enviPath | THE ENVIRONMENTAL CONTAMINANT BIOTRANSFORMATION PATHWAY RESOURCE

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eawag aquatic research

Data elements and packages in enviPath

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Overview

1. Data organization in enviPath
2. Data packages in enviPath
3. Navigating enviPath data

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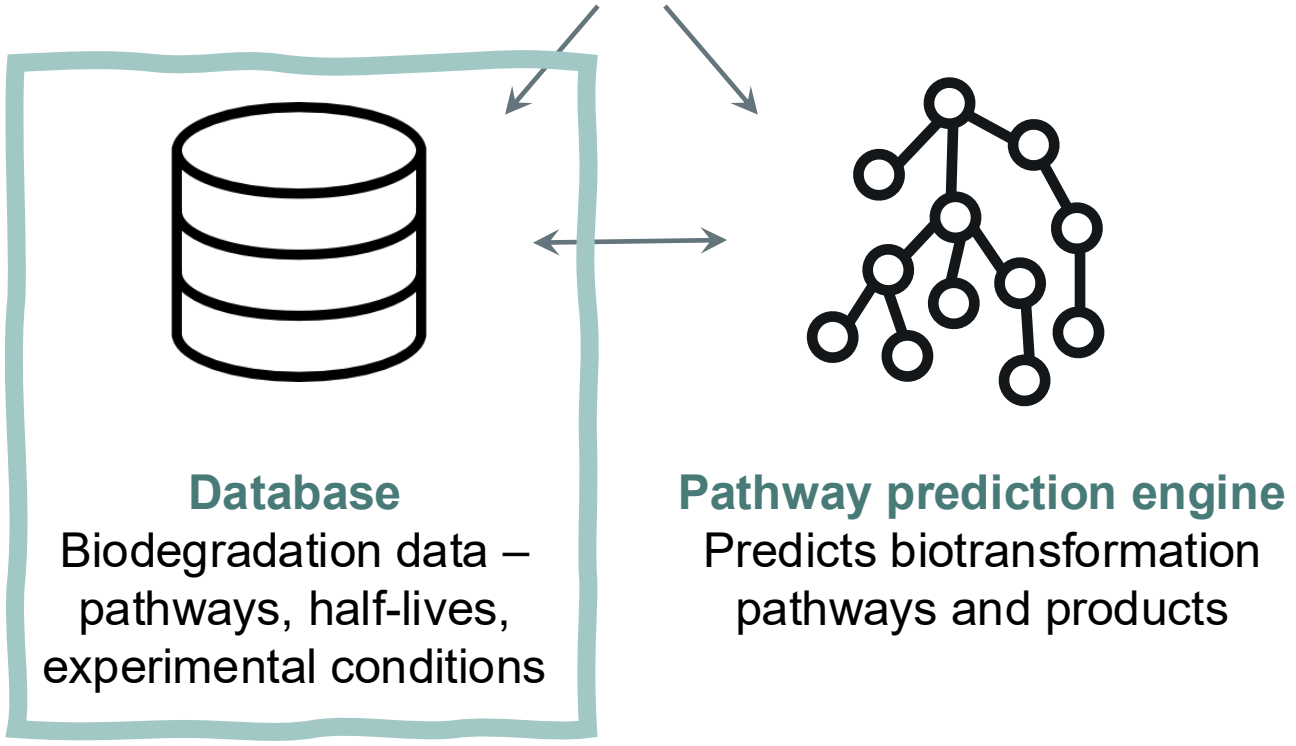
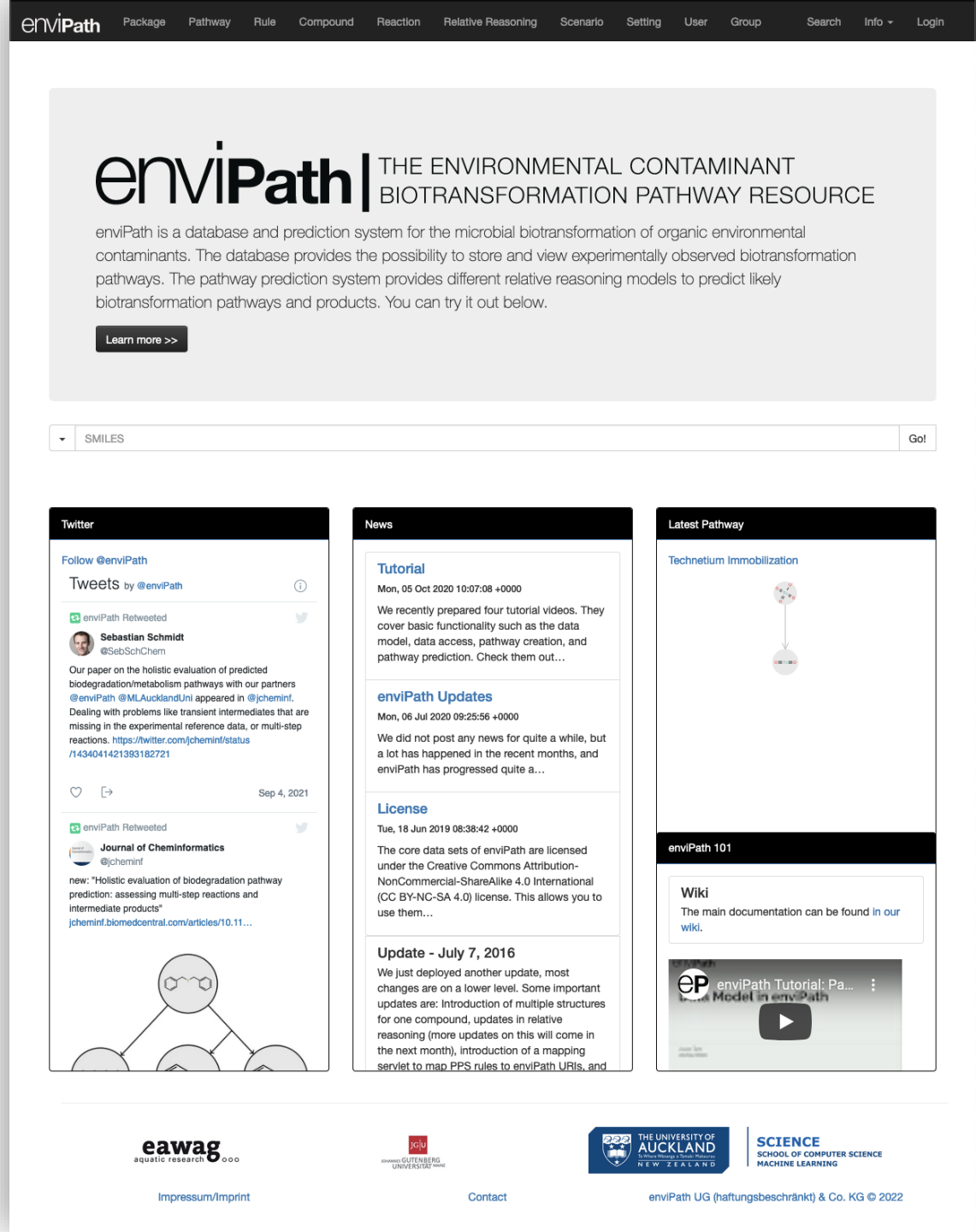
enviPath - a platform for environmental contaminant biotransformation

envipath.org



Database
Biodegradation data – pathways, half-lives, experimental conditions

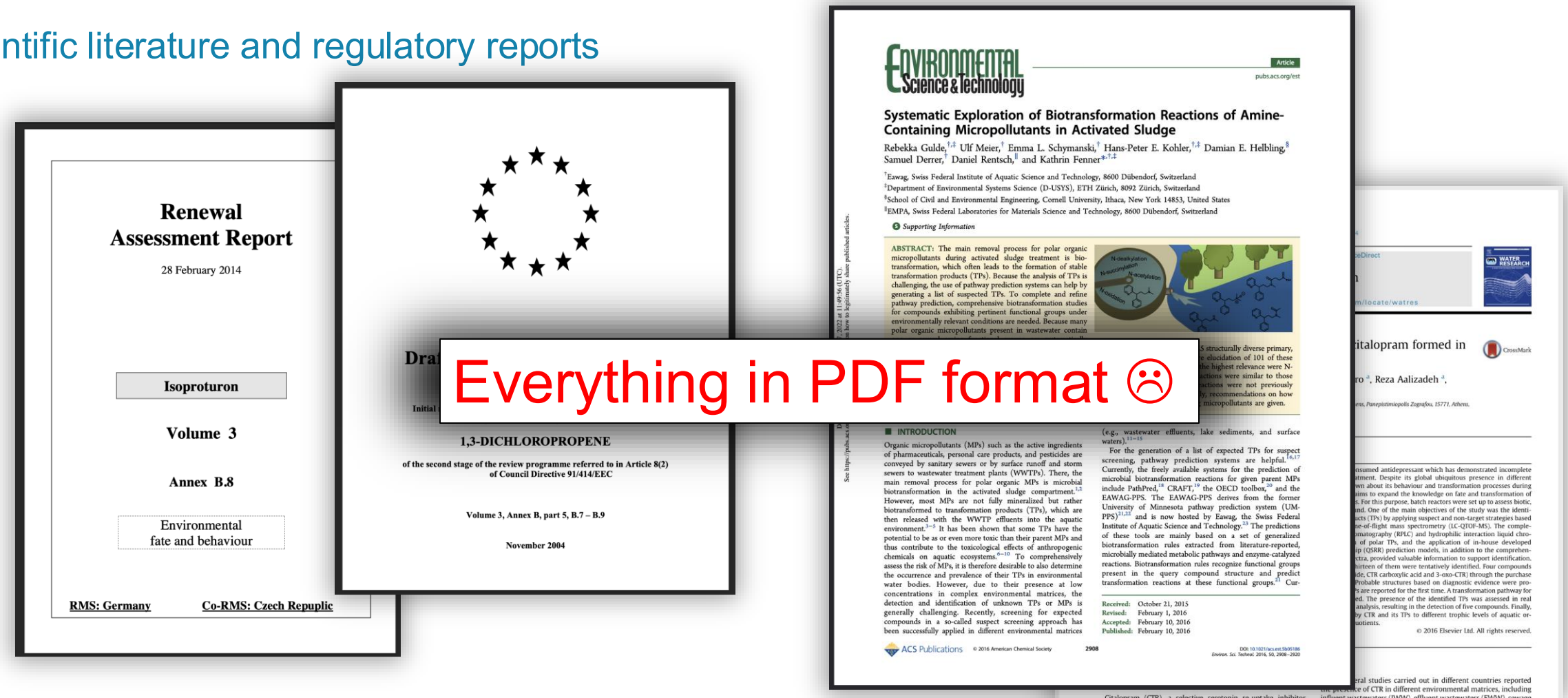
Pathway prediction engine
Predicts biotransformation pathways and products



1. Data organization in enviPath

Where does the biodegradation data come from ?

Scientific literature and regulatory reports



Everything in PDF format ☹

Systematic storage of standardized biodegradation data

Experimental standards

- OECD (or other) guidelines
- If non-standard setups: documentation of guideline modification and/or detailed account of experimental setups is crucial

Systematic organization of data

- Pre-defined set of experimental parameters (pH, temperature, OC content, …)
- Data-sets organized by environment (activated sludge, soil, water, …)

Machine-readable access

- Standard formats like CSV, JSON, …
- Database with API access (Application Programming Interface)

Schematic overview on database objects

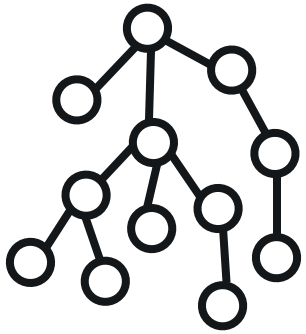
Compounds
structure

Reactions
observed or predicted

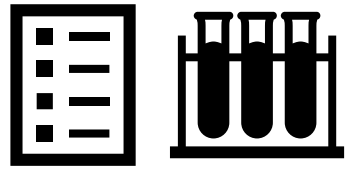
Biotransformation rules
for reaction prediction

Enzymes
EC classification

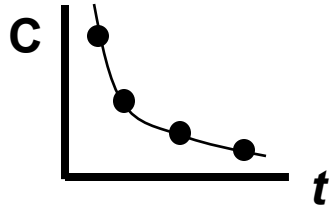
Pathways
observed or predicted



Scenarios
Experimental meta data

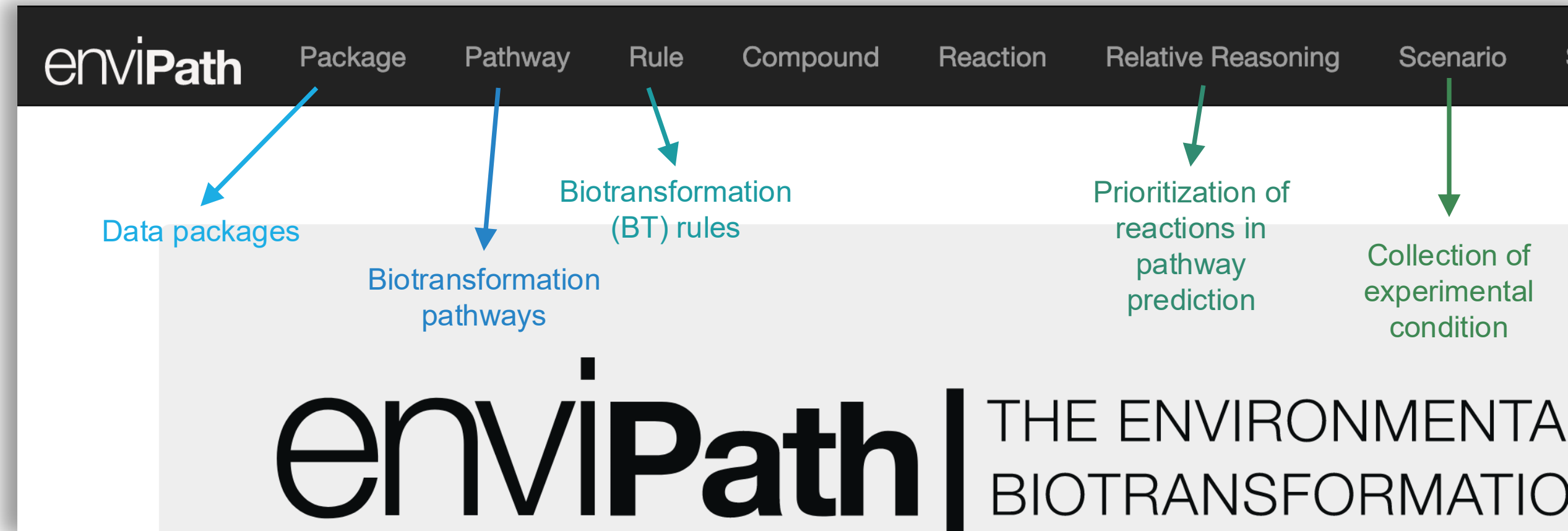


Biotransformation half-lives or rate constants
Obtained for specific scenario, primary DT_{50}



Data organization in enviPath

Overview on main objects in enviPath:

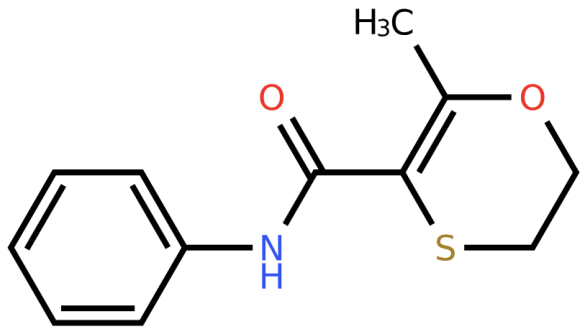


Compounds

Carboxin

Actions

Image representation



SMILES representation

CC1=C(C(=O)NC2=CC=CC=C2)SCCO1

Canonical SMILES

InChIKey

Pathways

External Identifiers

Half-lives

SMILES,
canonical SMILES (without stereochemical information),
InChIKey

Links to associated pathways, external database IDs and half-lives

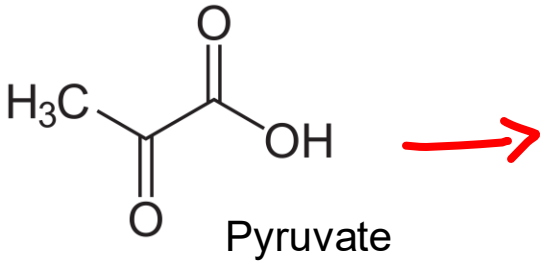
SMILES & SMIRKS

A quick introduction to cheminformatics

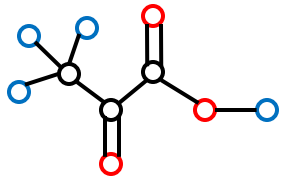
Graph representation
atoms = nodes
bonds = edges

SMILES
(String representation)

Compound SMILES

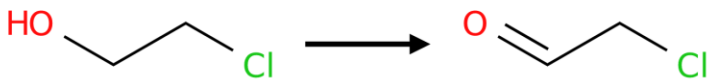


Pyruvate



CC(=O)C(=O)O

Reaction SMIRKS



SMIRKS

C(CO)Cl>>C(C=O)Cl

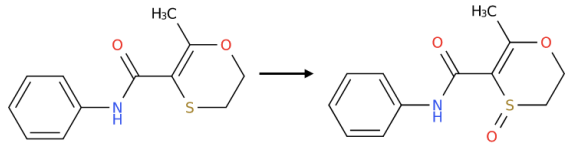
SMILES of reactant

SMILES of product

Reactions

reaction 0002303 ★

Image representation



Reaction Description

Carboxin → P/V-16 (Carboxin sulfoxide)

SMIRKS representation

CC1=C(C(=O)NC2=CC=CC=C2)SCCO1>>CC1=C(C(=O)NC2=CC=CC=C2)S(=O)CCO1

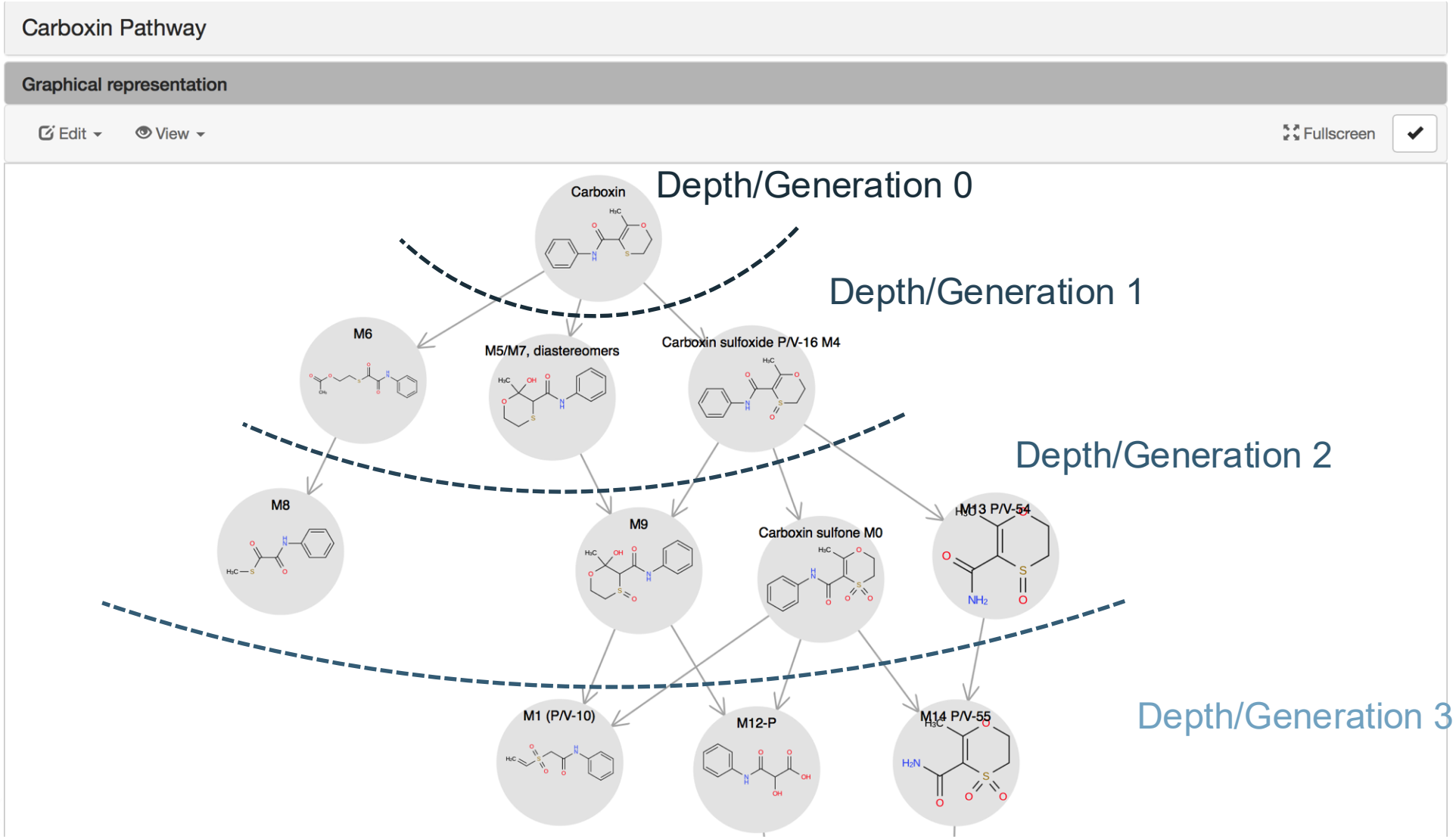
Rules

bt0162-4180

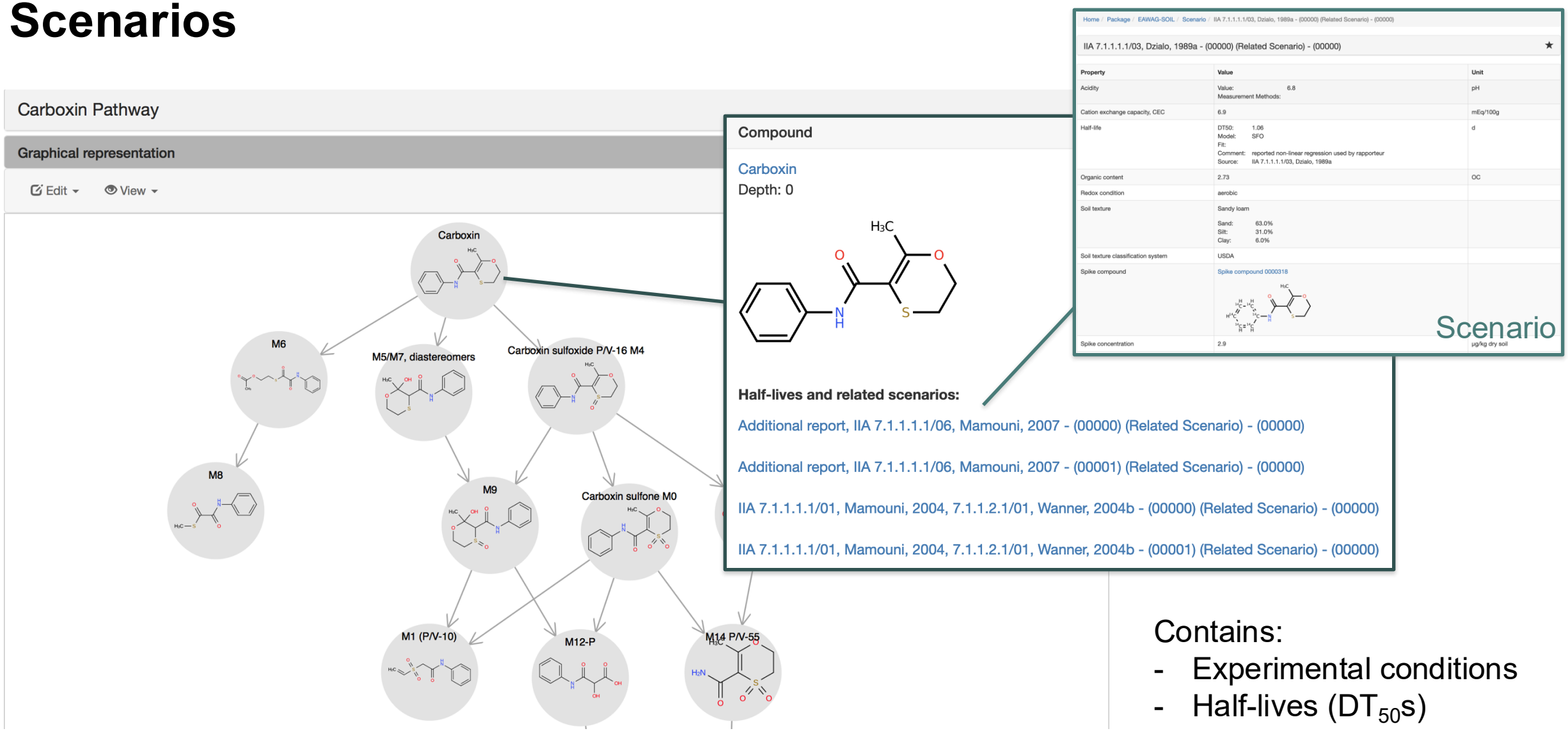
Pathways

Biotransformation rule(s) associated with this reaction

Pathways


Carboxin Pathway
Graphical representation
Edit
View
Fullscreen
Depth/Generation 0
Depth/Generation 1
Depth/Generation 2
Depth/Generation 3
Carboxin
M6
M5/M7, diastereomers
Carboxin sulfoxide P/V-16 M4
M8
M9
Carboxin sulfone M0
M13 P/V-54
M1 (P/V-10)
M12-P
M14 P/V-55

Scenarios



Contains:

- Experimental conditions
- Half-lives (DT_{50}s)

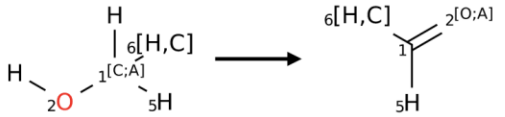
Biotransformation rules

bt0001-3568 ★

Description

primary Alcohol > Aldehyde

Representation



Reaction

SMIRKS

[H][#8:2][C:1]([H:5])([H])[#1,#6:6]>>[H:5][#6:1](-[#1,#6:6])=[O:2]

Reactants Smarts

Products Smarts

Included in Composite-Rule

Reactant Filter Smarts

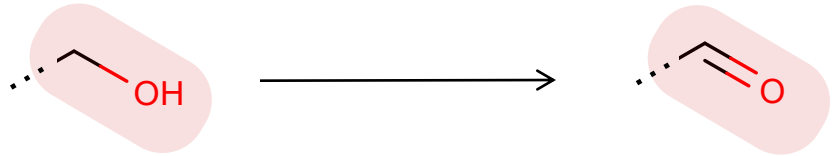
Scenarios

Reactions

Pathways

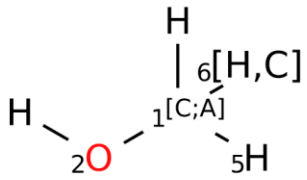
Biotransformation rules

Rule:



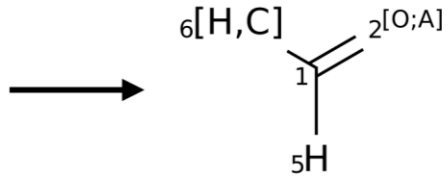
Recognition

Find -OH group on molecule



Transformation

Rearrange bonds to get =O group



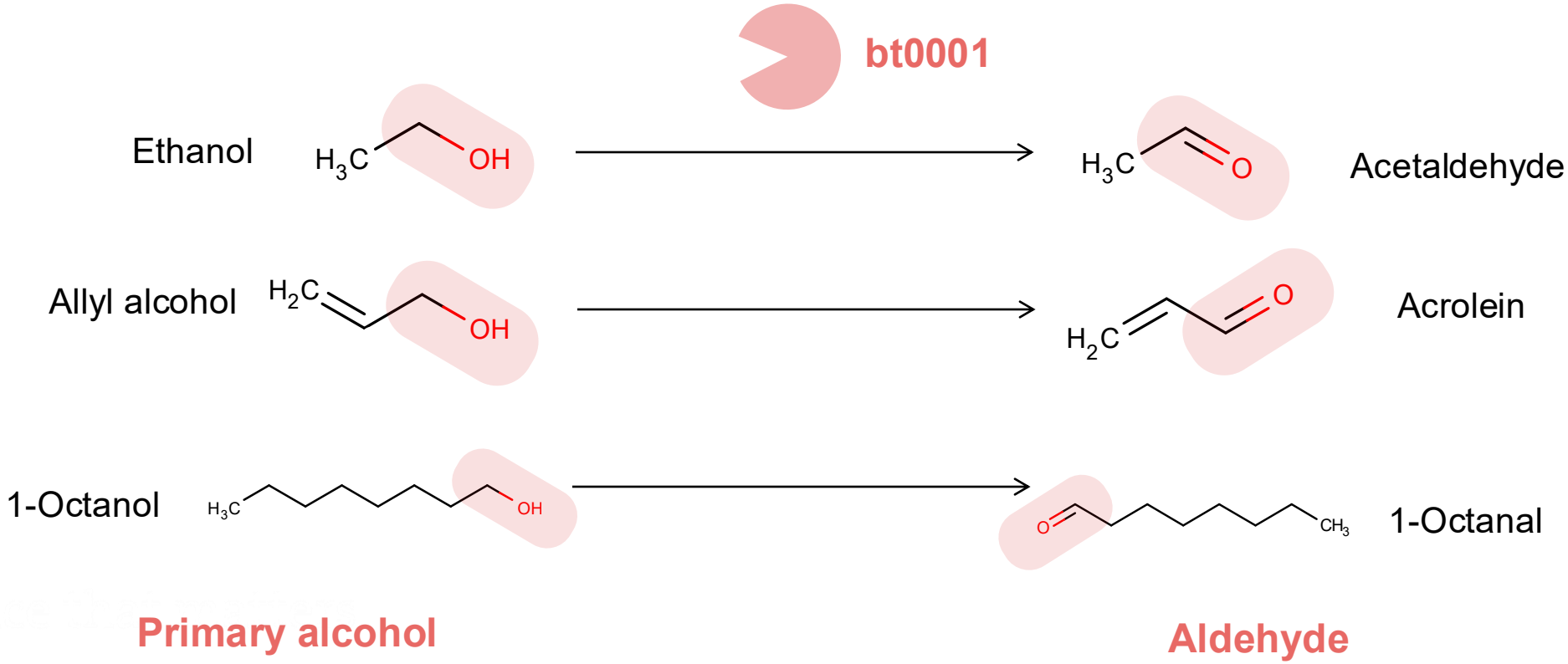
SMARTS

[H][#8:2][C:1]([H:5])([H])[#1,#6:6]

[H:5][#6:1](-[#1,#6:6])=[O:2]

Biotransformation rules

Example: Substrate-promiscuous action of an alcohol dehydrogenase

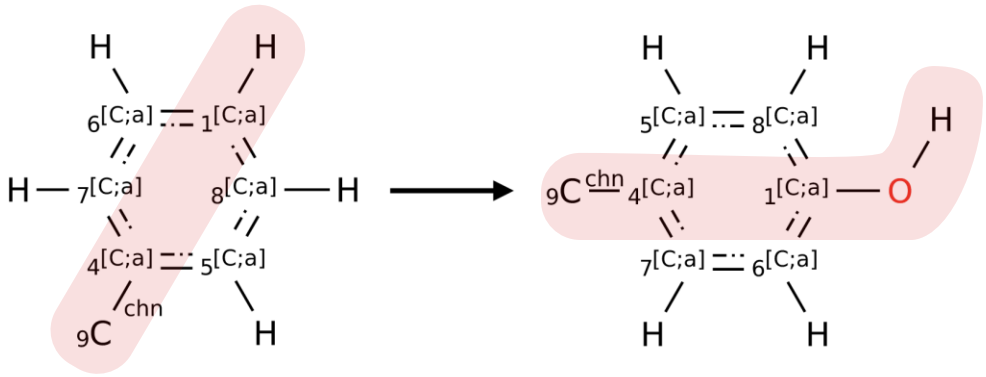


Biotransformation (BT) rules in enviPath

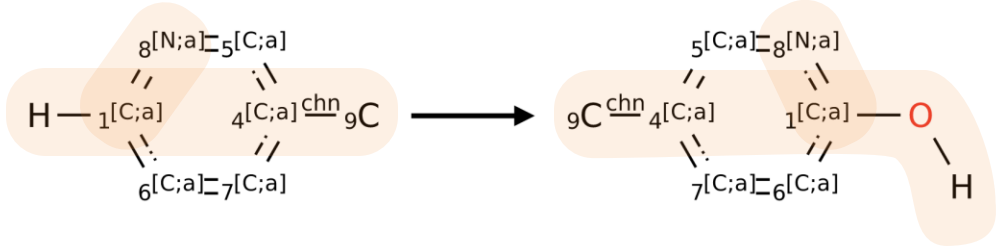
499 expert-curated biotransformation rules

- Rule names start with bt….
- They can consist of several sub-rules (“parallel rules”), for example bt0013:

bt0013-4165
monosubstituted Benzenoid → Add p-OH



bt0013-4165.2
substituted Pyridine → Add p-OH



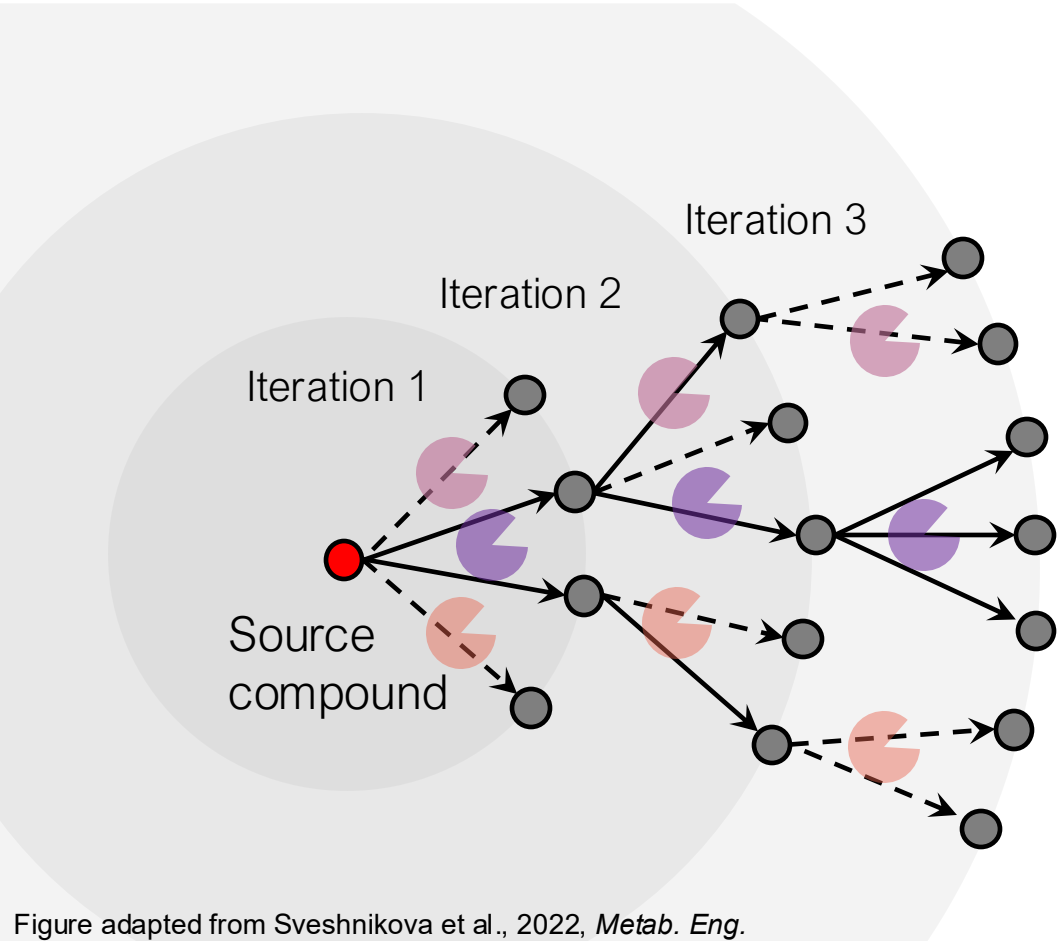
Rules linked to EC classification (enviLink)

Example: bt0001

EC Numbers			
1.1.1.-			
1.1.1.1	alcohol dehydrogenase	enviPath	EAWAG-BBD 2020-10-21 enviLink
1.1.1.1	alcohol dehydrogenase	KEGG	KEGG 2020-10-21 enviLink
1.1.1.2	alcohol dehydrogenase (NADP+)	KEGG	KEGG 2020-10-21 enviLink
...			
1.1.2.-		enviPath	
1.1.2.7	methanol dehydrogenase	enviPath	EAWAG-BBD 2020-10-21 enviLink
1.1.3.-			
1.1.3.7	aryl-alcohol oxidase	KEGG	KEGG 2020-10-21 enviLink
1.1.3.9	galactose oxidase	KEGG	KEGG 2020-10-21 enviLink
...			

From reaction to pathway prediction

Degradation pathway prediction through iterative rule application



1. **biotransformation rules,** expert-curated, 499 rules

2. **Relative reasoning rules**: Prioritization of biotransformation reactions

→ **More on this later today!**

Figure adapted from Sveshnikova et al., 2022, *Metab. Eng.*

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2. Data packages in enviPath

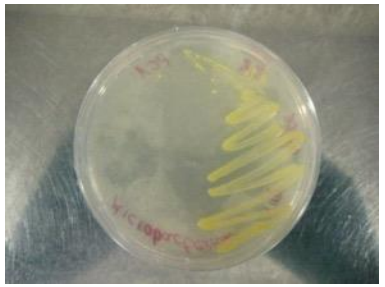
Available data packages

EAWAG-BBD

Data obtained from **original UMBBD**

Pathways observed mostly in **pure or enrichment cultures**

Pathways	✓
Compounds	✓
Reactions	✓
BT rules	✓
Scenarios	✗
Enzymes	✓



EAWAG-SOIL, EAWAG-SLUDGE, EAWAG-SEDIMENT

Data obtained from **literature** and **regulatory reports**

Pathways and half-lives observed in **complex natural or technical** (WWTP) **cultures**

Pathways	✓
Compounds	✓
Reactions	✓
BT rules	(✓)
Scenarios	✓
Enzymes	✗

EAWAG-BBD: Heritage from UM-BBD/PPS

Data in EAWAG-BBD

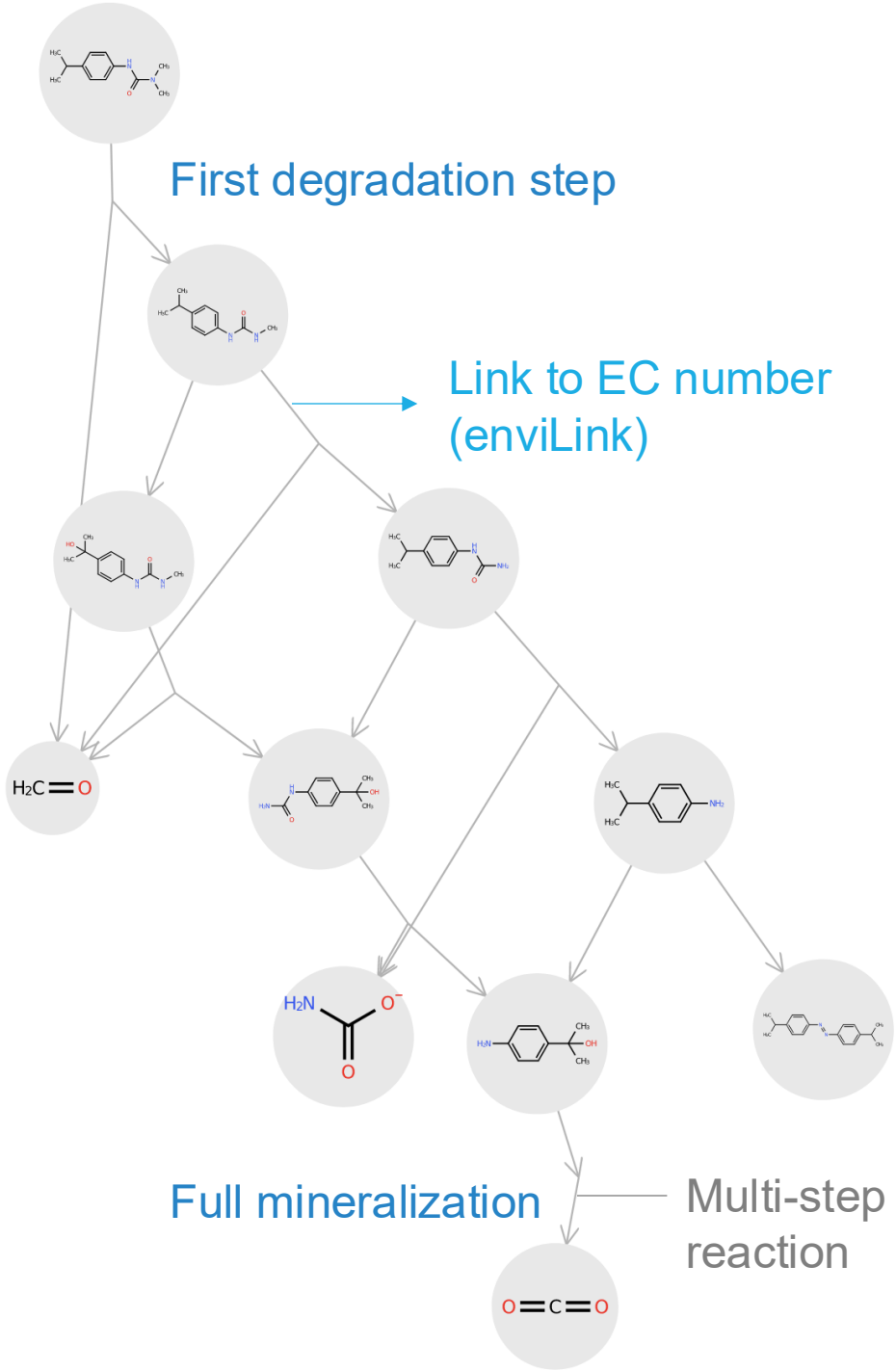
	EAWAG-BBD
Experimental guideline	**None** - pathways obtained mostly from pure and enrichment cultures
Type of chemicals	**Diverse** - Industrial chemicals, pesticides, pharmaceuticals, natural products
Source	**Scientific literature** (publication date ranging from 1957 to 2011)
# Pathways	220
# Compounds	648
# Reactions	1480 (associated with ~ 900 enzymes)
# BT rules	499

Example: Isoproturon pathway

Available information: Compilation of 4 studies

Description

The phenylurea herbicide isoproturon (IPU) is used against annual grasses and broad-leaved weeds in cereal production across Europe, resulting in both surface water and ground water pollution (Sorensen et al., 2001). Isoproturon in soil is degraded, producing carbon dioxide and degradation products (Perrin-Gainer et al., 2001). The major biodegradation pathway of isoproturon is isoproturon -> mono-demethyl-isoproturon -> hydroxy-monodemethyl-isoproturon -> 4`-(2-hydroxyisopropylphenyl)urea -> 4`-(2-hydroxyisopropylphenyl)aniline. Other minor pathways exist. Through one of these, 4,4`-diisopropylazobenzene can accumulate in soil (Perrin-Ganier et al., 2001). Attempts to isolate microorganisms which metabolize isoproturon have often failed. Recently, Sphingomnas sp. strain SRS2 was found to mineralize isoproturon. Sphingomnas sp. strain SRS2 is auxotrophic; it requires strain SRS1 to supply amino acids needed for the pathway (Sorensen et al., 2002).



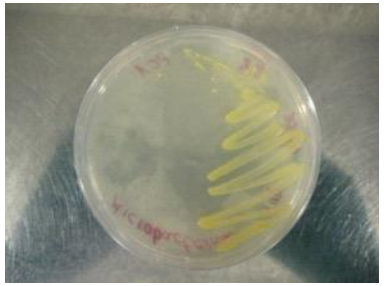
Available data packages

EAWAG-BBD

Data obtained from **original UMBBD**

Pathways observed mostly in **pure or enrichment cultures**

Pathways	✓
Compounds	✓
Reactions	✓
BT rules	✓
Scenarios	✗
Enzymes	✓



EAWAG-SOIL, EAWAG-SLUDGE, EAWAG-SEDIMENT

Data obtained from **literature** and **regulatory reports**

Pathways and half-lives observed in **complex natural or technical** (WWTP) **cultures**

Pathways	✓
Compounds	✓
Reactions	✓
BT rules	(✓)
Scenarios	✓
Enzymes	✗

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Data collections in enviPath

3 environment-specific data packages

enviPath

	EAWAG-SOIL	EAWAG-SLUDGE	EAWAG-SEDIMENT
Guideline	OECD 307	N/A	OECD 308
Type of chemicals	Pesticides	Micropollutants in general	Pesticides
Source	Regulatory reports	Scientific literature	Regulatory reports
# Pathways	317	183	179
# Compounds	1780	1067	579
# Cpds with half-lives	**895**	**158**	**181**
Status	Published (2017)	Published (2023)	Published (2025)

NEW

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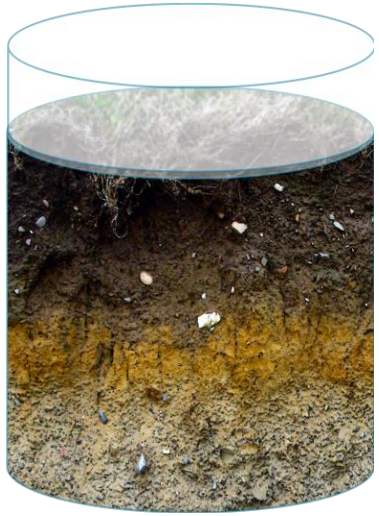
Data in EAWAG-SOIL

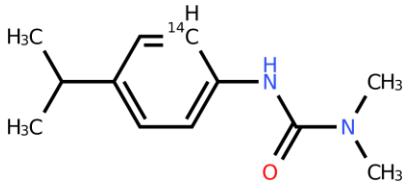


Biodegradation experiments in soil

Guideline: OECD 307

^{14}C-labeled spike compound

- Structure
- Spike concentration



Experimental conditions

- Temperature
- pH
- Redox condition

Experimental outcome

- **Half-life**
  - determined from concentration-time series
  - Model used for HL determination, model fit, comments
- **Transformation products**
  - Structure
  - % radioactivity (major/minor classification)

Soil parameters

- Soil texture (% sand, silt, clay)
- Organic carbon content
- Cation exchange capacity (CEC)
- Water storage capacity

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EAWAG-SOIL

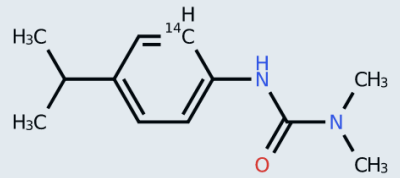
Scenario

Spike compound

Experimental conditions

Soil parameters

Experimental outcome

Property	Value	Unit
Acidity	Value: 6.8 Measurement Methods:	pH
Cation exchange capacity, CEC	12.5	mEq/100g
Half-life	DT50: 10.9 Model: SFO Fit: Comment: Source: Galicia (1989); Callow & Jarvis (2011)	d
Organic content	1.3	OC
Redox condition	aerobic	
Soil origin	SLH	
Soil texture	Silt loam Sand: 14.8% Silt: 65.5% Clay: 19.7%	
Spike compound	Spike compound 0000381 	
Spike concentration	2.0	µg/kg dry soil
Temperature	20.0	°C
Water storage capacity	water hold capacity 13.4 conditions % actual WC maximum water hold capacity	g water/100g dry soil

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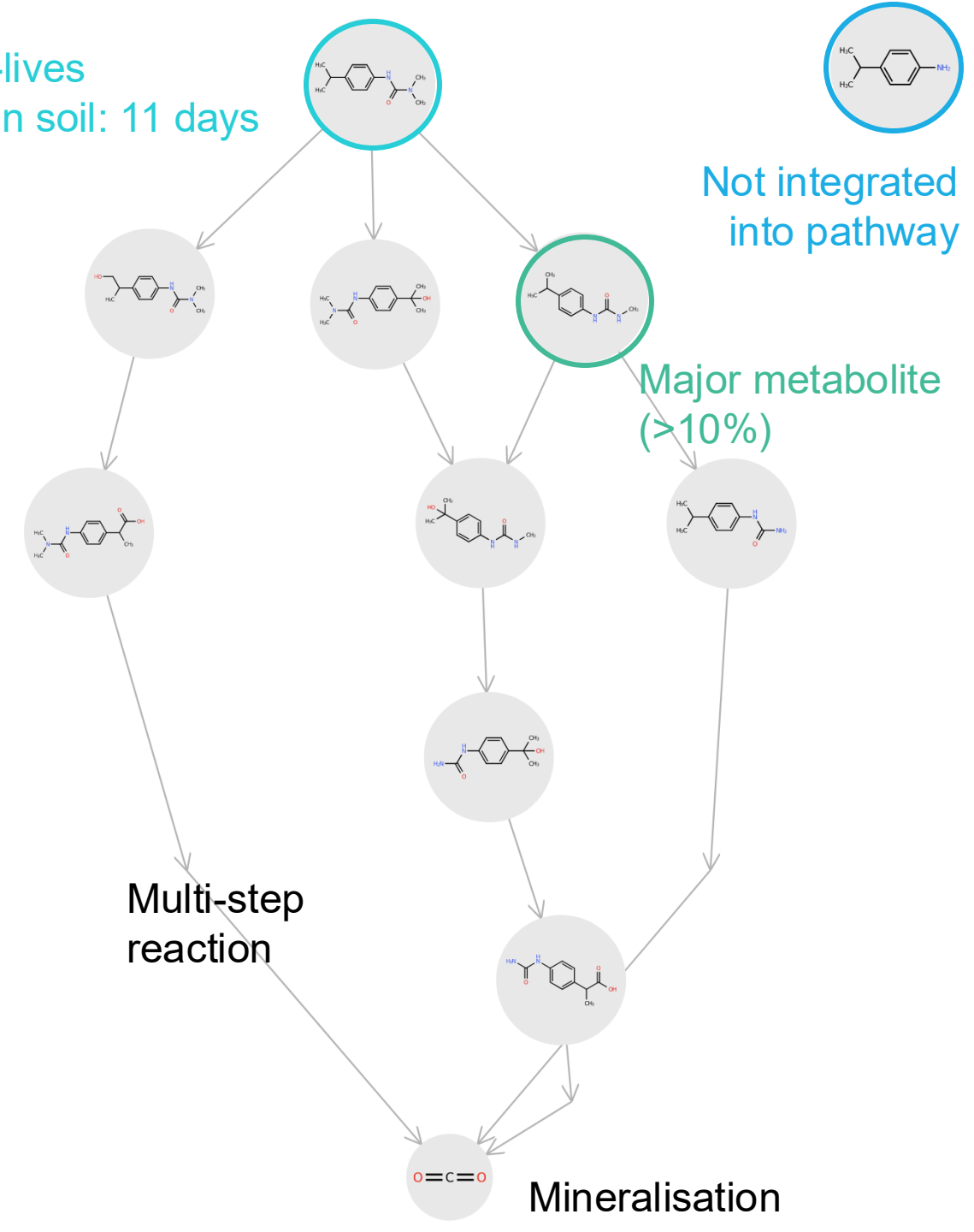
- 14 reported half-lives
- Median half-life in soil: 11 days

Example: Isoproturon pathway

Compilation of several studies

Description

Aerobic degradation studies in soil demonstrated that isoproturon was degraded via biological processes, with 10 to 45% mineralisation after 58 to 100 days and unextractable residues of 48 to 73% of applied radioactivity after 58 to 100 days. In the Review Report for isoproturon (SANCO/3045/99-final 12 March 2002), only the metabolite desmethyl-isoproturon was classified as a major metabolite (occurring in amounts >10% of applied substance). [...] The degradation pathway of isoproturon involves demethylation (to produce desmethyl-isoproturon) and hydroxylation (to produce 1-OH-isoproturon and 2-OH-isoproturon) forming three primary metabolites (which were identified as potentially relevant). Desmethyl-isoproturon is transformed to didesmethyl-isoproturon in a second demethylation step. 1-OH-isoproturon degrades further to proanoic acid isoproturon, whereas 2-OH-isoproturon is transformed to minor metabolites.



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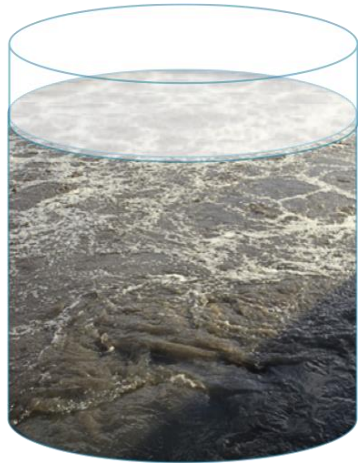
Data in EAWAG-SLUDGE

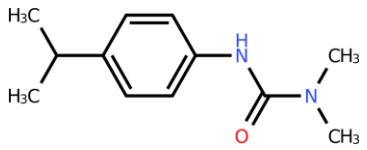


Biodegradation experiments in activated sludge

(OECD 314b)

Spike compound (unlabeled)

- Structure
- Spike concentration
- Type of compound addition



Experimental outcome

- **Rate constant or half-life**
  - determined from concentration-time series
  - Model used for HL determination, model fit, comments
- **Transformation products**
  - Structure
  - Confidence level

Experimental conditions

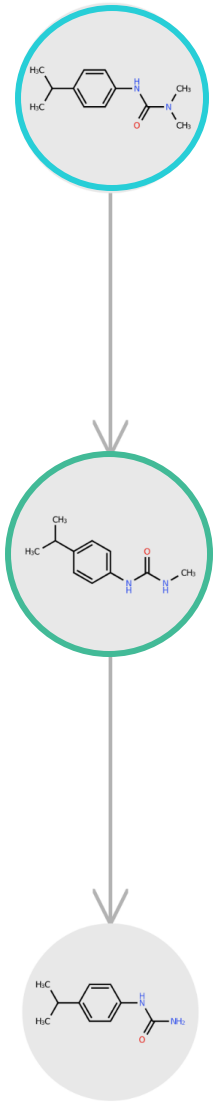
- Temperature
- pH
- Redox condition

Sludge parameters

- Setup
  - Bioreactor type
  - Aeration
- Origin
  - Location
  - Treatment technology
- Sludge properties
  - N, P content
  - Total suspended solids concentration (TSS)

Example: Isoproturon pathway

Compilation of several studies



- 14 reported rate constants or half-lives
- Median half-life in sludge: 6.8 days

<u>Sometimes</u>
Level of confidence for metabolite identification*

* According to Schymanski *et al. Environ. Sci. Technol.* **48**, 2097–2098 (2014).

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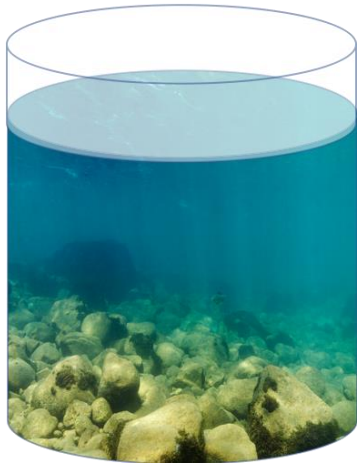
Data in EAWAG-SEDIMENT

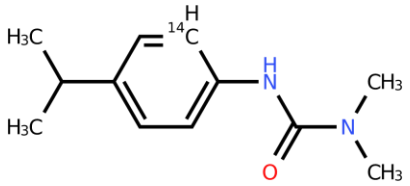


Biodegradation experiments in water-sediment systems

Guideline: OECD 308

^{14}C-labeled spike compound

- Structure
- Spike concentration



Experimental outcome

- **Half-lives** (total system, water, sediment)
  - determined from concentration-time series
  - Model used for HL determination, model fit, comments
- **Transformation products**
  - Structure
  - % radioactivity (major/minor classification)

Experimental conditions

- Temperature
- pH (water and sediment)
- Redox potential
- Oxygen content

Water-sediment parameters

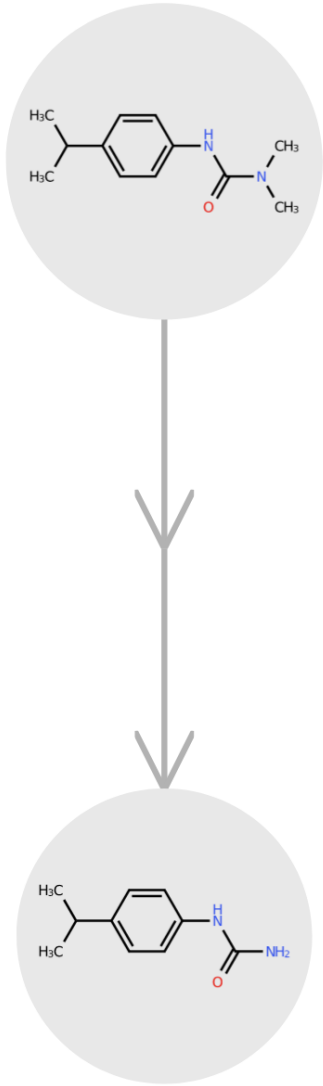
- Sample location
- Sediment texture
- Ratio water to sediment
- Organic content
- Sediment porosity

Example: Isoproturon pathway

One study in a water-sediment system

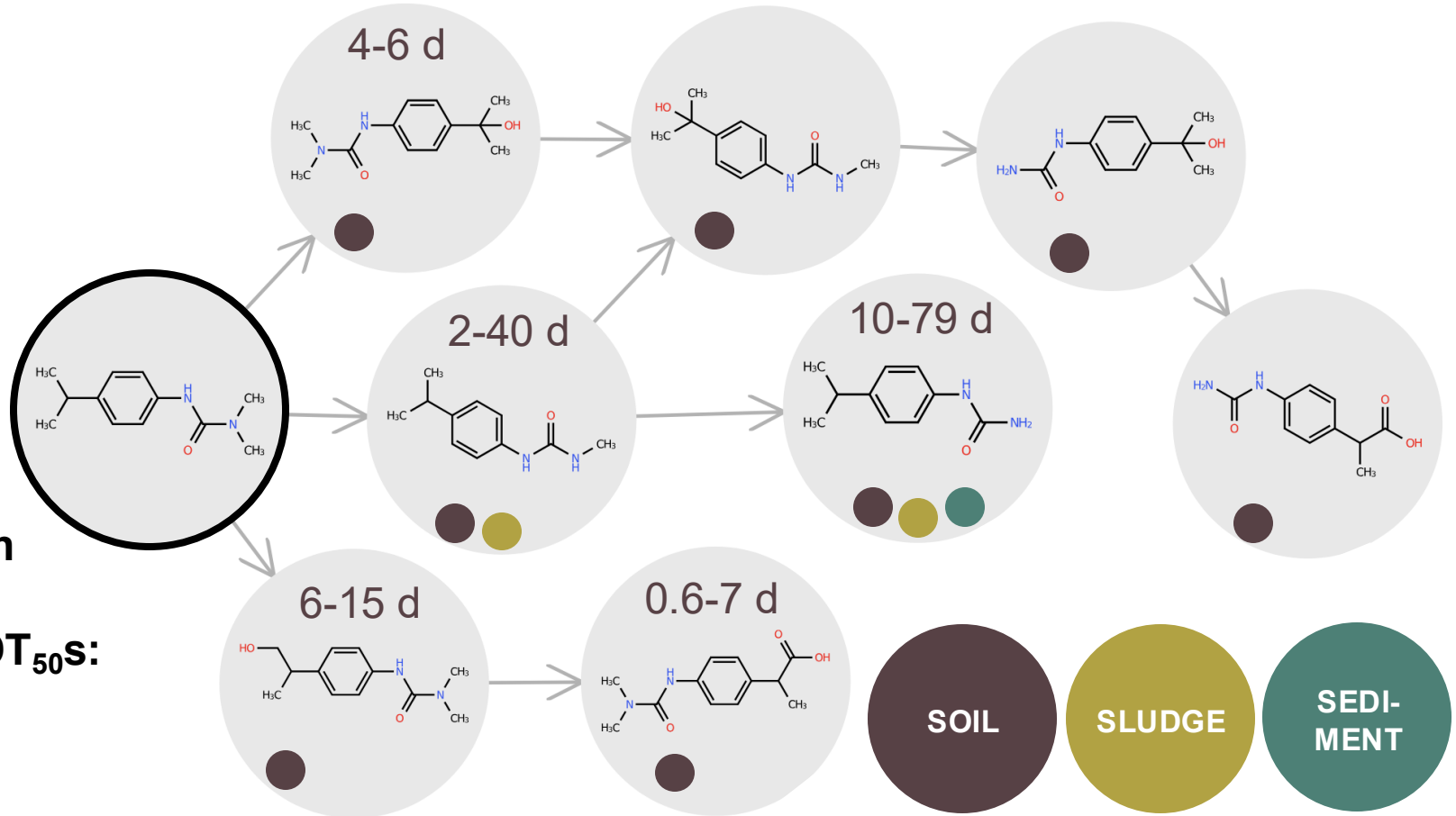
Description

The route and rate of degradation of 14C-isoproturon in two aquatic systems (Bury Pond: fine texture, Emperor Lake: coarse texture) under aerobic conditions were investigated at 20 °C in the dark. In the entire system the half-lives of 14C-isoproturon were calculated to be 101 and 279 days for pond and lake systems. Two metabolites exceed the 5 or 10 % AR in water or sediment: Desmethyl-isoproturon (whole system: 20.9%) and BPh1 (whole system: 9.5%).



→ Systematic comparison between packages ?

Comparison of Isoproturon pathways



Isoproturon

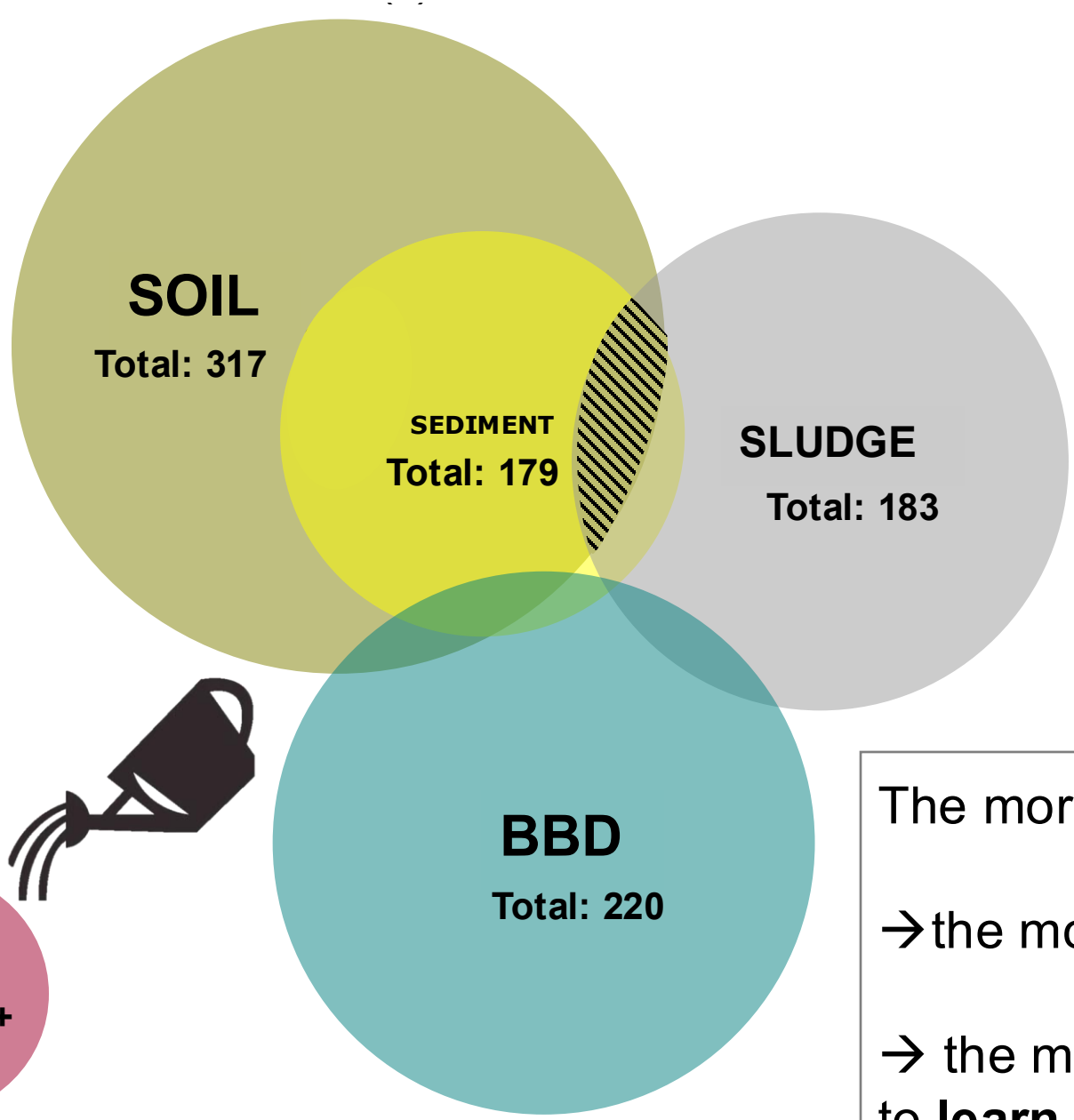
Reported DT_{50}s:

7-30 d

0.6-35 d

124-218 d

Overlap between BBD, SOIL, SLUDGE, and SEDIMENT



Common pathways

Talk by Stephanie in the afternoon

The more **data**

→ the more **overlap**

→ the more opportunities to **learn** from data

SOIL vs. SLUDGE vs. SEDIMENT

Comparing data packages – opportunities for read-across

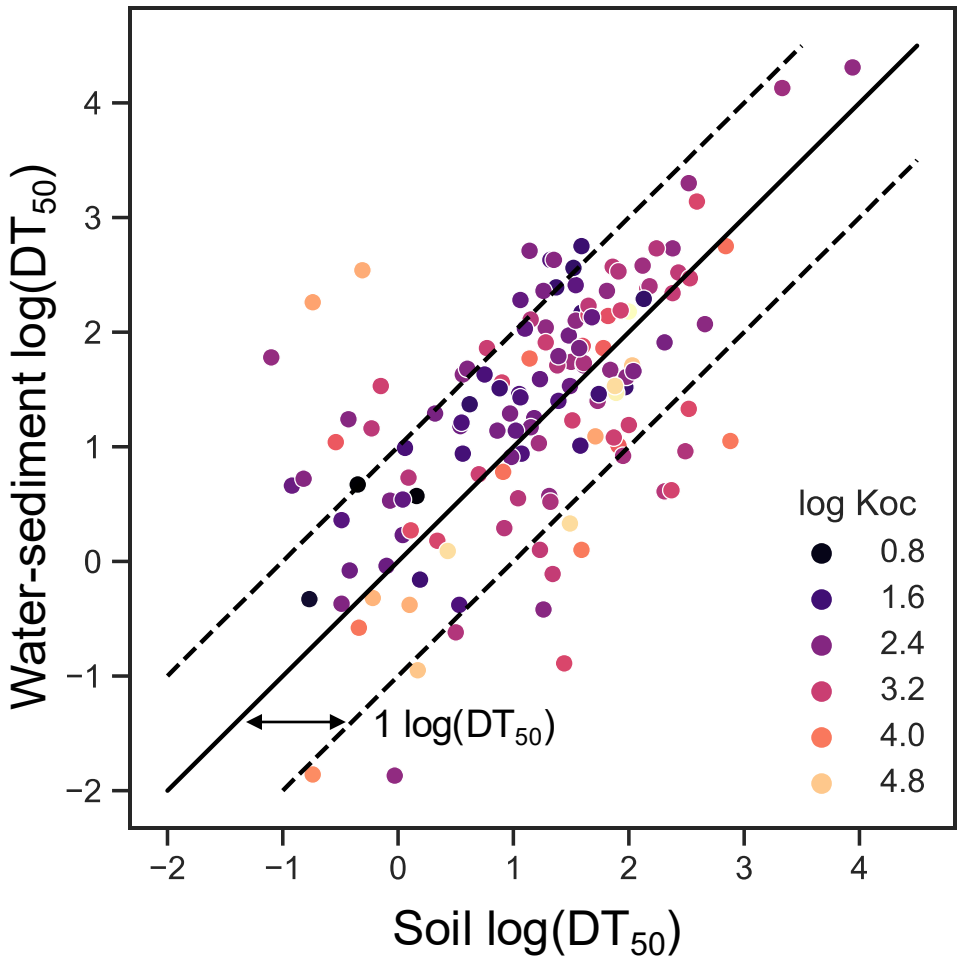
8 common pathways*	SOIL	SLUDGE	SEDIMENT
Average number of TPs	6.6	2.3	1.1
Average half-lives	12 days	3 days	52 days

→ Shortest **half-lives** in activated sludge, longest in water-sediment systems

→ Most **transformation products** detected in soil, very few in sediment

* Carbetamide, Clomazone, Diazinon, Ethofumesate, Isoproturon, Napropamide, Spiroxamine, Trinexapac-ethyl

SOIL vs. SEDIMENT half-lives



Information

148 Pesticides and pesticide TPs

logDT50 values: Bayesian mean, in log(days)

logKoc values predicted by OPERA

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3. Navigating enviPath data

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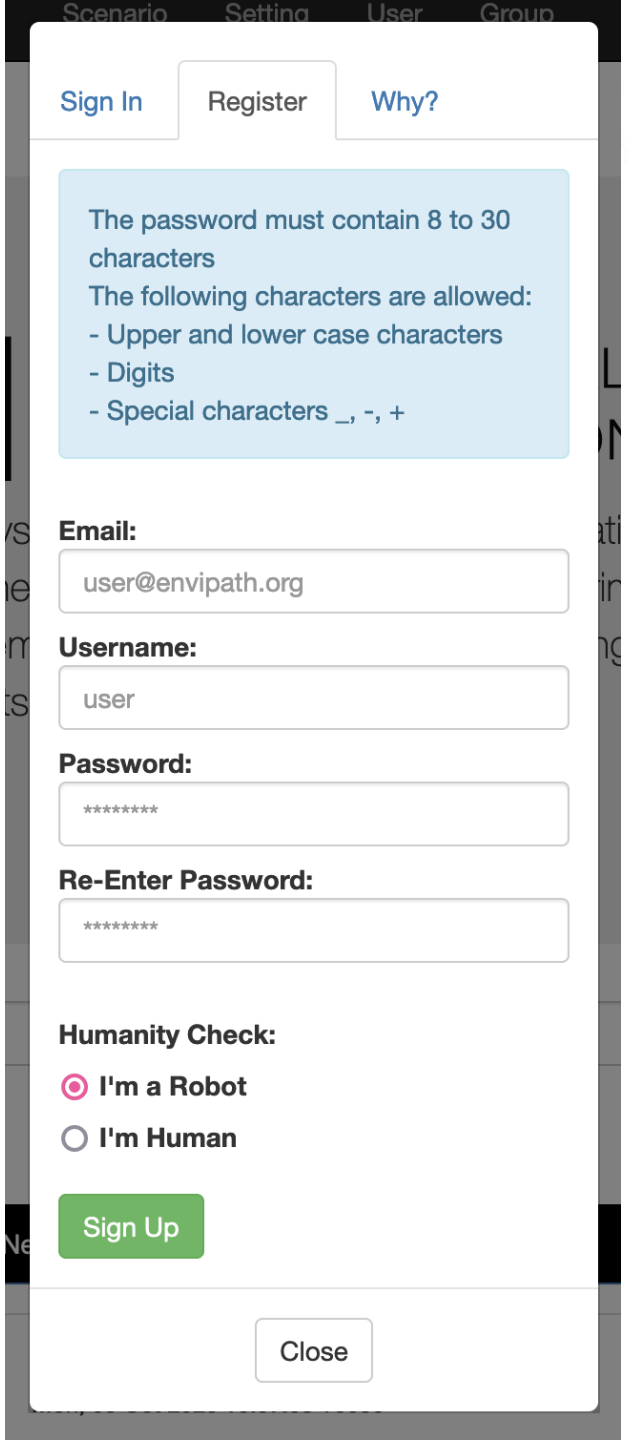
How to register →

User administration

Users can …

- register and create own packages
- establish groups
- give reading and writing rights for their packages
- submit packages for review and publication on enviPath
- Define default settings for their package



enviPath Python API

API: Application Programming interface

Freely available at https://github.com/enviPath/enviPath-python

Tutorials can be found here: https://envipath-python.readthedocs.io

```
# Define the instance to use
INSTANCE_HOST = 'https://envipath.org'
# Each journey starts with setting up the enviPath instance
eP = enviPath(INSTANCE_HOST)
# Define package URIs
BBD_URI = 'http://envipath.org/package/32de3cf4-e3e6-4168-956e-32fa5ddb0ce1'
# Load package BBD
bbd = Package(eP.requester, id=BBD_URI)
# Retrieve data from enviPath
bbd_compounds = bbd.get_compounds()
bbd_pathways = bbd.get_pathways()
```

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Take-home message

- ✓ enviPath is a growing **resource** for biodegradation data
- ✓ The data can be used to develop predictive **models** (TPs, half-lives)
- ✓ Maybe **YOU can contribute** to expand our knowledge base in the future !

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