer – Training Set

features	class
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)CC	
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)C	C
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)	C
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O)	
CCC(O)CO.CCC1CO1>>CCC(O)COCC(O	
CCC(O)CO.CCC1CO1>>CCC(O)COCC (	
CCC(O)CO.CCC1CO1>>CCC(O)COC	C
CCC(O)CO.CCC1CO1>>CCC(O)CO	C
CCC(O)CO.CCC1CO1>>CCC(O)C	O
CCC(O)CO.CCC1CO1>>CCC(O)	C
CCC(O)CO.CCC1CO1>>CCC(O)	
CCC(O)CO.CCC1CO1>>CCC(O	
...	

enviFormer – Method



enviFormer

- Overcome small dataset size with pre-training on generic reaction data set
- Advantage: Remove the need of manual rule creation, just need a data set with reactions
- Disadvantage: Loss of interpretability

enviPath

- enviPath is an active research project run by University of Auckland, Eawag, and University of Zürich

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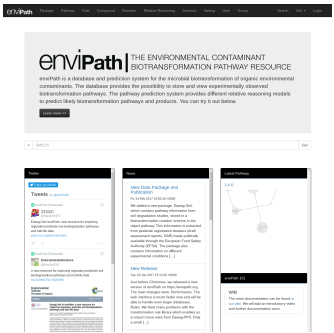
- *Reach out to us if you are interested!*

Outlook

- Current work
  - Implementing enviFormer into enviPath
  - Adding more data
  - Adding more improvements into the prediction engine
- Complete reimplementation of the system
  - Faster, more robust, more reliable
  - Frequently changing (and breaking) beta-version at `https://playground.envipath.org`



enviPath

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NEW ZEALAND

SCIENCE

Thank you for listening! Any questions?

https://envipath.org
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