Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg

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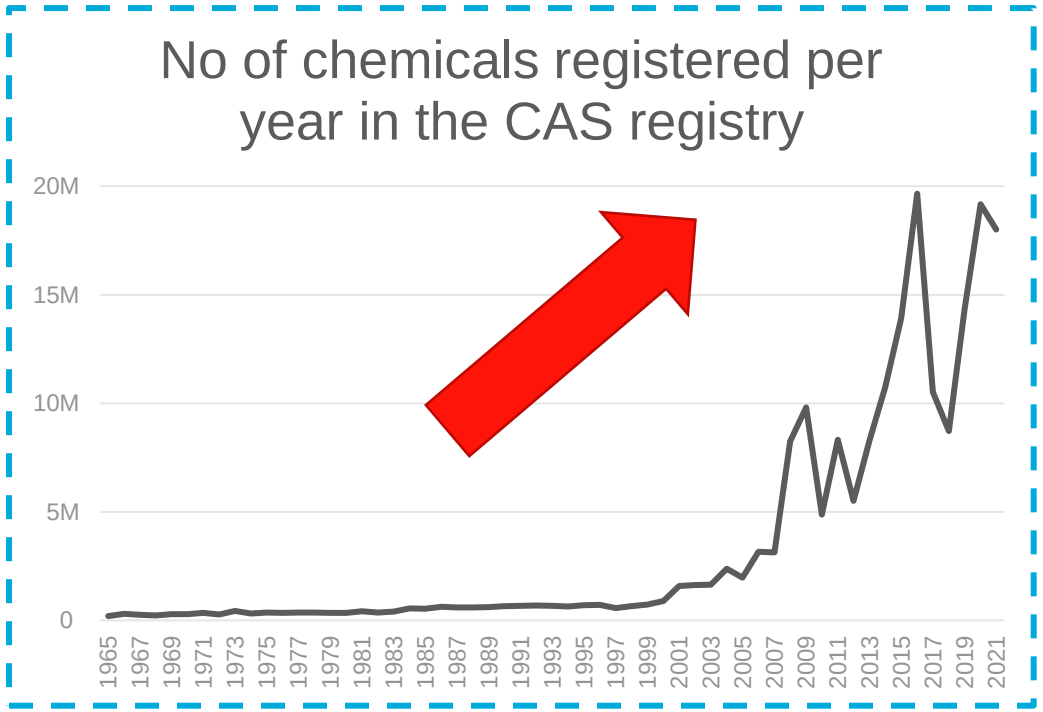
Oral Presentation at ICNTS23, Erding
NTS in Environmental Analysis session, 18 October 2023

INTRODUCTION

- Study of exposome-related pollutants in surface water



WHY?

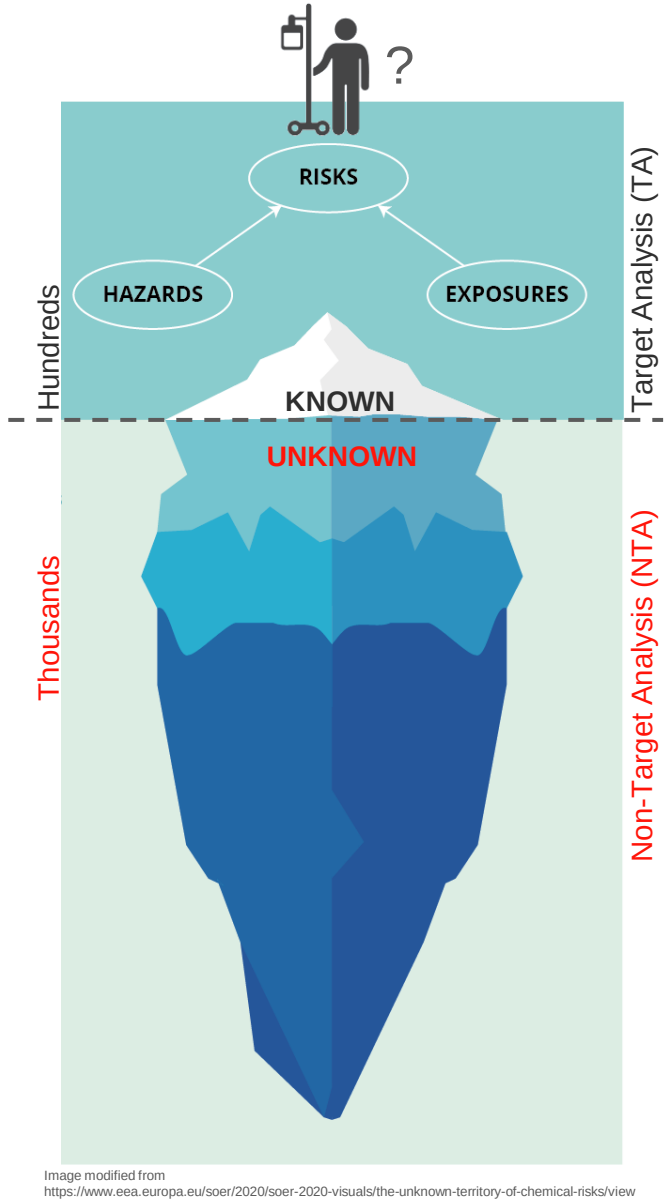
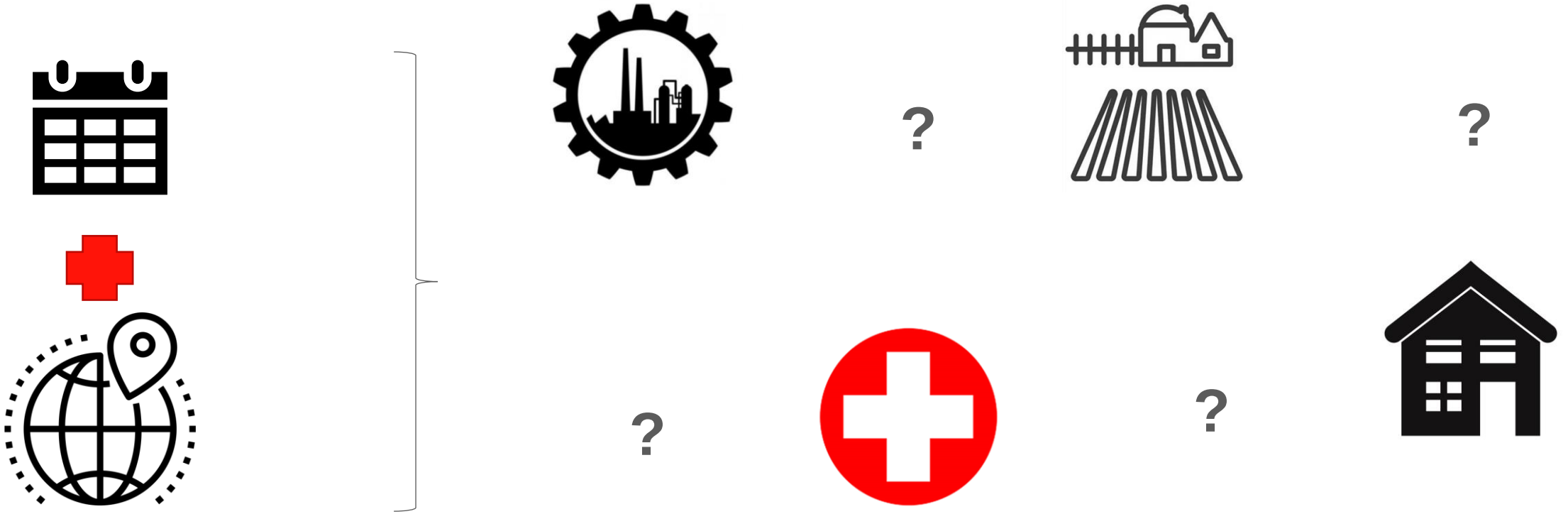


Image modified from
https://www.eea.europa.eu/soer/2020/soer-2020-visuals/the-unknown-territory-of-chemical-risks/view

INTRODUCTION

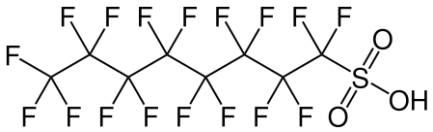
- Use of temporal patterns and geographical data
  - Understand pollution sources and risks



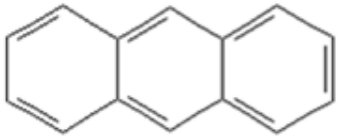
INTRODUCTION

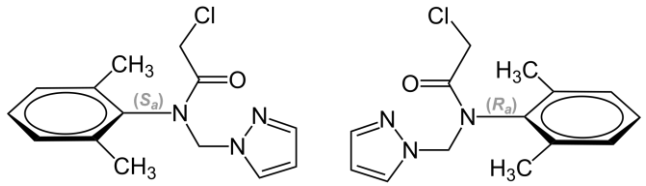
- 102 natural (nearly unmodified) surface water bodies in Luxembourg

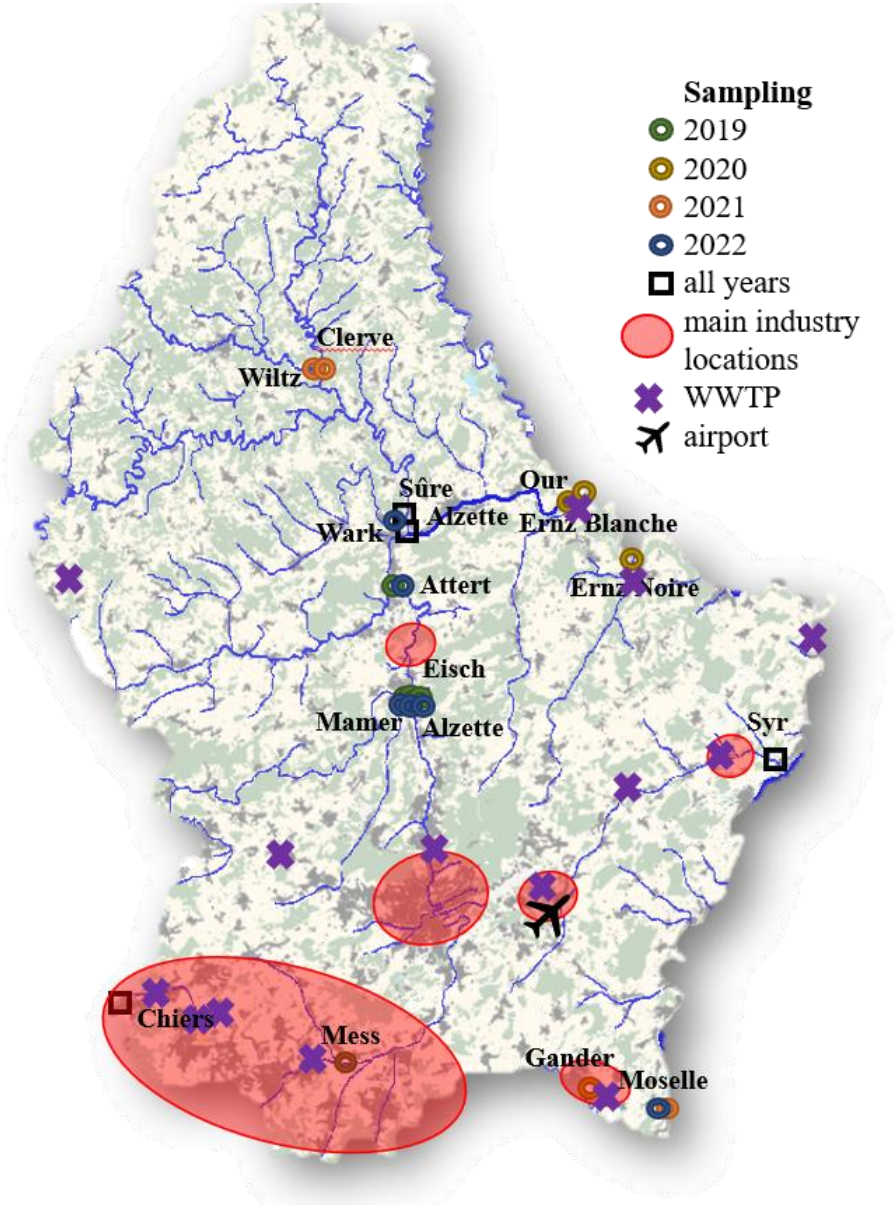
- 2022 report on water quality: NO river in good condition*



concentration values exceeded for e.g.







*: L'Administration de la gestion de l'eau (AGE), Luxembourg (2022) Elaboration du 3e plan de gestion.

INTRODUCTION

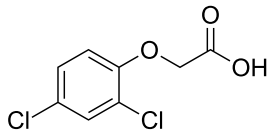
- Target monitoring of Luxembourgish waters by AGE

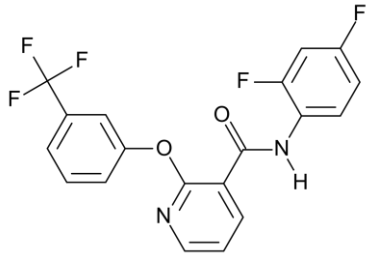
LE GOUVERNEMENT
DU GRAND-DUCHÉ DE LUXEMBOURG
Ministère de l'Environnement, du Climat
et du Développement durable

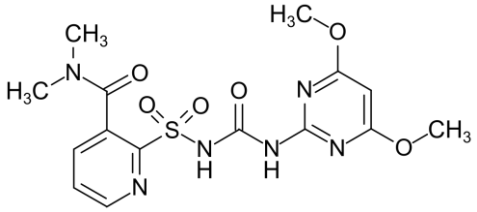
Administration de la gestion de l'eau

➢Priority chemicals

➢Catchment specific chemicals







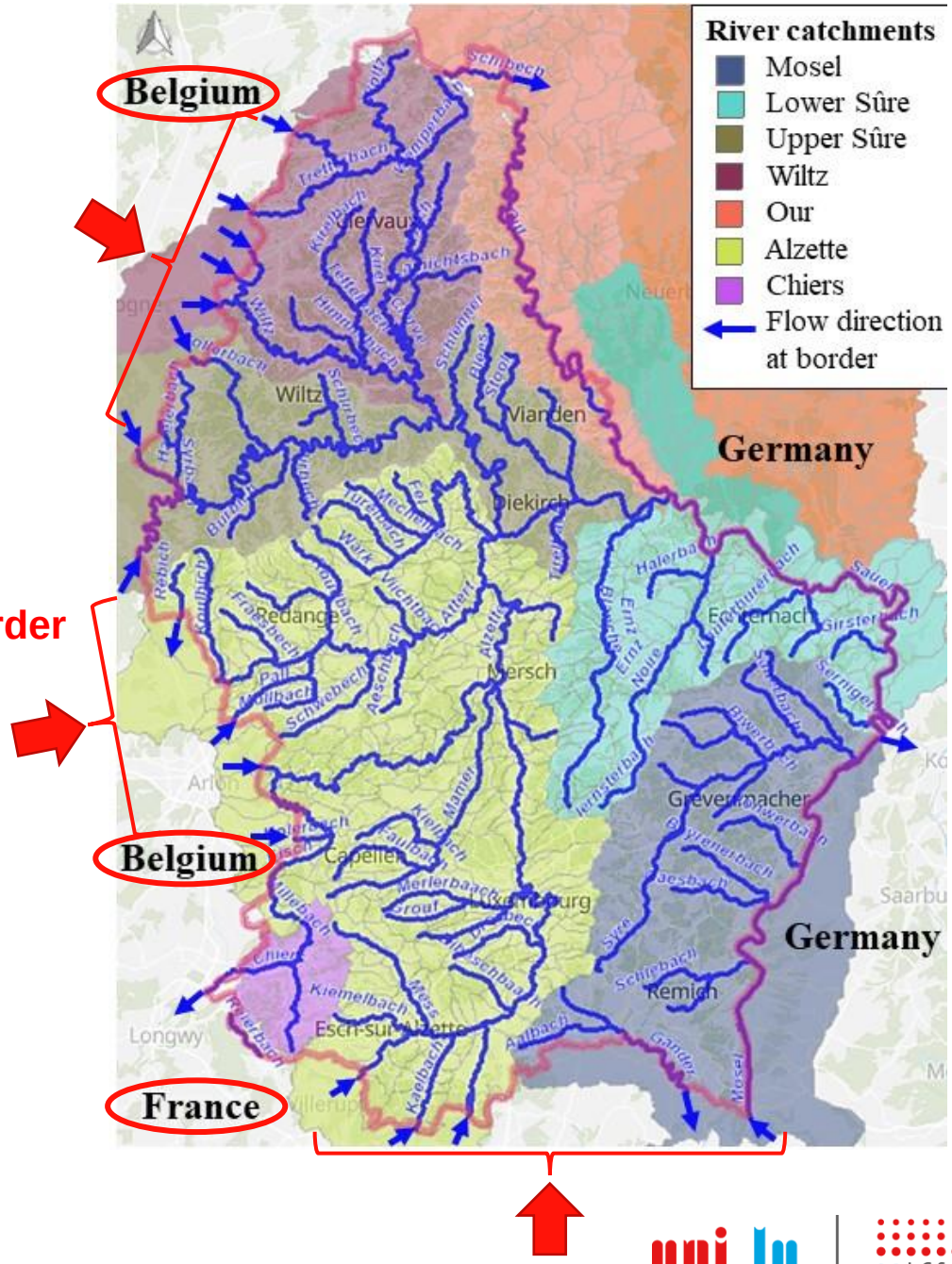
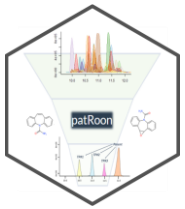


Image taken from Aurich D., et al. forthcoming, *Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg.* Preprint DOI: 10.21203/rs.3.rs-3136123/v1

Research Objectives

- employ NTA as a complementary approach to routine target monitoring
  - propose open source and adaptable NT workflow



- Identify temporal and/or spatial patterns (potential sources)

- classify chemicals using different tools

classyfireR 0.3.8

PubChemLite EXPOSOMICS

LE GOUVERNEMENT
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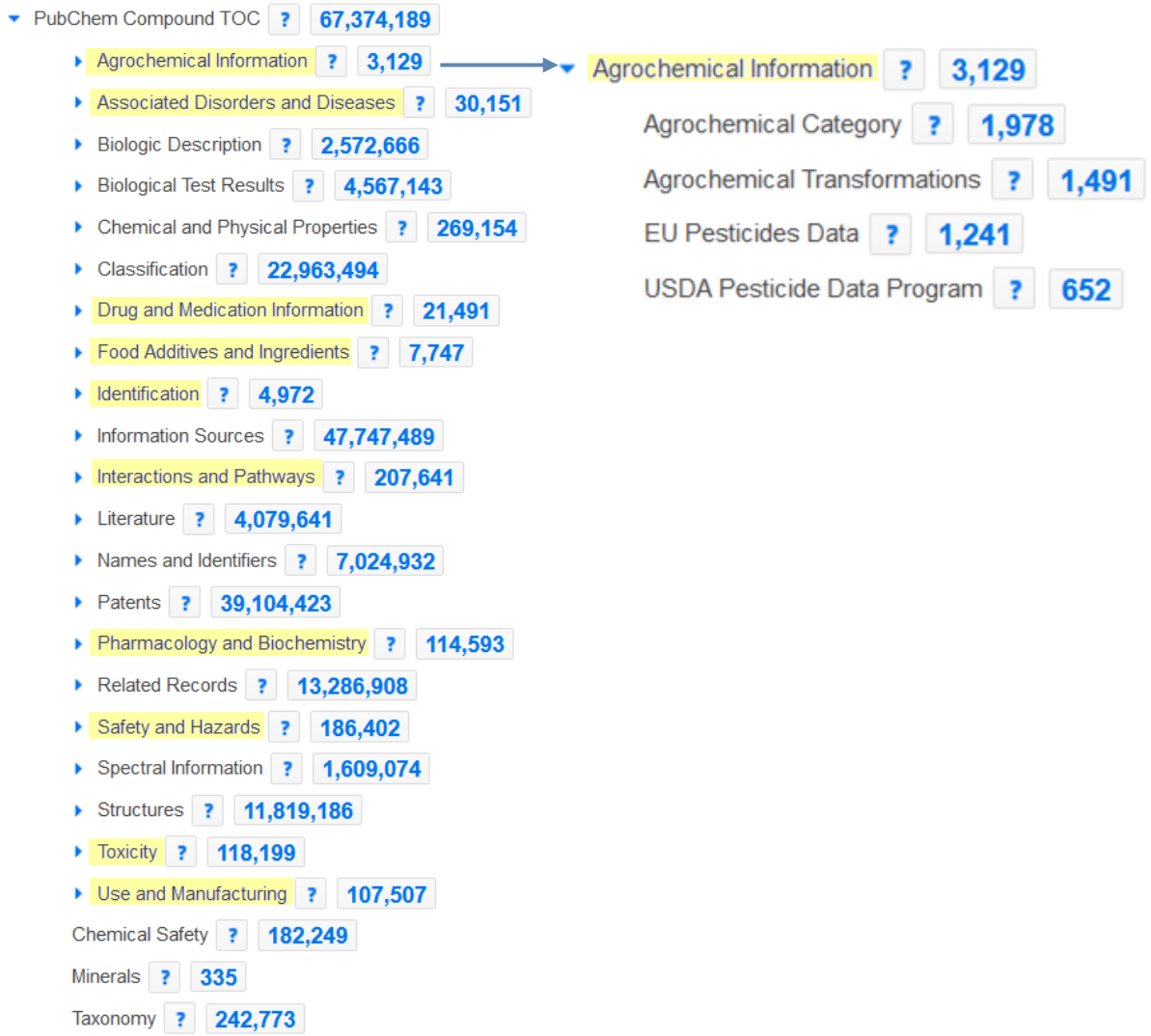
Ministère de l'Environnement, du Climat
et du Développement durable
Administration de la gestion de l'eau

PubChemLite
EXPOSOMICS



PubChemLite EXPOSOMICS

116M Compounds | 309M Substances | 292M Bioactivities | 36M Literature | 38M Patents

PubChem

- PubChem Compound TOC ? 67,374,189
  - Agrochemical Information ? 3,129
  - Associated Disorders and Diseases ? 30,151
  - Biologic Description ? 2,572,666
  - Biological Test Results ? 4,567,143
  - Chemical and Physical Properties ? 269,154
  - Classification ? 22,963,494
  - Drug and Medication Information ? 21,491
  - Food Additives and Ingredients ? 7,747
  - Identification ? 4,972
  - Information Sources ? 47,747,489
  - Interactions and Pathways ? 207,641
  - Literature ? 4,079,641
  - Names and Identifiers ? 7,024,932
  - Patents ? 39,104,423
  - Pharmacology and Biochemistry ? 114,593
  - Related Records ? 13,286,908
  - Safety and Hazards ? 186,402
  - Spectral Information ? 1,609,074
  - Structures ? 11,819,186
  - Toxicity ? 118,199
  - Use and Manufacturing ? 107,507
  - Chemical Safety ? 182,249
  - Minerals ? 335
  - Taxonomy ? 242,773

Agrochemical Information ? 3,129

- Agrochemical Category ? 1,978
- Agrochemical Transformations ? 1,491
- EU Pesticides Data ? 1,241
- USDA Pesticide Data Program ? 652

Metolachlor (Compound)

8.3 EU Pesticides Data

Active Substance
metolachlor

Status
Not approved [Reg. (EC) No 1107/2009]

Legislation
2002/2076

▸ EU Pesticides Database

Glyphosate (Compound)

9.3 EU Pesticides Data

Active Substance
glyphosate

Status
Date of Approval: 16/12/2017 Expiration of Approval: 15/12/2022 [Reg. (EC) No 1107/2009]

Legislation
01/99/EC, 2010/77/EU, Reg. (EU) 2015/1885, Reg. (EU) 2016/1056, Reg. (EU) 2016/1313, Reg. (EU) 2017/2324, Reg. (EU) 2019/724, Reg. (EU) No 540/2011

ADI
0.5 mg/kg bw/day [Reg. (EU) 2017/2324]

ARfD
0.5 mg/kg bw [Reg. (EU) 2017/2324]

AOEL
0.1 mg/kg bw/day [Reg. (EU) 2017/2324]

▸ EU Pesticides Database

PubChemLite EXPOSOMICS

371,663 compounds

116M Compounds | 309M Substances | 292M Bioactivities | 36M Literature | 38M Patents

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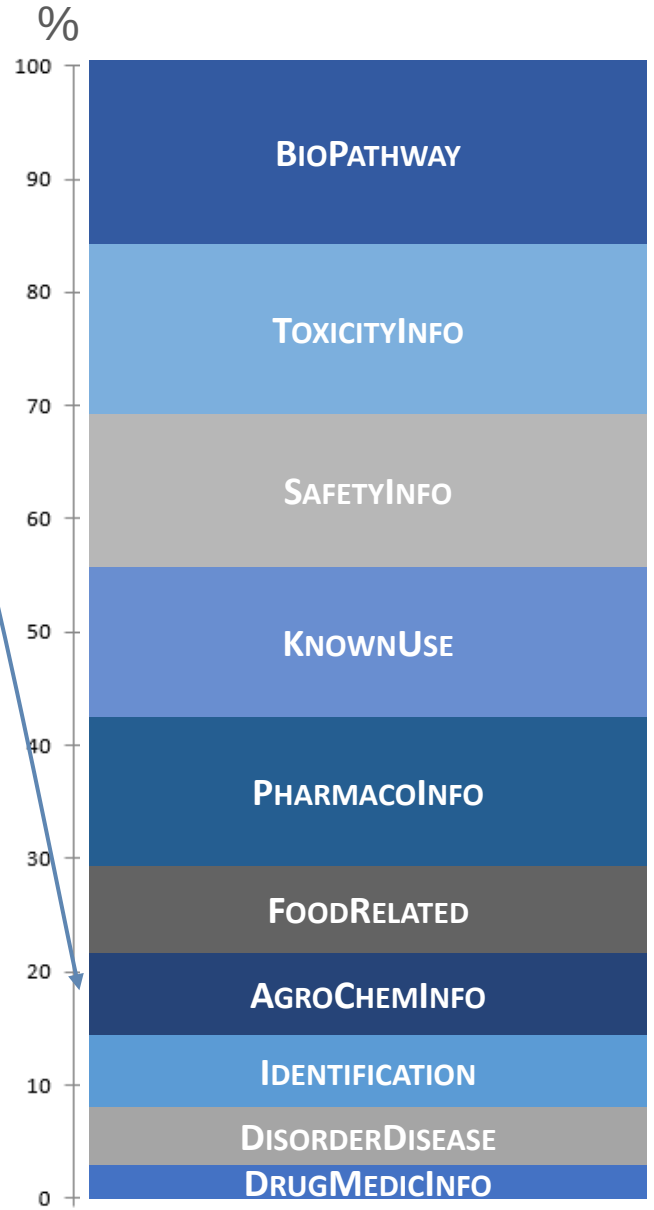
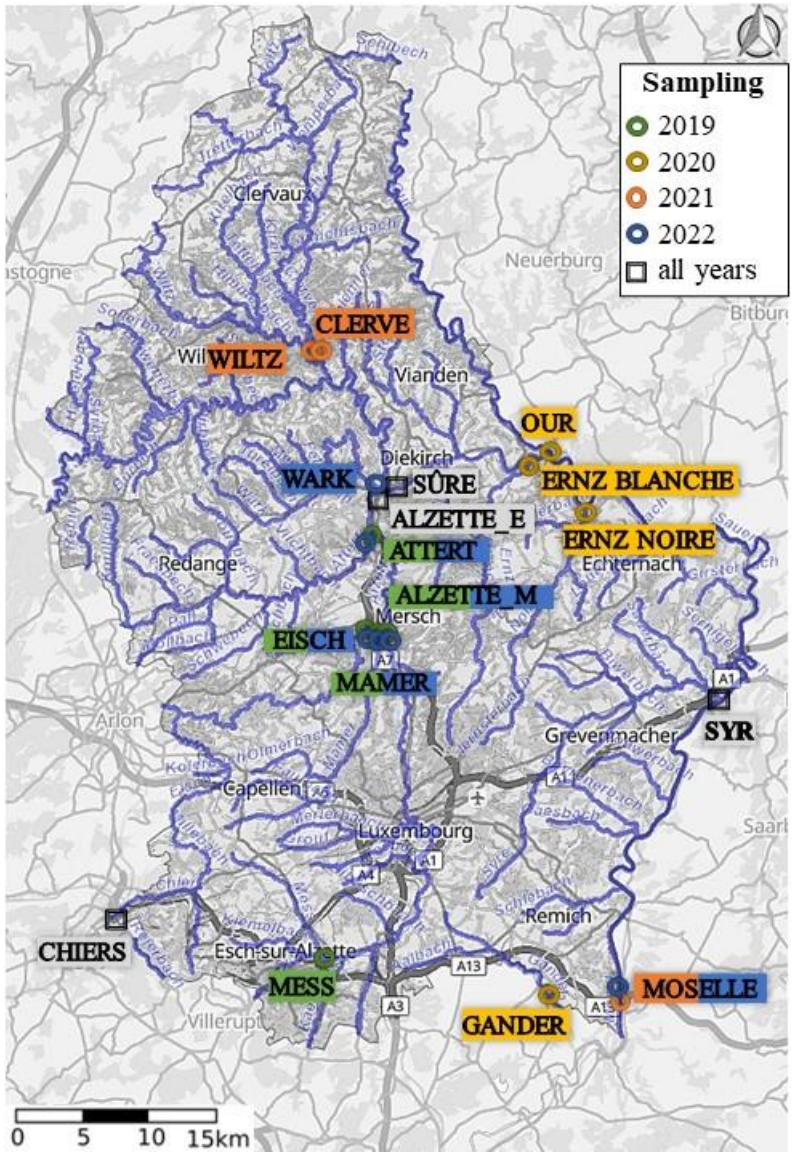


PubChemLite EXPOSOMICS

DATA COLLECTION

mzML → GNPS

doi:10.25345/C55X25P62



- 271 surface water samples (2019-2022)
- Extraction

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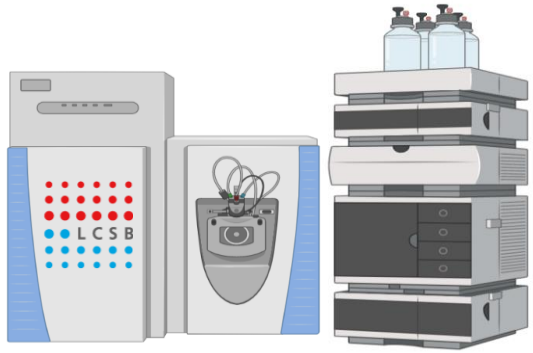
Administration de la gestion de l'eau

- HRMS analysis



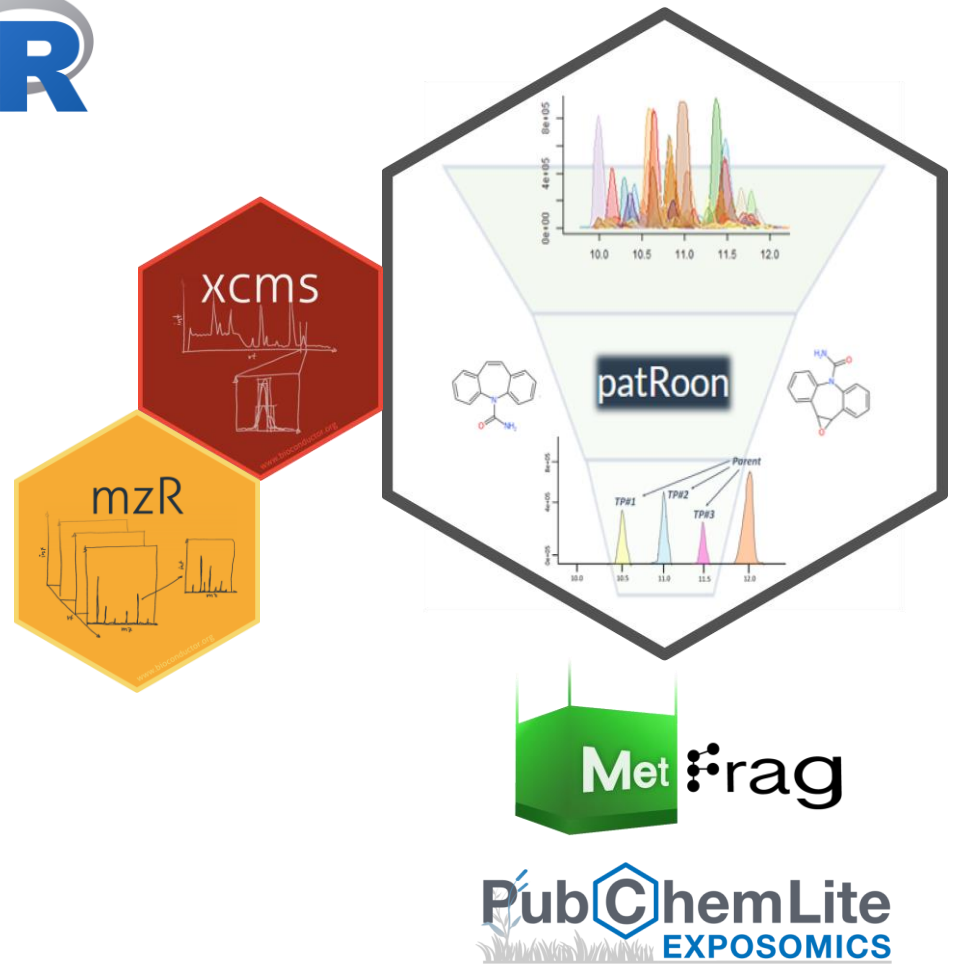
data analysis

Image taken from Aurich D., et al. forthcoming, *Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg.* Preprint DOI: 10.21203/rs.3.rs-3136123/v1

DATA ANALYSIS

code

- Open source HRMS data processing workflow in R
- NTA via patRoon:
  - ‘Sets’ workflow (positive and negative)
  - **xcms** for feature finding (optimized) and grouping
  - **mzR** to generate peak lists
  - **MetFrag (PubChemLite)** for compound annotation
  - adapted **identification level scheme*** :



Level	individualMoNAScore
2	> 0.9
3a	0.7-0.9
3b	0.4-0.7

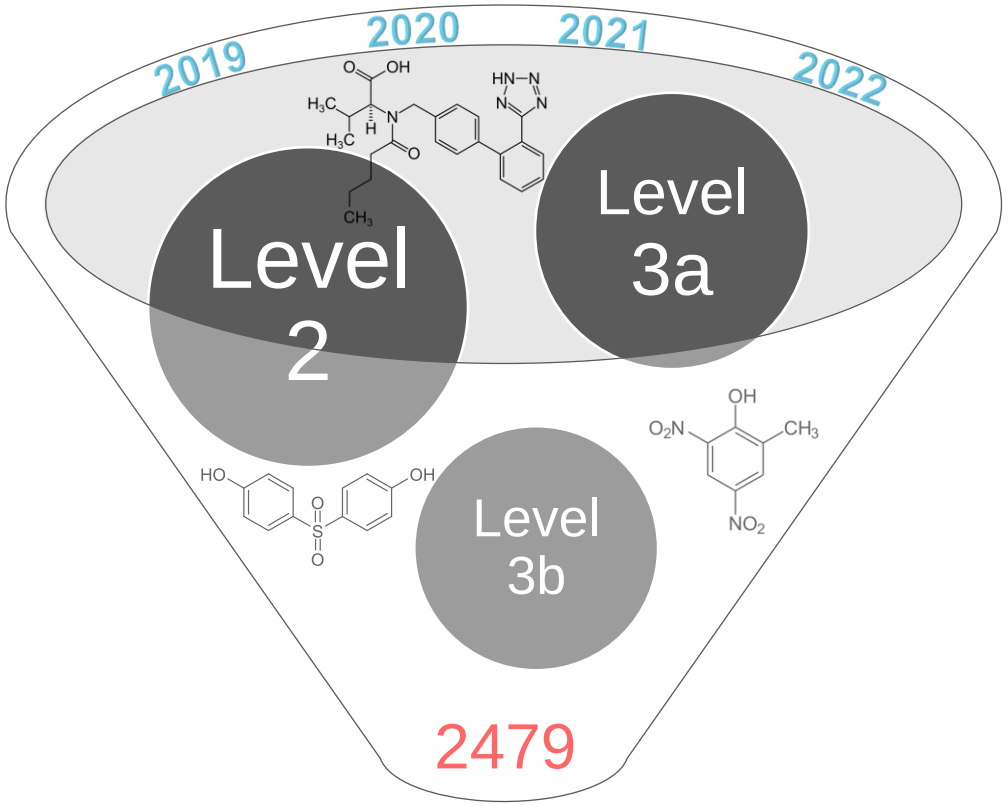
good MSMS library match

poor MSMS library match

*Talavera Andújar et al., DOI: 10.1007/s00216-022-04207-z

ANNOTATIONS

data



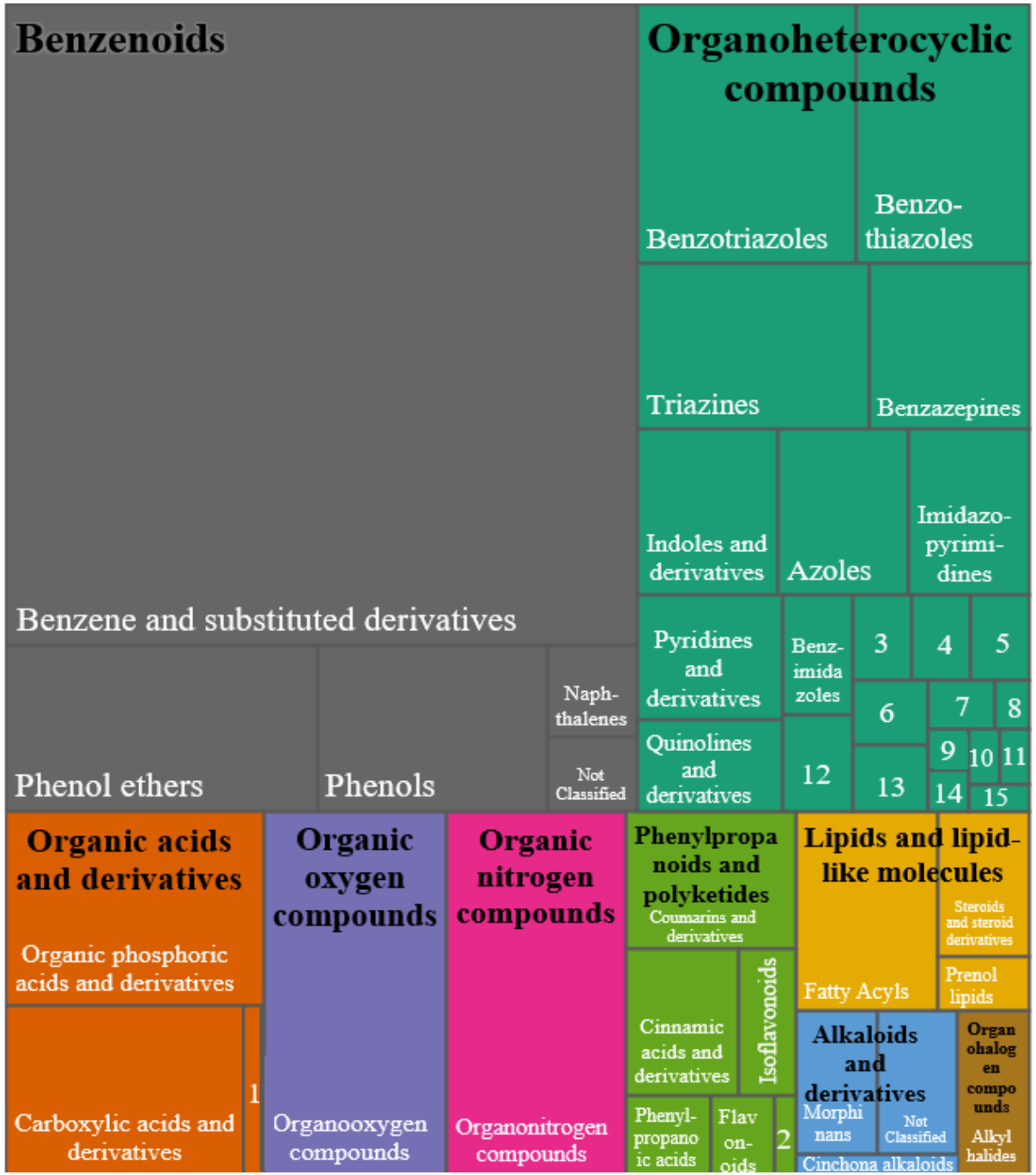
378 unique (exposome-related) chemicals

PubChemLite EXPOSOMICS

CLASSIFICATION

http://classyfire.wishartlab.com/

classyfireR 0.3.8

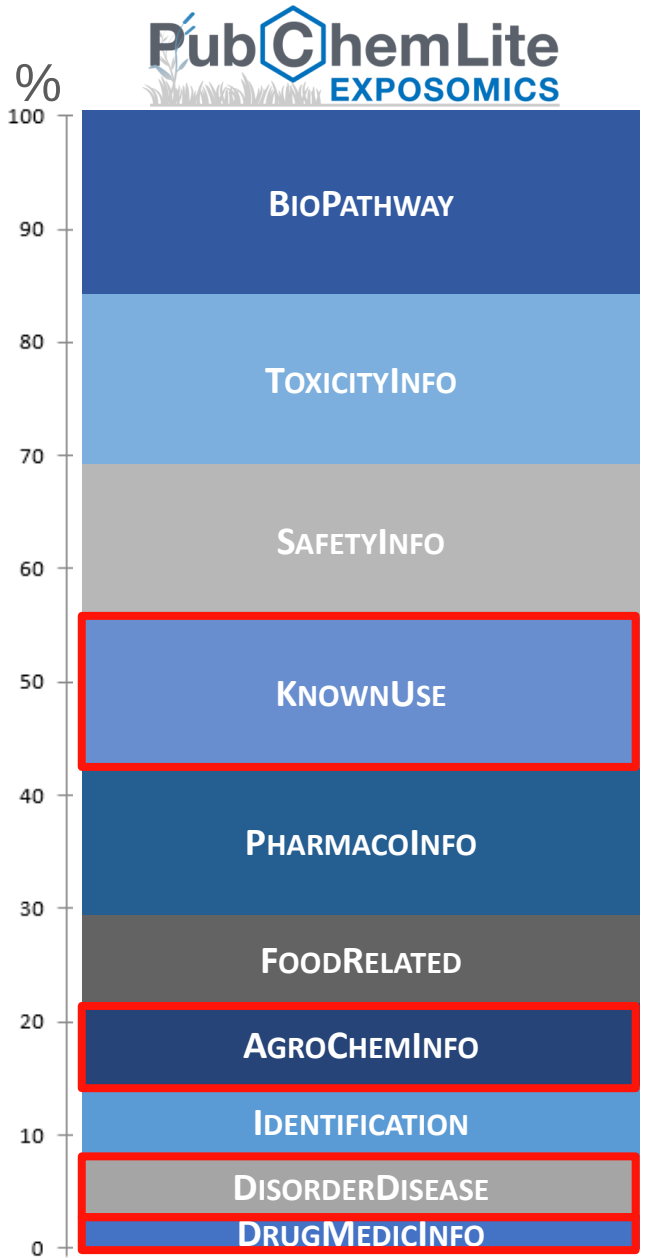


1 Hydroxy acids and derivatives
2 Cinnamaldehydes
3 Isoquinolines and derivatives
4 Heteroaromatic compounds
5 Imidazothiazoles
6 Thiochromenes
7 Pyrazolopyrimidines
8 Isocoumarans
9 Piperidines
10 Thiadiazines
11 Oxepanes
12 Piperazinoazepines
13 Benzodiazepines
14 Diazines
15 Pyrroles

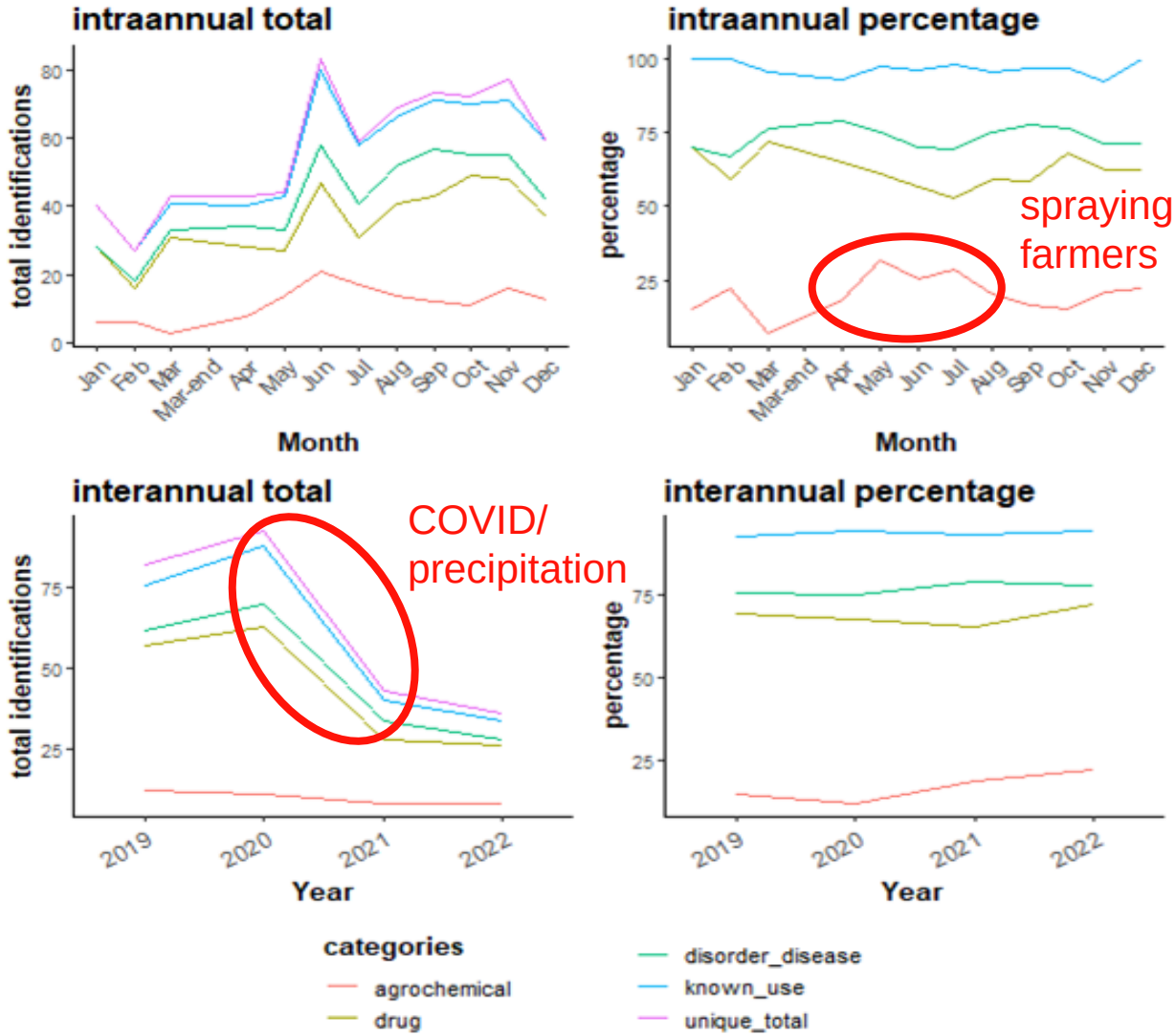
Example for 2021

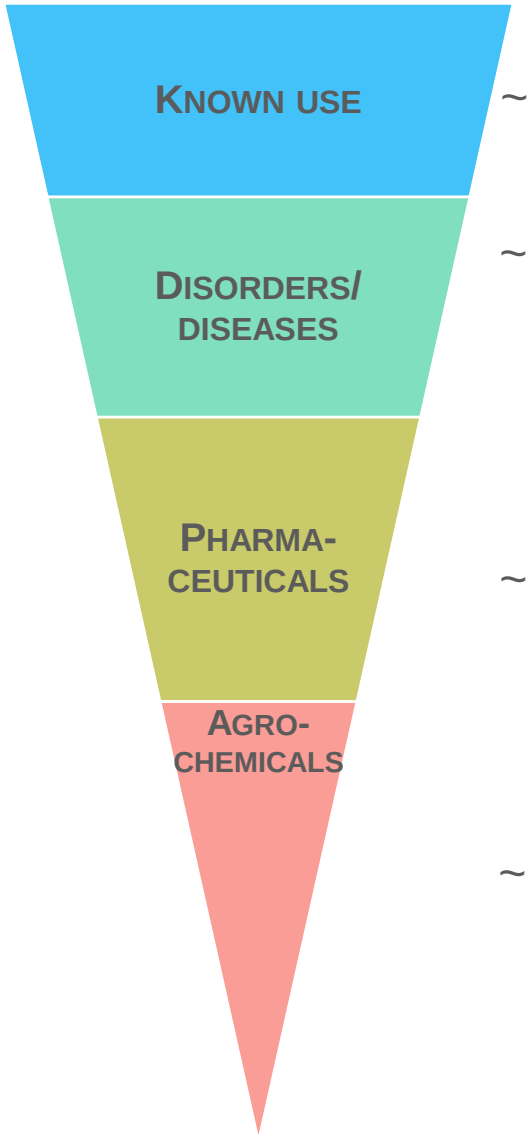
Image taken from Aurich D., et al. forthcoming, *Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg.* Preprint DOI: 10.21203/rs.3.rs-3136123/v1

CLASSIFICATION



TEMPORAL VARIATIONS





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Pollutants in Surface Waters

- Comparison to AGE monitoring lists (2019, 2020) and 2022 water report
  - ➢40 chemicals overlapping
  - ➢including 8 (of 16) catchment specific pollutants
  - ➢338 chemicals not covered by lists
    - ➢evaluation based on frequency of occurrence

      (number of months out of 34)
    - ➢exclusion of chemicals without environmental/health effect (PubChem)

Pollutants in Surface Waters

- Chemicals with high occurrence (not monitored by AGE):

Synonym	Use	Parent Name	PubChem CID	No of occurences
Irbesartan	pharmaceutical	-	3749	32
Amisulpride	pharmaceutical	-	2159	31
Telmisartan	pharmaceutical	-	65999	26
Celiprolol	pharmaceutical	-	2663	25
Fluconazole	pharmaceutical	-	3365	25
Trimethoprim	pharmaceutical	-	5578	24
4-Acetamidoantipyrine	pharmaceutical	Metamizole	65743	23
4-NP	industrial	-	980	22
Desvenlafaxine	pharmaceutical	Venlafaxine	125017	22
TCEP	flame retardant	-	8295	19
TCPP	flame retardant	-	26176	19
triethyl phosphate	industrial	-	6535	18
Adipic acid	industrial	-	196	18
4-Formylaminoantipyrine	pharmaceutical	Aminopyrine	72666	17
Carbamazepine-10,11-epoxide	pharmaceutical	Carbamazepine	2555	15
Dibutyl phthalate	industrial	-	3026	14
PFOA	industrial	-	9554	14
2-Hydroxycarbamazepine	pharmaceutical	Carbamazepine	129274	14
3-Hydroxypyridine	industrial	-	7971	13
Tributylamine	industrial	-	7622	13
D617	pharmaceutical	Verapamil	93168	13
Sulisobenzone	consumer products	-	19988	13
Ensulizole	consumer products	-	33919	13

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- some TPs appear more often than their (monitored) parent

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- OPFRs

Pollutants in Surface Waters

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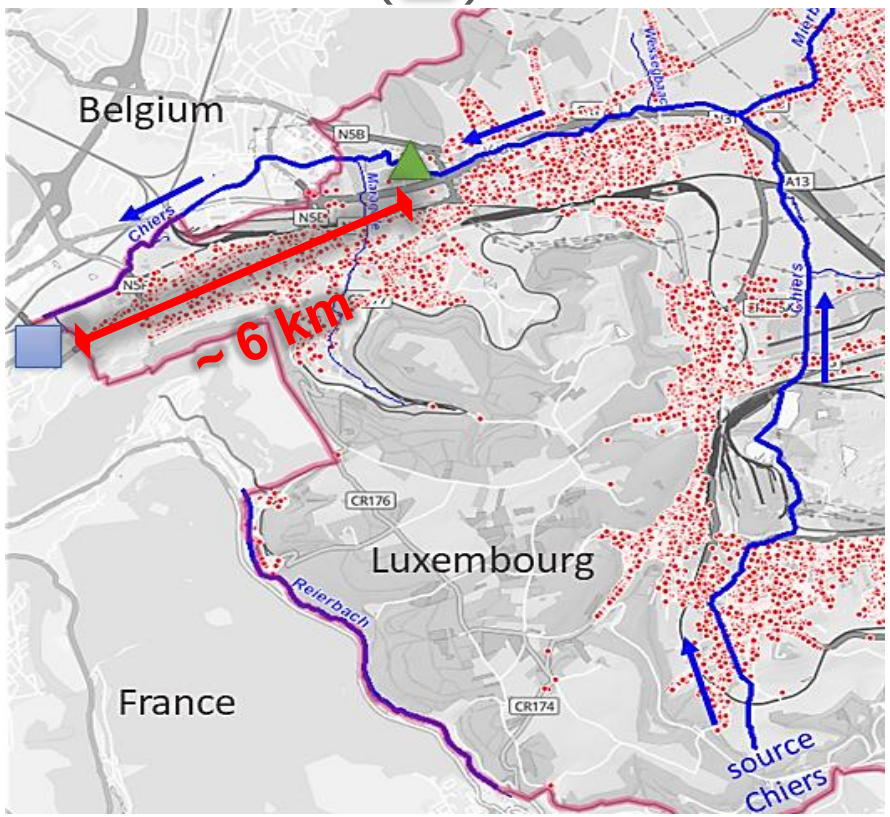
- industrial chemicals examples: 4-NP, DBP, PFOA…
- pharmaceuticals dominating

GEOGRAPHICAL VARIATIONS

- Example:
  - river Chiers (border to France)
  - comparison of results (▢) to WWTP inlet sampling ▲ (different 2022 study)



▲ WWTP Petange (sampling point) → 409 chemicals
▢ Sampling point AGE → 343 chemicals
↑ Flow direction Chiers
Addresses: Populated Region

Image modified from Aurich D., et al. forthcoming, *Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg.*
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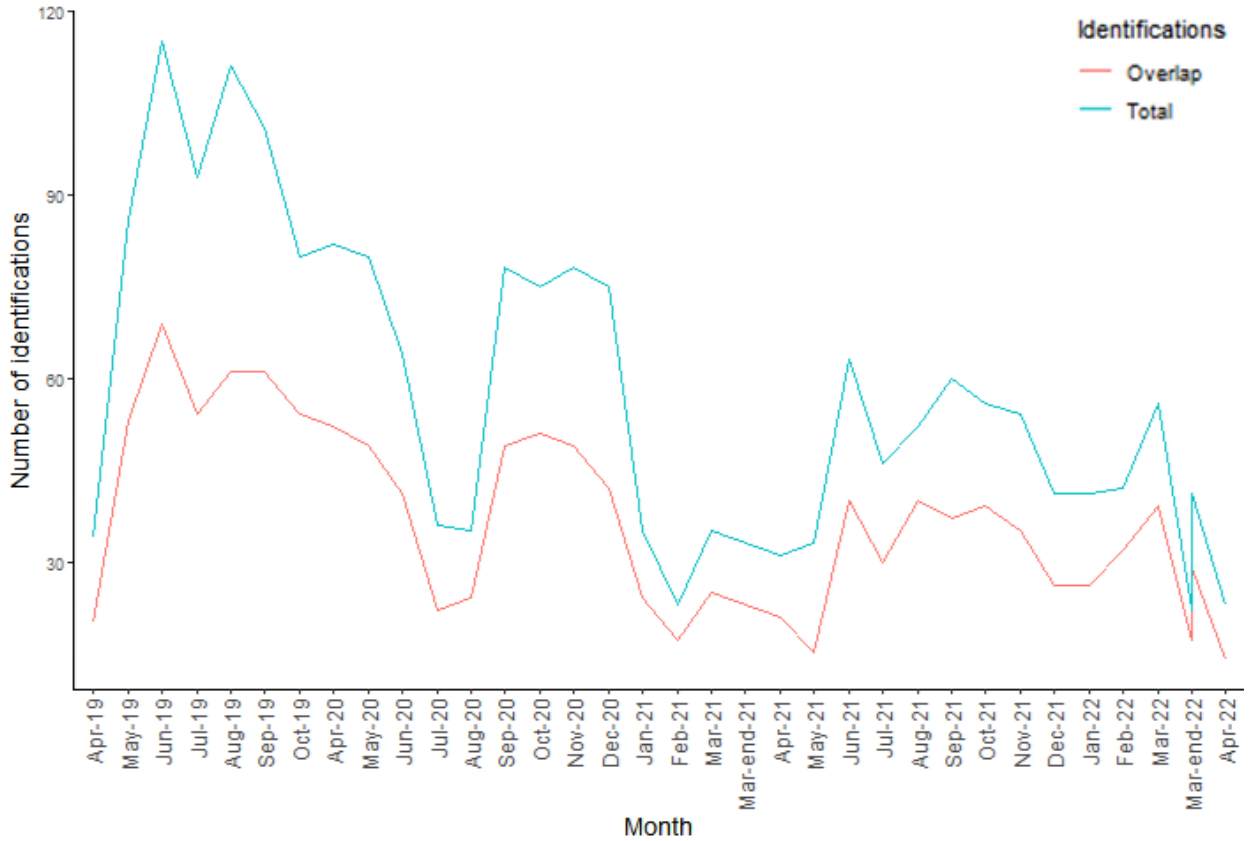
Potential Sources of Pollutants

- Example:
  - river Chiers (border to France)
  - comparison to prior WWTP inlet sampling (different study)



178 overlapping chemicals
(36 agrochemicals, 130 pharmaceuticals)

165 chemicals found only at border
(e.g. pregabalin, tramadol, benzotriazoles, PFNA, PFHpA…)

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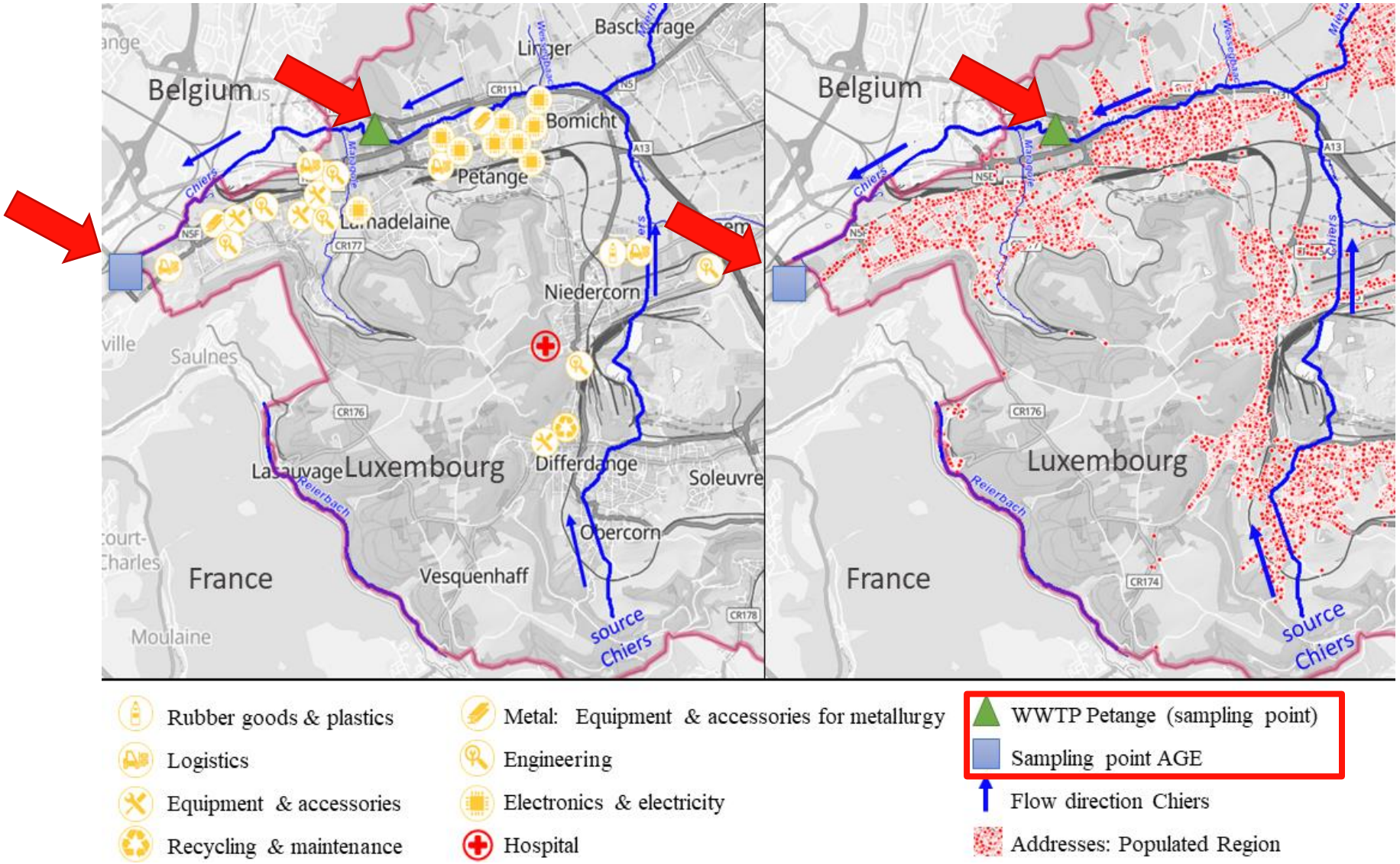

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Conclusion and Perspectives

- ✓ Study of exposome-related pollutants in surface water
  - ➢ annotation of 378 exposome-related chemicals
- ✓ Use of classification schemes, temporal patterns & geographical data
  - ➢ understand pollution sources and risks
- ✓ Use of NTA method as an addition to routine monitoring
- ❑ Future work:
  - ❑ Confirm and quantify annotated chemicals
  - ❑ Expand the monitoring list

Conclusion and Perspectives

- ✓ Study of exposome-related pollutants in surface water
  - ➢ annotation of 378 exposome-related chemicals
- ✓ Use of classification schemes, temporal patterns & geographical data
  - ➢ understand pollution sources and risks
- ✓ Use of NTA method as an addition to routine monitoring
- Future work:
  - Confirm and quantify annotated chemicals
  - Expand the monitoring list

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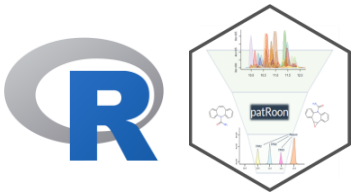

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ACKNOWLEDGEMENTS

University of Amsterdam

IBED

LE GOUVERNEMENT
DU GRAND-DUCHÉ DE LUXEMBOURG
Ministère de l'Environnement, du Climat
et du Développement durable

Administration de la gestion de l'eau

preprint

preprint

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code and data

DATA

GNPS

doi:10.25345/C55X25P62

UNIVERSITY OF LUXEMBOURG
Institute for Advanced Studies

LUXEMBOURG INSTITUTE OF SCIENCE AND TECHNOLOGY
LIST

C²DH uni.lu LCSB

Additional Material

Additional Material

- Target monitoring of Luxembourgish waters by AGE

LE GOUVERNEMENT
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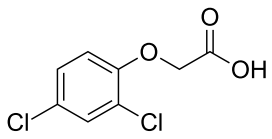
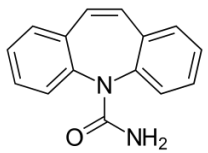
- Priority chemicals:
  - 2019 list: ~ 100 chemicals
  - 2020 list: ~ 200 chemicals

- 2022 water quality report:
  - ~ 80 chemicals/ chemical classes
  - 16 catchment specific chemicals





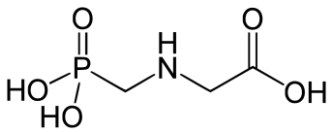
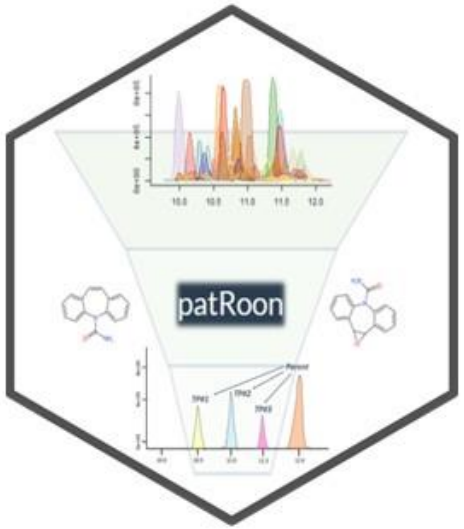
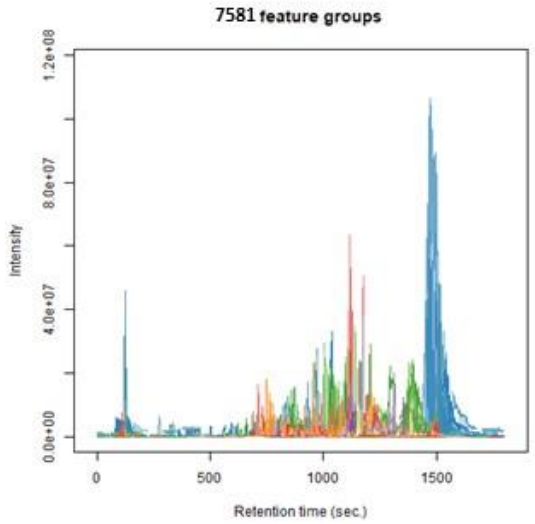


Image taken from Aurich D., et al. forthcoming, *Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg.* Preprint DOI: 10.21203/rs.3.rs-3136123/v1

ADDITIONAL MATERIAL





Raw files pre-treatment
`.mzML`
Example April 2020: **10** samples

Feature finding
`findFeatures()`
fListPos **75263** elements | fListNeg **43697** elements
fList **118960**

Feature grouping
`groupFeatures()`
60138 features in **9651** fGroups

Feature group filtering
`filter()`
24005 features in **7581** fGroups

Retrieve MS peak lists
`generateMSPeakLists()`
2144832 elements for
6290 pos features| **2782** neg features

MS peak list filtering
`filter()`
864274 elements for
959 pos features| **774** neg features

Retrieve compound structure candidates
`generateCompounds()`
15140 pos compounds | **12546** neg compounds
26097 elements

Tentative identification*
`Level 2, 3a or 3b`
76 pos compounds | **73** neg compounds
93 unique compounds

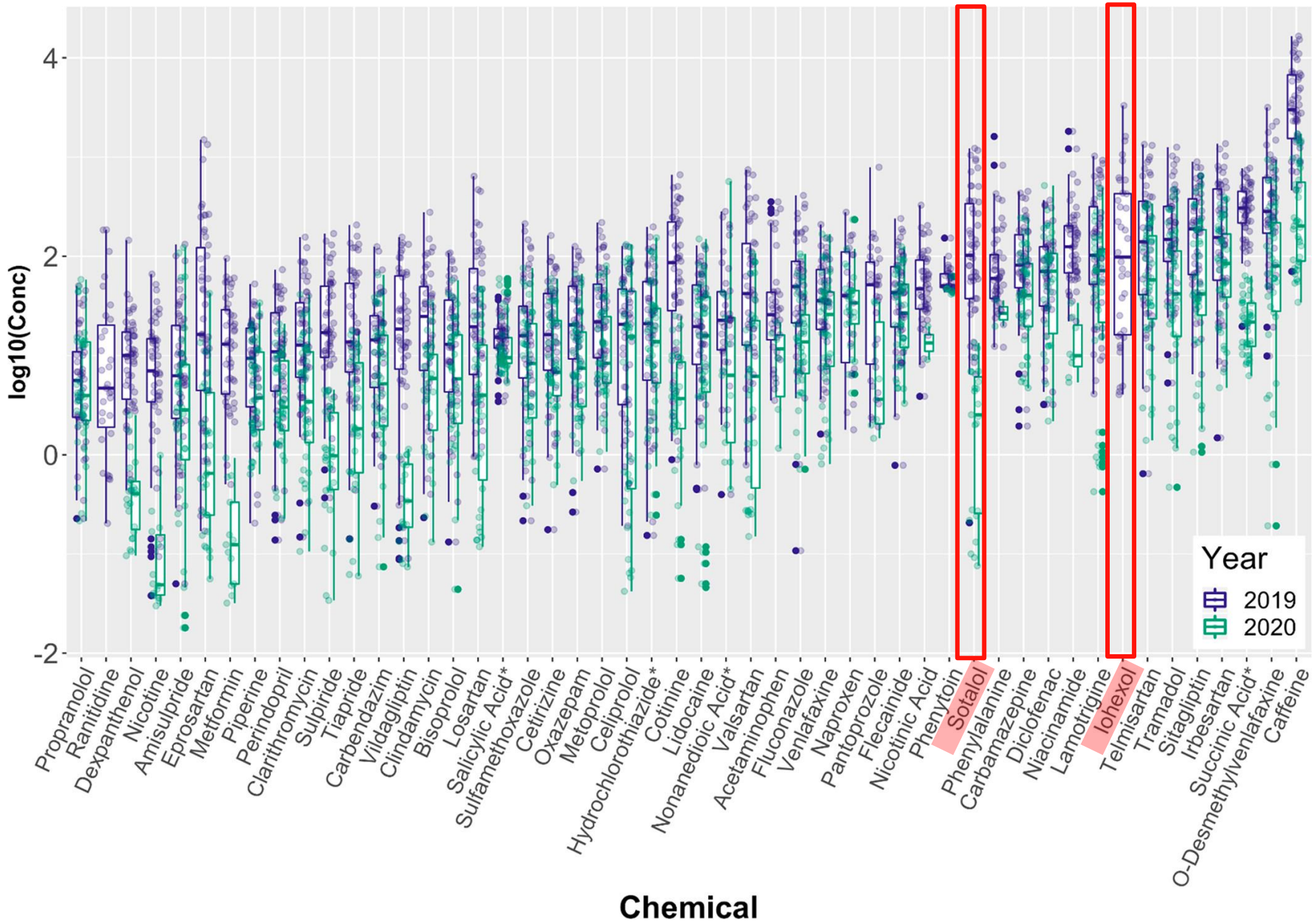
Example for April 2020

* Talavera Andújar et al.
DOI: 10.1007/s00216-022-04207-z

Image taken from Aurich D., et al. forthcoming, *Non-Target Screening of Surface Water Samples to Identify Exposome-Related Pollutants: A Case Study from Luxembourg.*
Preprint DOI: 10.21203/rs.3.rs-3136123/v1

Additional Material

Singh et al. 2021
DOI:10.1021/acsenvironau.1c00008



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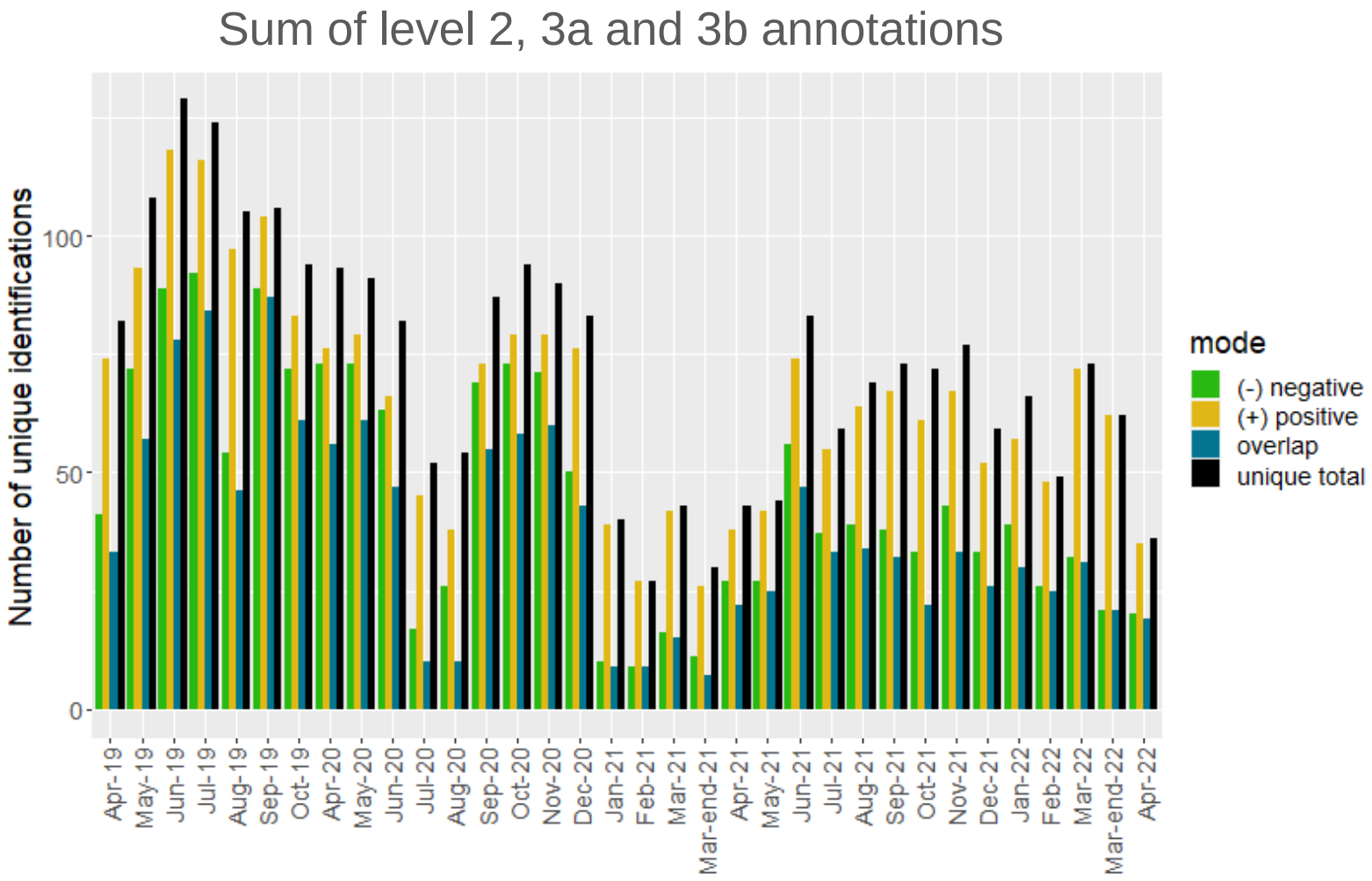

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Additional Material

- Focus only on agrochemicals (Krier et al.) or pharmaceuticals (Singh et al.)