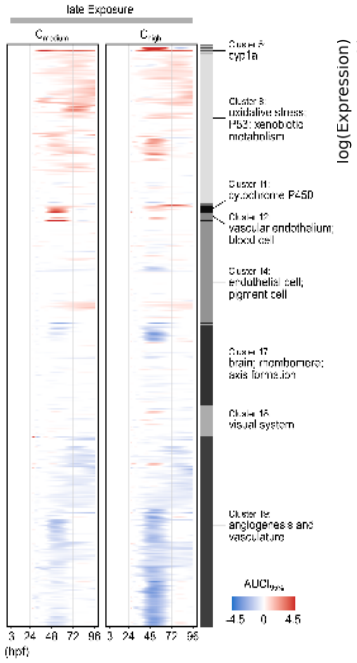
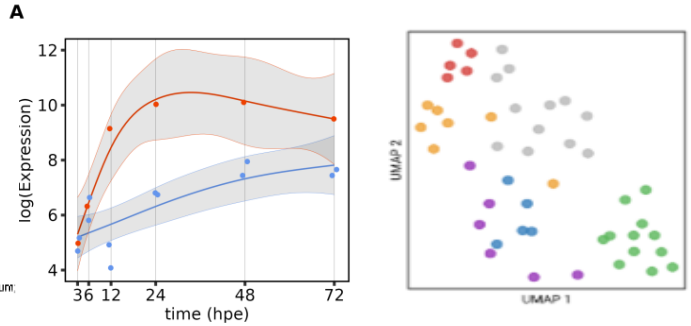
Integrative toxicology (iTOX) working group

Head:
Wibke Busch

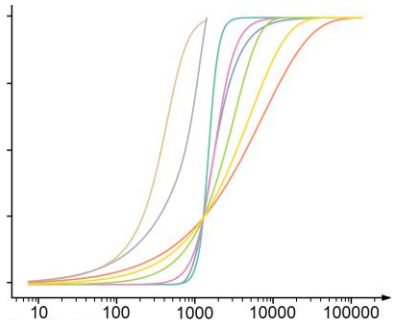
Toxicogenomics and data-driven toxicology with zebrafish embryos





- Software, statistics and AI for phenotypic data (e.g. gene expression, morphology)
- Patterns of responses linked to modes of action?

Mixture toxicology and environmental risk assessment



scientific data

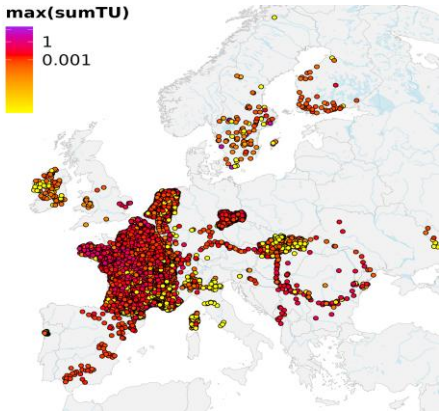
www.nature.com

OPEN

DATA DESCRIPTOR

Curated mode-of-action data and effect concentrations for chemicals relevant for the aquatic environment

- Mixture toxicology in the lab at different scales
- Data curation and mixture risk assessment with regulatory impact



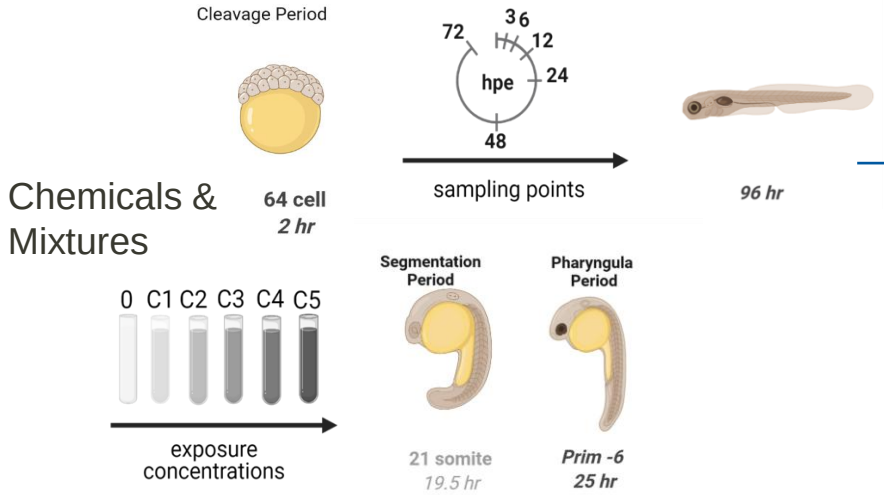
Integrative toxicology (iTOX) working group

Head: Wibke Busch

Toxicogenomics and data-driven toxicology with zebrafish embryos

NOT here today:
Samuel (PhD student)
Janet (Technician)

Small & large scale experiments (e.g. 3000 embryos)



Endpoints, Phenotypes

- Lethality
- Morphology
- Transcriptome
- Dose-Response
- Time-Response
- Internal conc.

Software and data analytics

INTOB

tfpbrowser

toxprofileR2

→ Talks by:

- Nils
- Arslan
- Berfin
- Paul
- Jasmin

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Head: Wibke Busch

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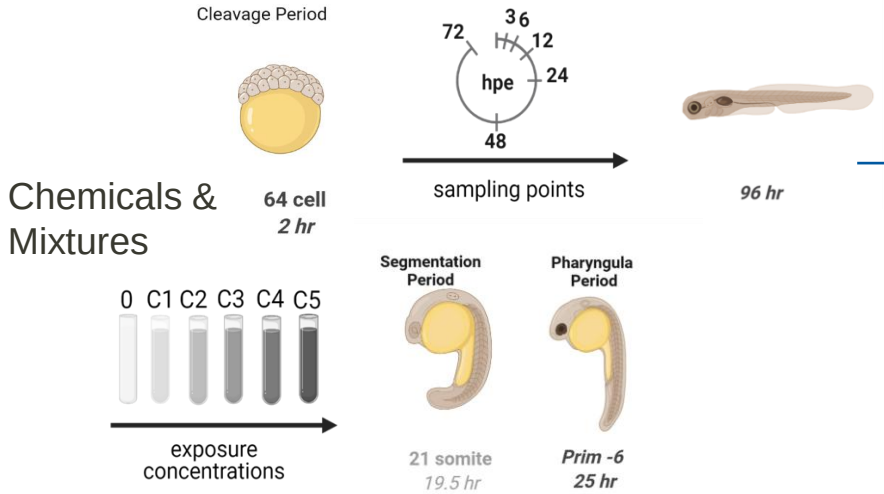

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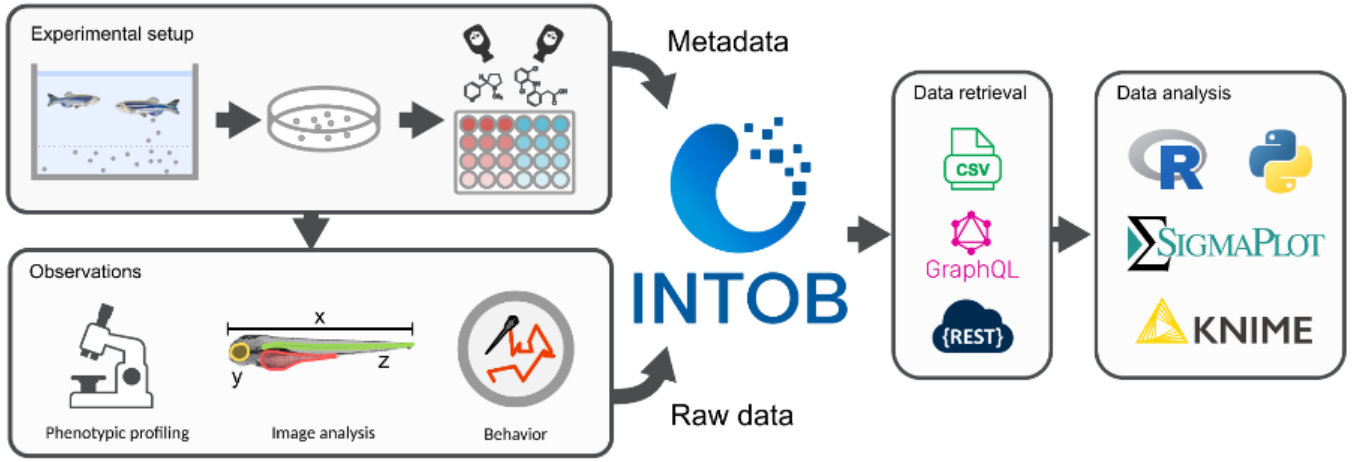
Mixture toxicology and environmental risk assessment

- Wibke

INTOB

Integrated effect data base for toxicological observations on organism scale

https://www.ufz.de/intob/



Findable
Accessible
Interoperable
Reusable

iTOX integrative toxicology

InfAI Institut für Angewandte Informatik

RDM Research Data Management

transfun inspiring ideas | accelerating application

- Own development 2019-2024 → market launch in mid 2024
- In house zebrafish effect data
  - 1417 experiments, 542 substances
- New features to be implemented (behaviour data, organisms, cells)
- FAIR principles for data management

INTOB

Integrated effect data base for toxicological observations on organism scale

https://www.ufz.de/intob/

Environmental Science & Technology

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pubs.acs.org/est

Article

Leveraging Zebrafish Embryo Phenotypic Observations to Advance Data-Driven Analyses in Toxicology

Paul Michaelis,[⊥] Nils Klüver,[*,⊥] Silke Aulhorn, Hannes Bohring, Jan Bumberger, Kristina Haase, Tobias Kuhnert, Eberhard Küster, Janet Krüger, Till Luckenbach, Riccardo Massei, Lukas Nerlich, Sven Petruschke, Thomas Schnicke, Anton Schnurpel, Stefan Scholz, Nicole Schweiger, Daniel Sielaff, and Wibke Busch[*]

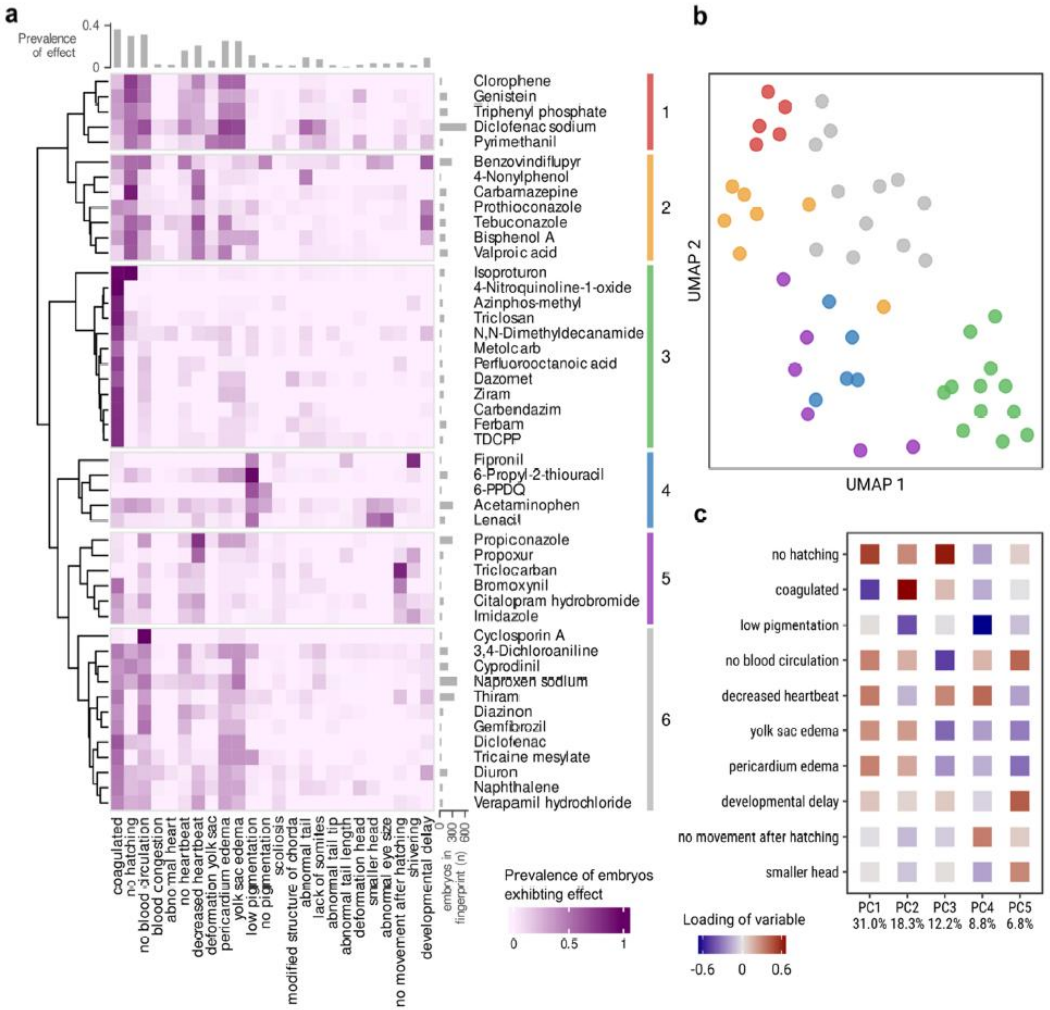
Cite This: *Environ. Sci. Technol.* 2025, 59, 4304–4317

Read Online

https://doi.org/10.1021/acs.est.4c11757

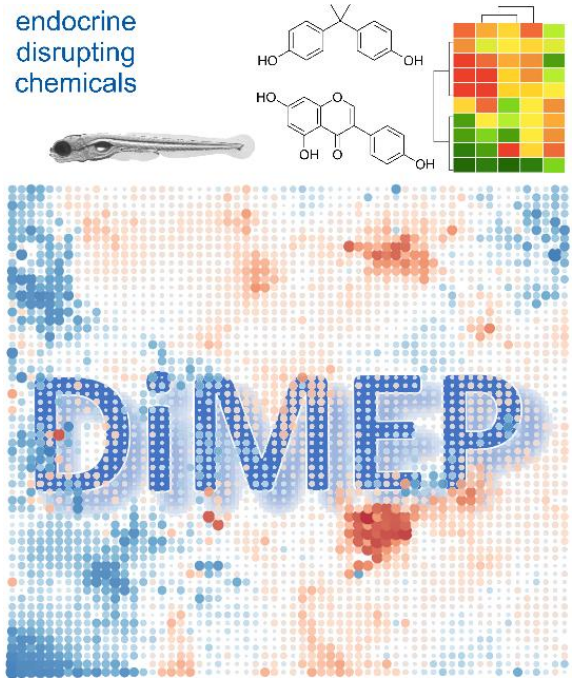
- Used only manually phenotypic effects assessment
- Phenotypic fingerprint of chemical effects
- potential to be used to infer MoA
- INTOB enables improved data management of toxicological data including metadata

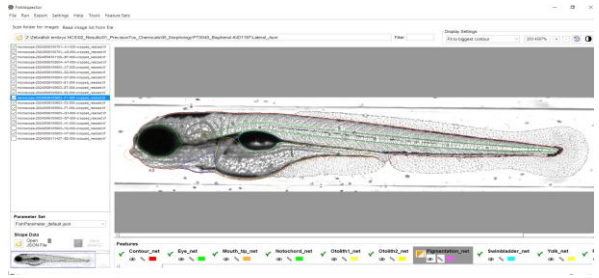
→ Precision Tox; DiMEP;…

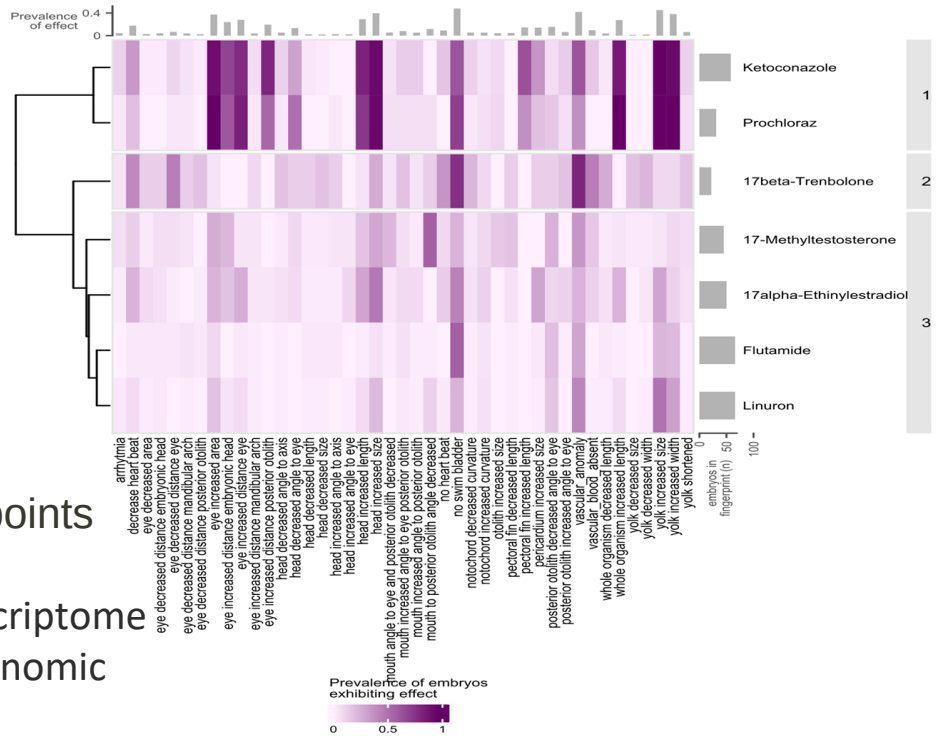


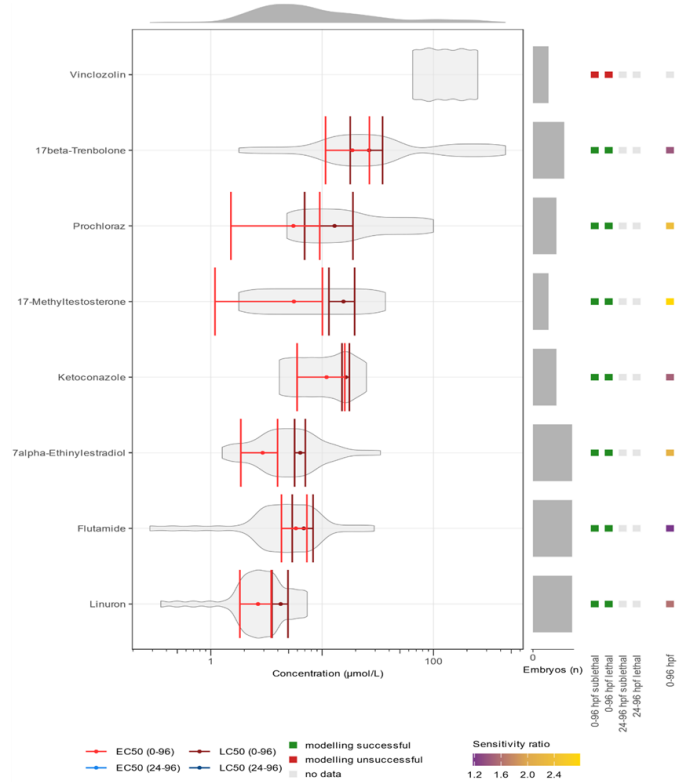
DiMEP

„phenotypic and molecular effect endpoints of EDCs in ZFE“









- Image based analysis (FishInspector)
  - More than 40 morphological endpoints

- Selecting sublethal concentration for transcriptome analysis → Data analysis pipeline (Toxicogenomic Fingerprint Browser)

Federal Ministry of Education and Research

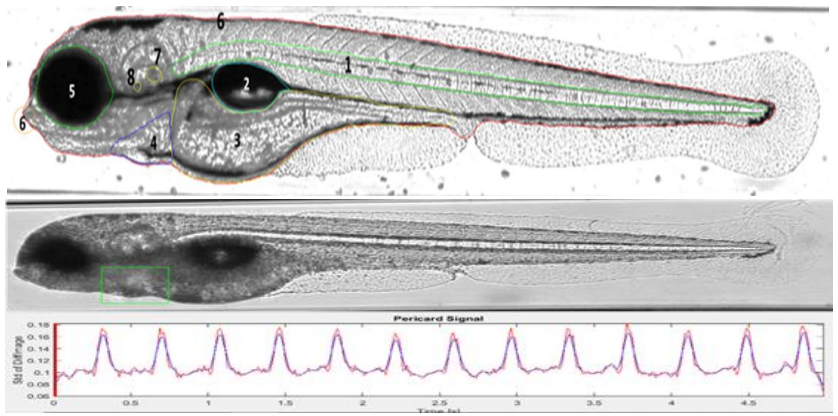
Introduction & Objective

Old Data on Z: Drive

Lack of Systematic Naming

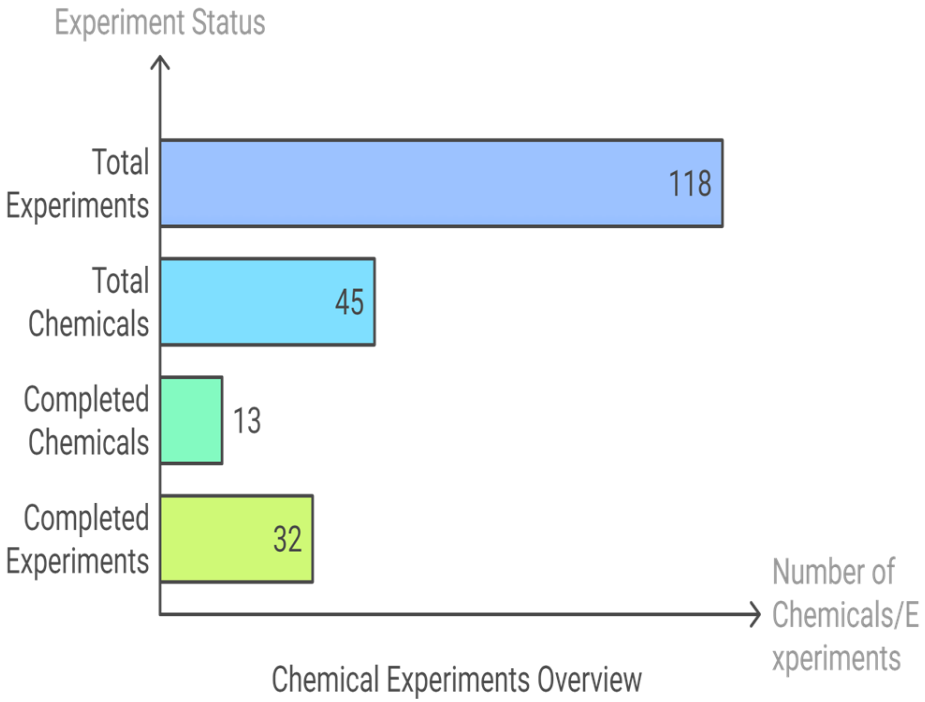
Data Needs Analysis

Uploading



Annotations

Heart Rate



Chemical Experiments Overview

Baseline Ranges & Analysis

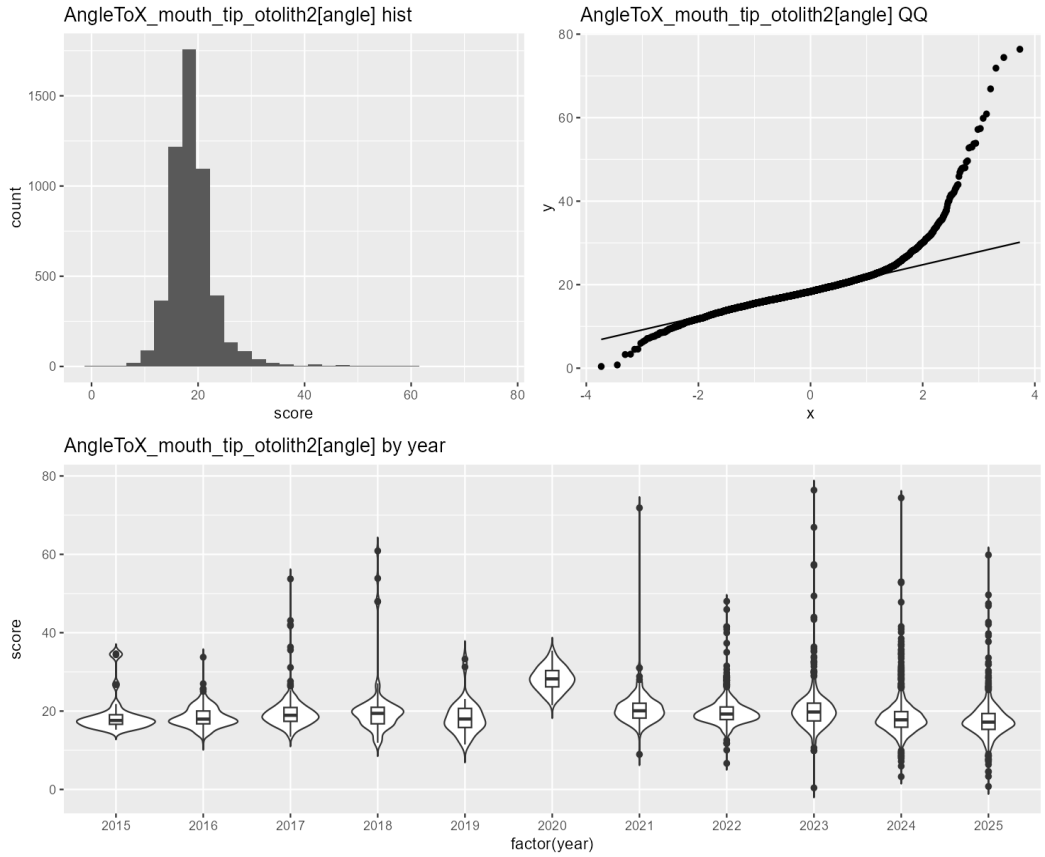
Converting the DATA into Binary:

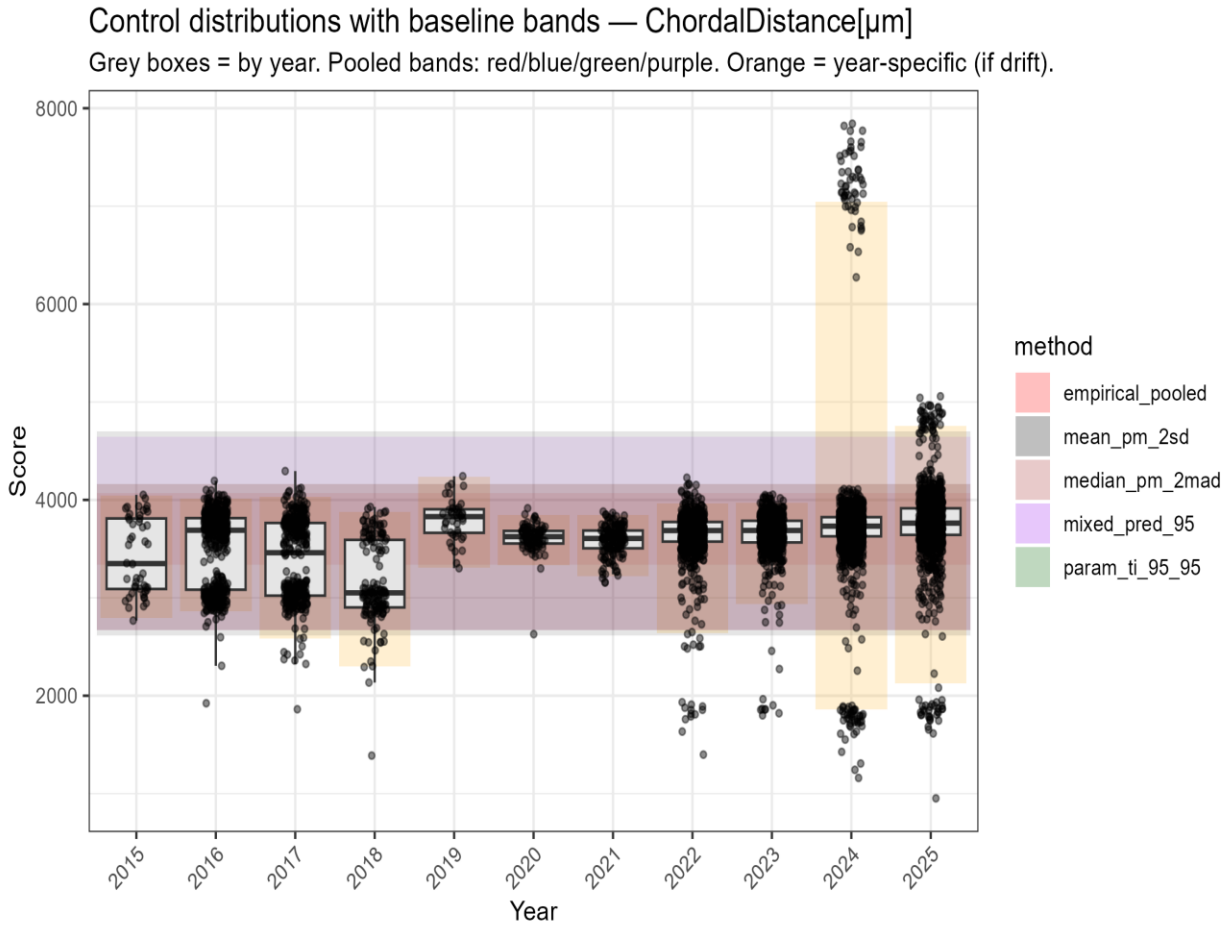
Uses Ranges of Historical Control DATA (HCD):

Observed data > Ranges (Mean + 2SD) = 1 (increasing)

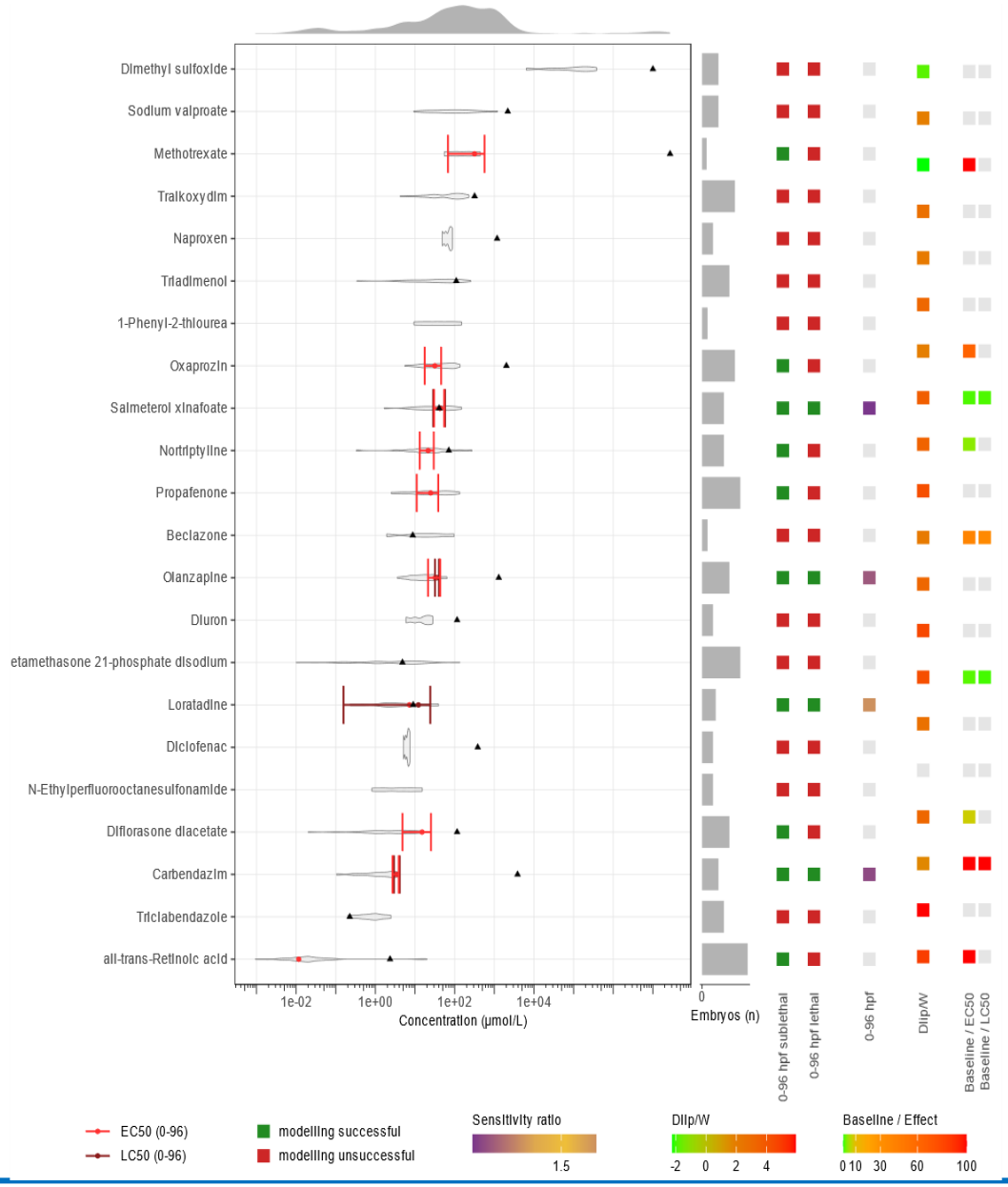
Observed data < Ranges (Mean + 2SD) = 1 (Decreasing)

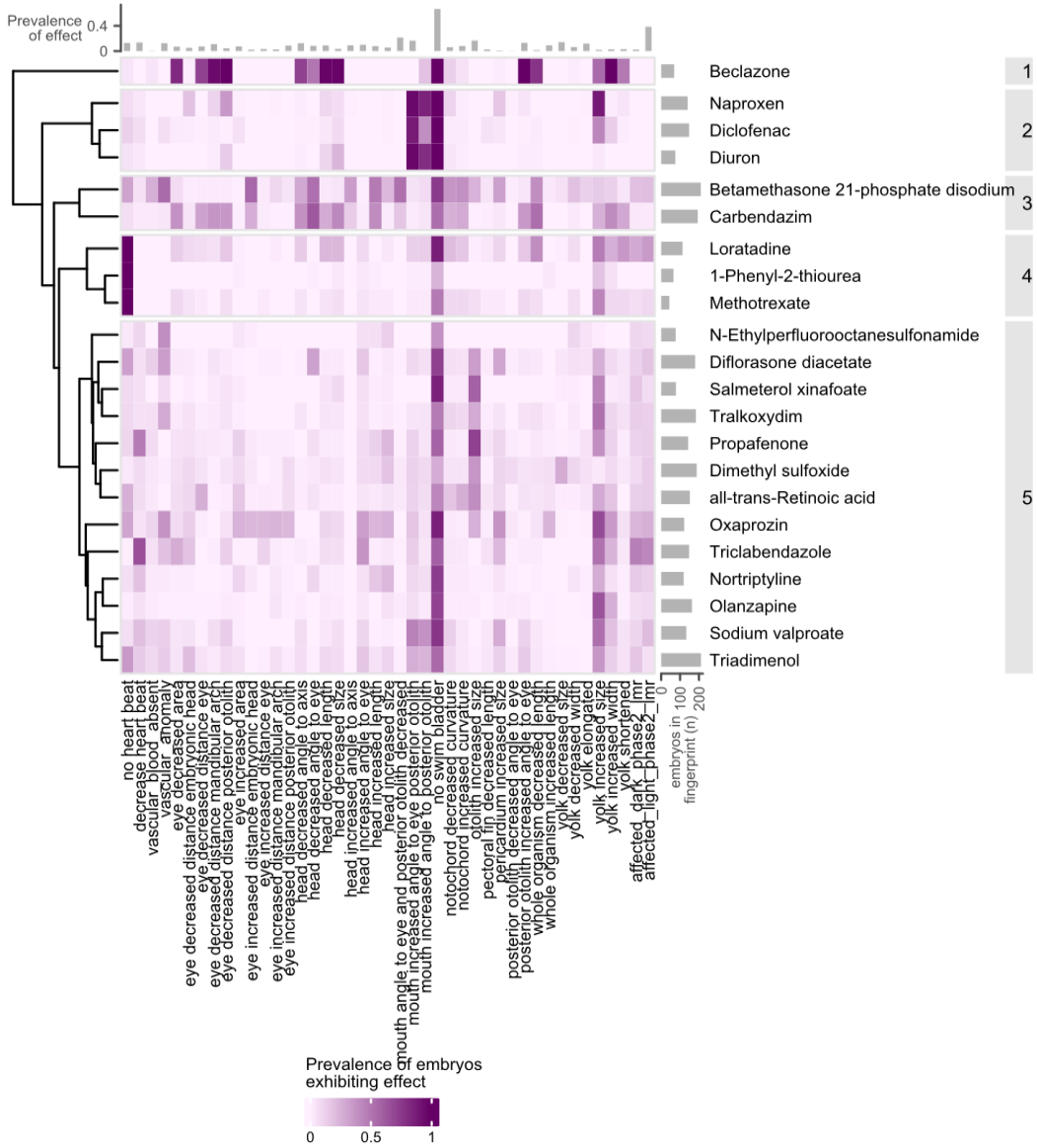
Observed data <> Ranges (Mean + 2SD) = 0





Digital Phenotypic Fingerprints



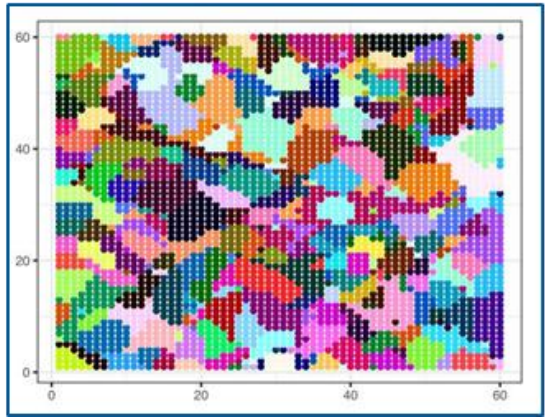


Toxicological map of the zebrafish transcriptome

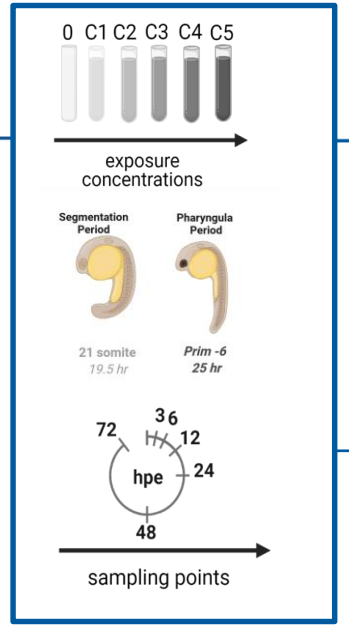
(ToxSOM)

Training Data
Gene expression data from zebrafish embryos exposed to various chemicals

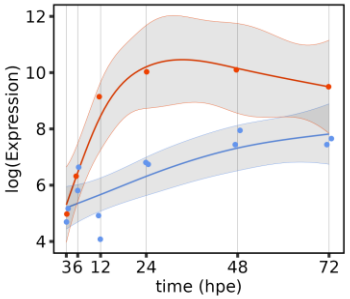
SOM Mapping
Gene response profiles organized on 60x60 SOM based on co-expression patterns in training data



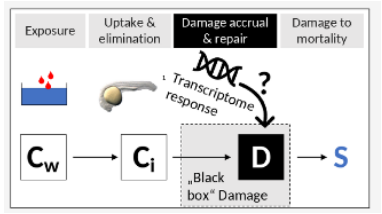
Schüttler et al. 2019, GigaScience



New Data Visualization
Map new data onto existing SOM



Nöth et al. 2025, Archives in Toxicology



Schunck et al. 2024, ES&T

The ZFE toxicogenomic browser

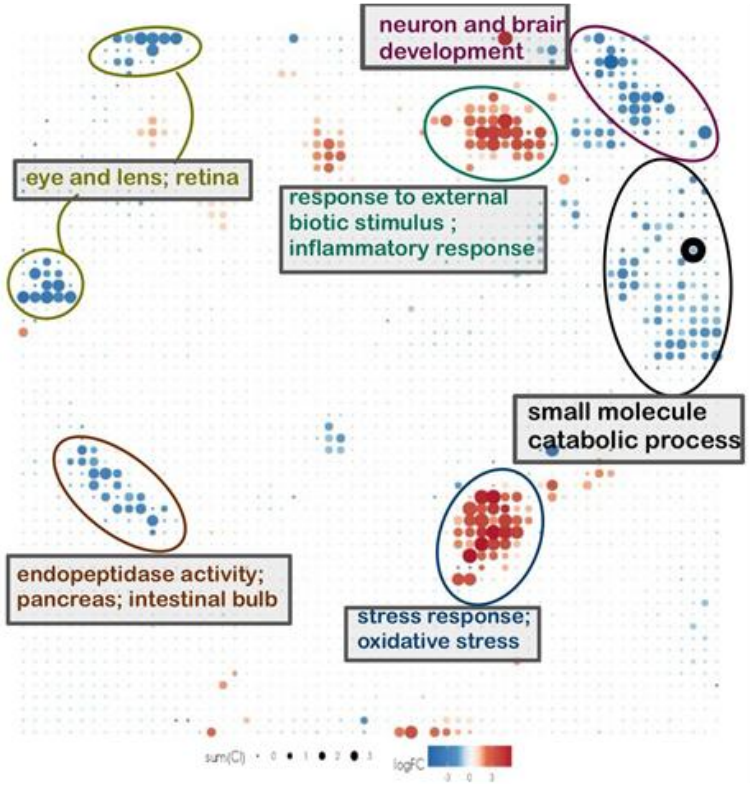
webapp.ufz.de/itox/tfpbrowser/

- ➔ 92 compounds
- ➔ 35 studies

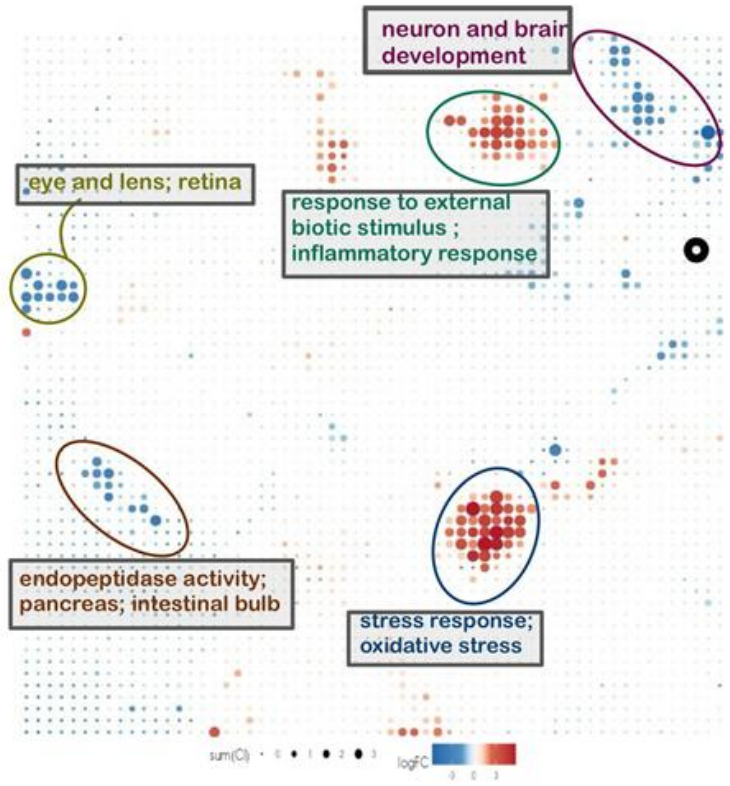
ToxSOM fingerprints

Common responses

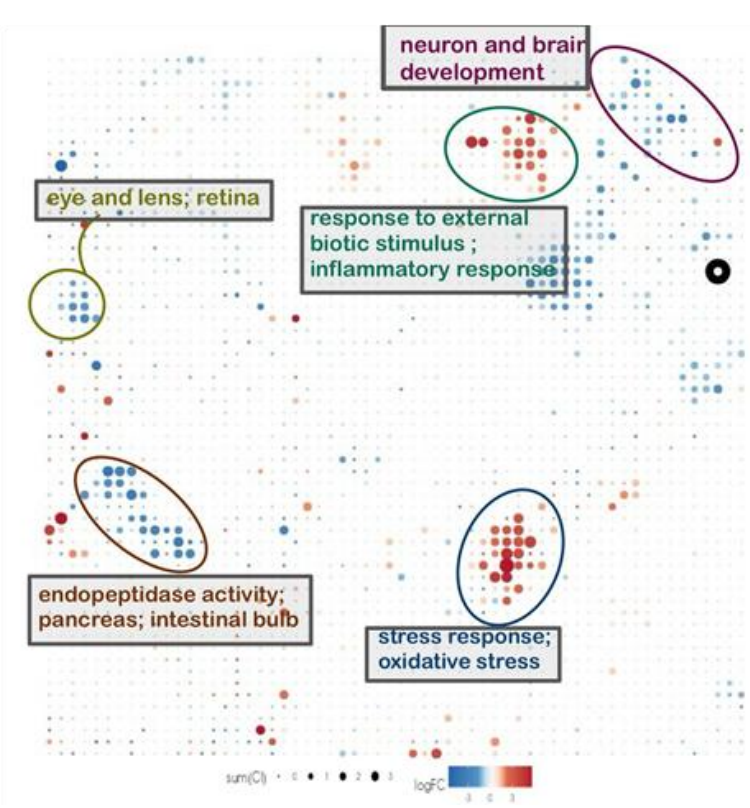
Mixture of 13 chemicals 96 hpf



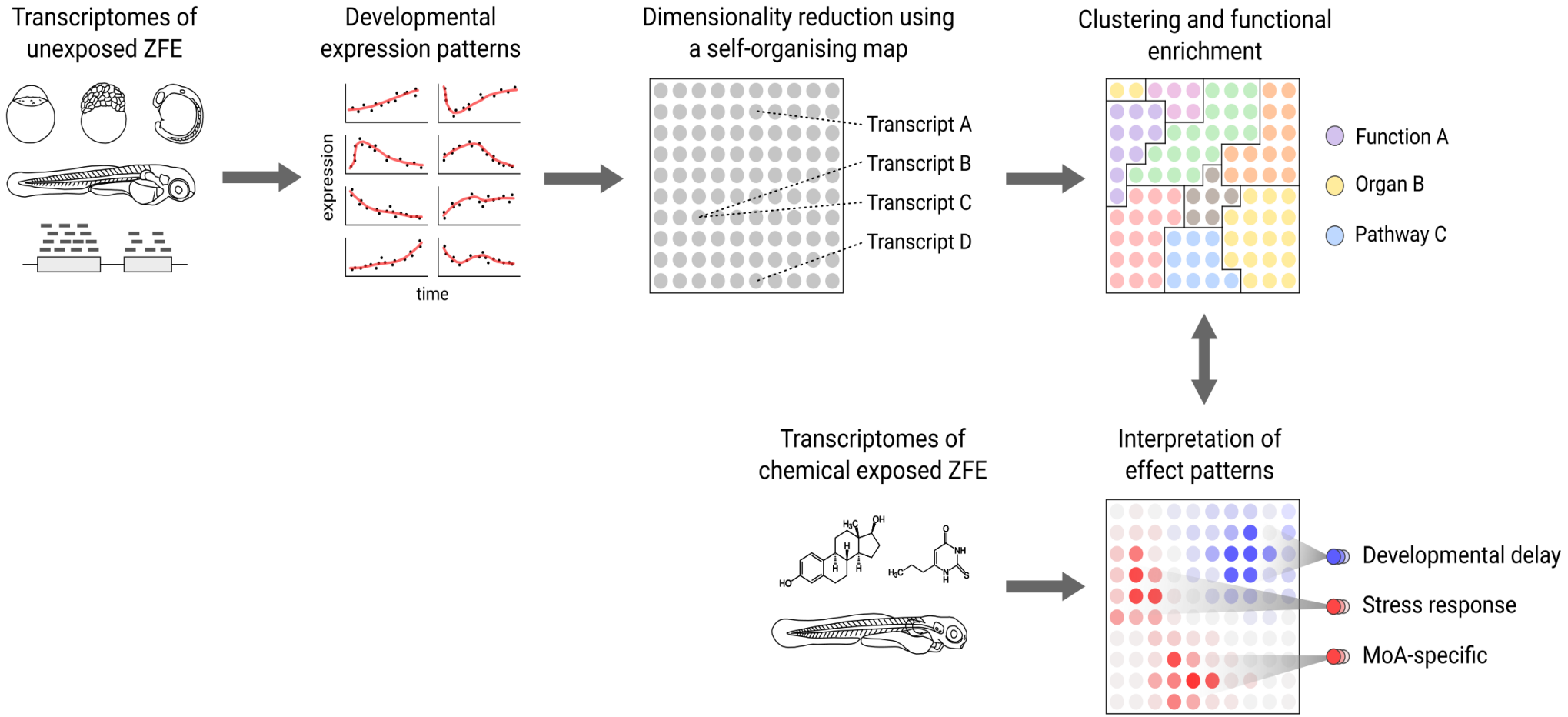
Naproxen Sodium 96 hpf



Flutamide 96 hpf



The developmental self-organising map (devSOM)



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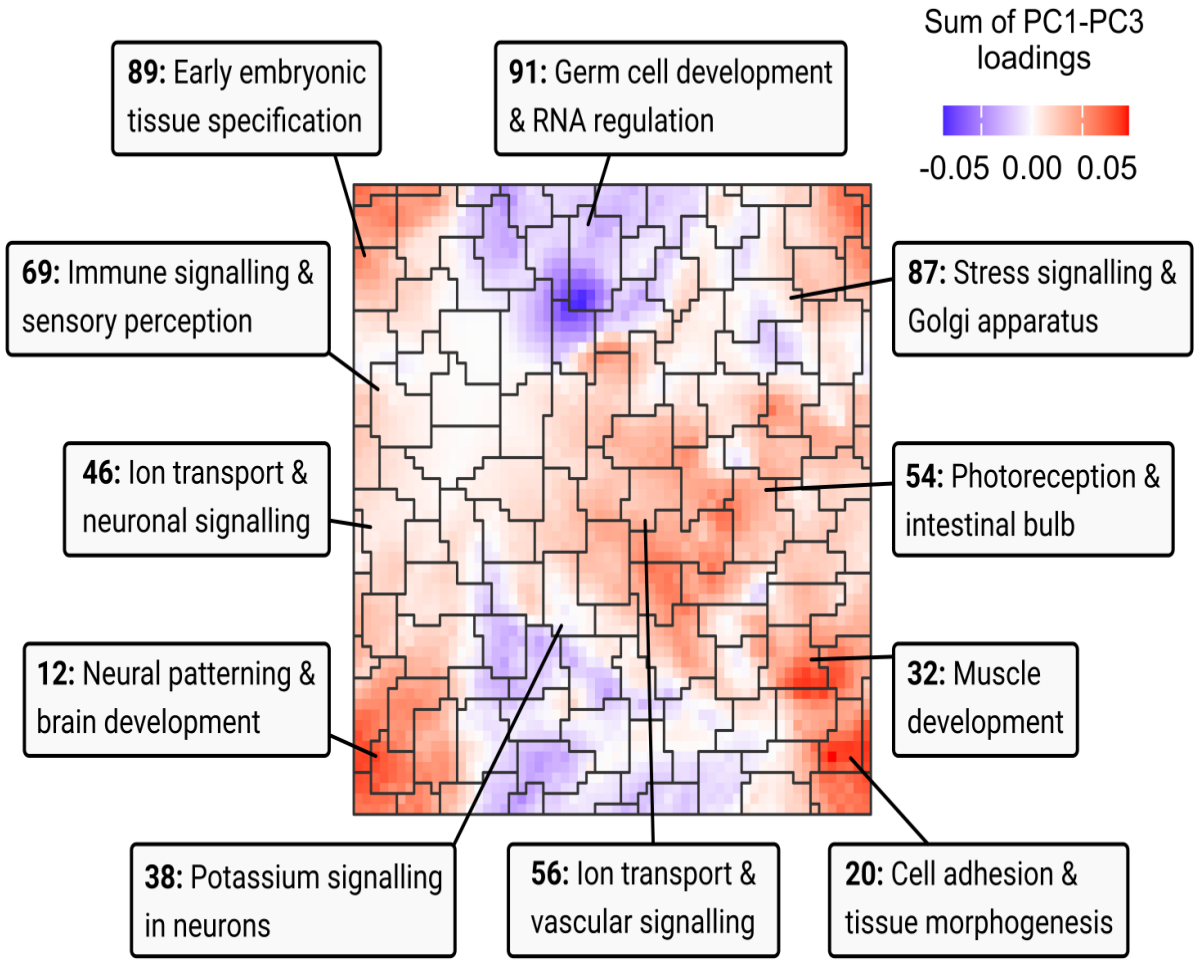
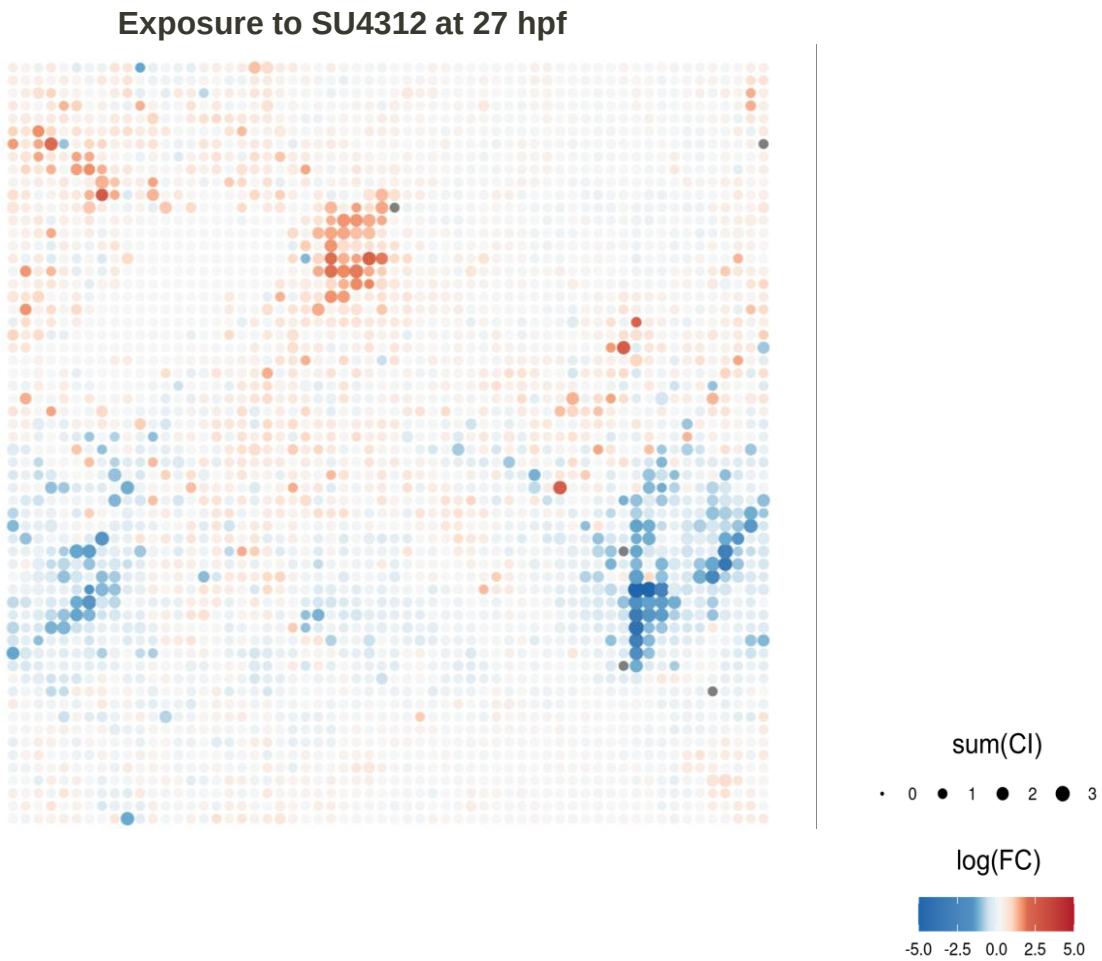
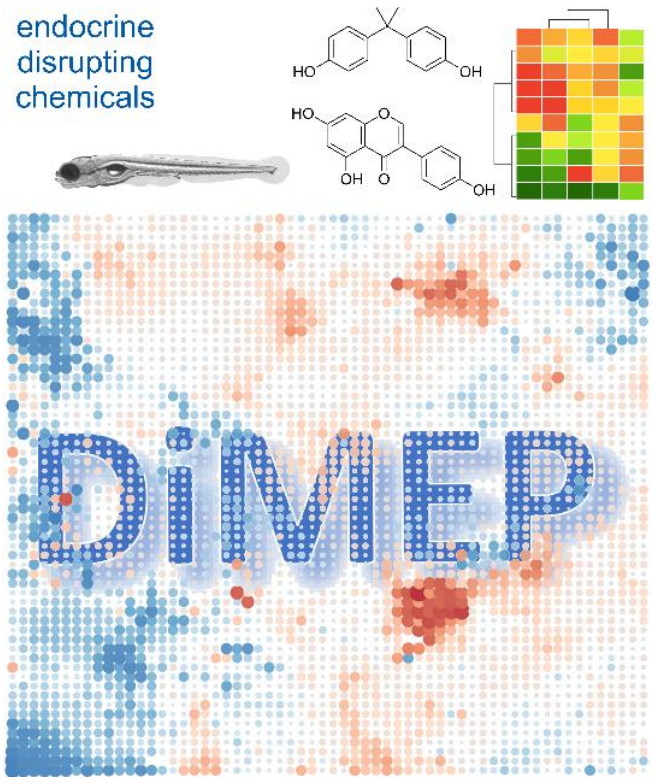




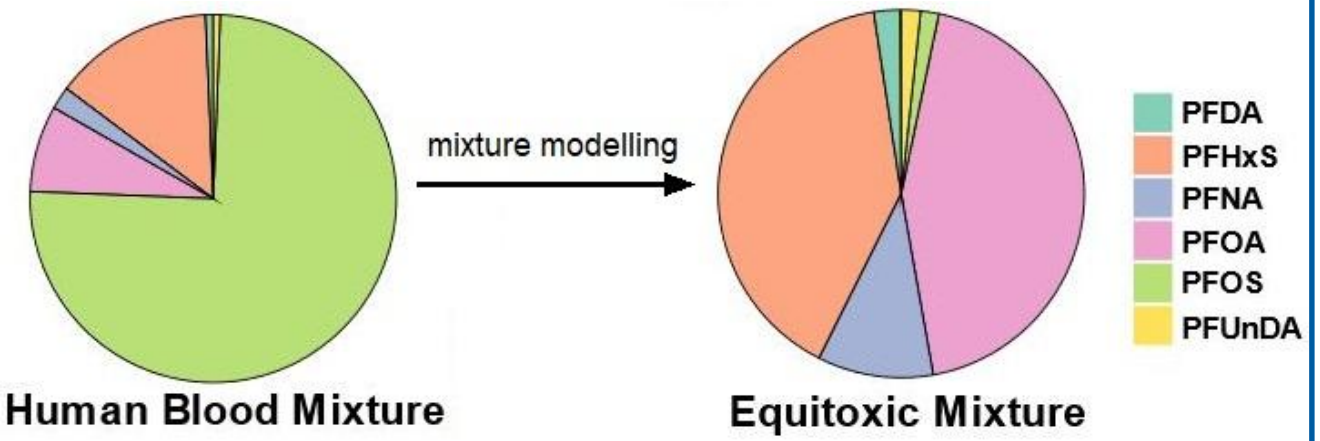
SOM fingerprints – coming soon

Specific responses on ToxSOM and DevSOM?

endocrine disrupting chemicals



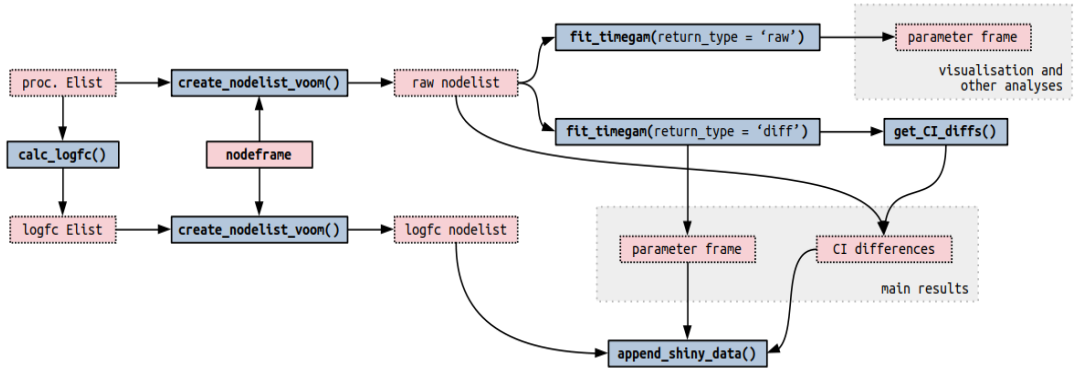
PFAS mixtures

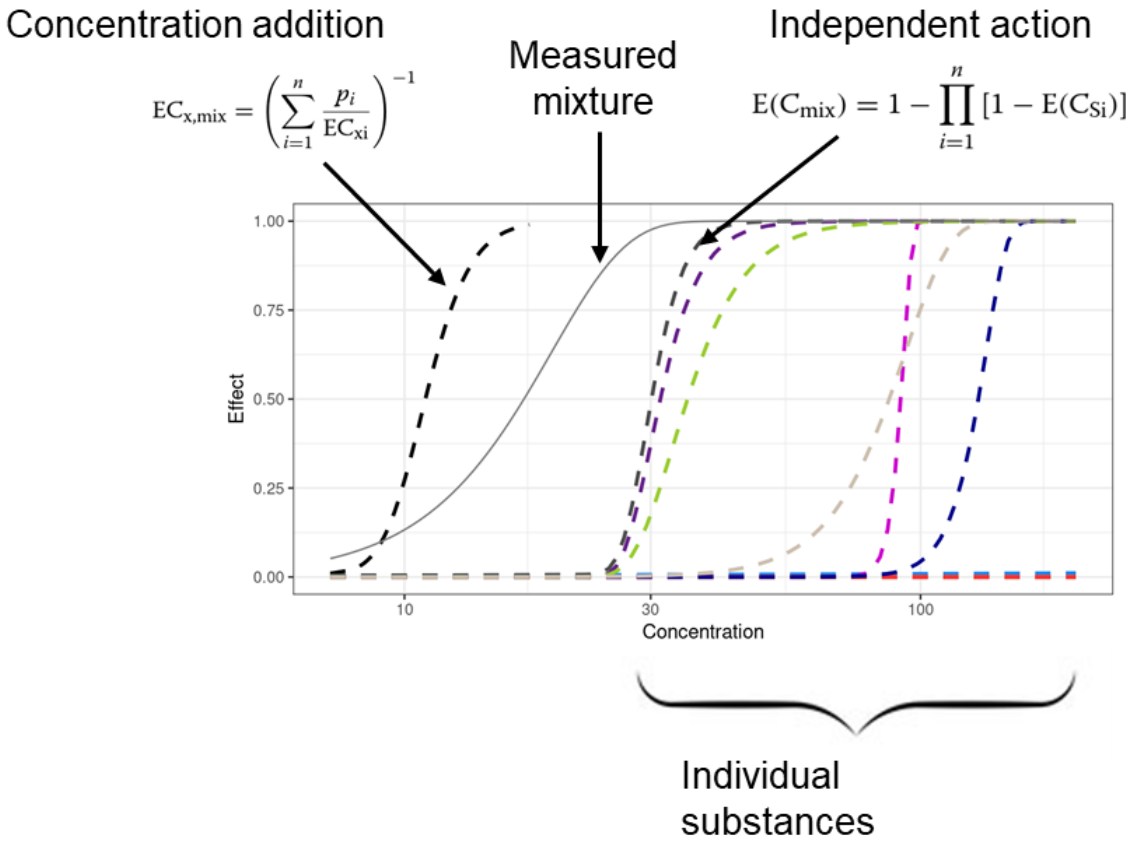


Plant protection products

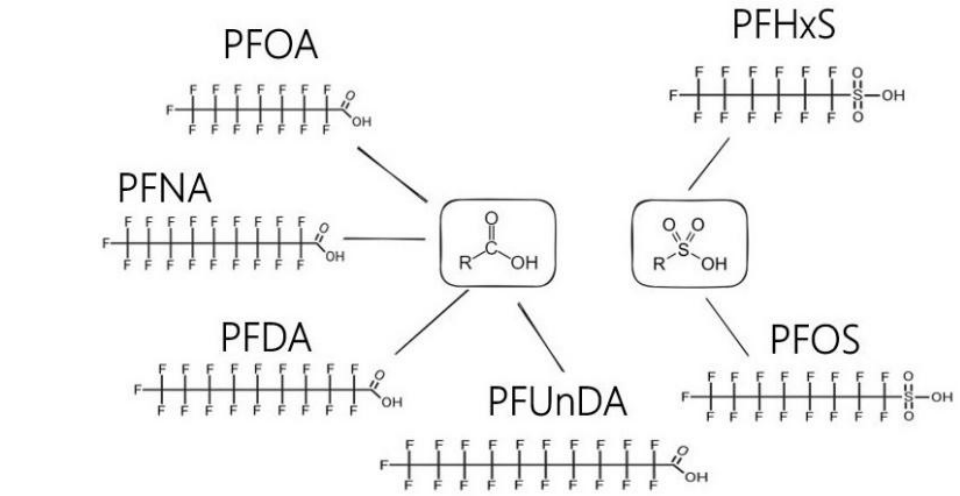
Data science and bioinformatics

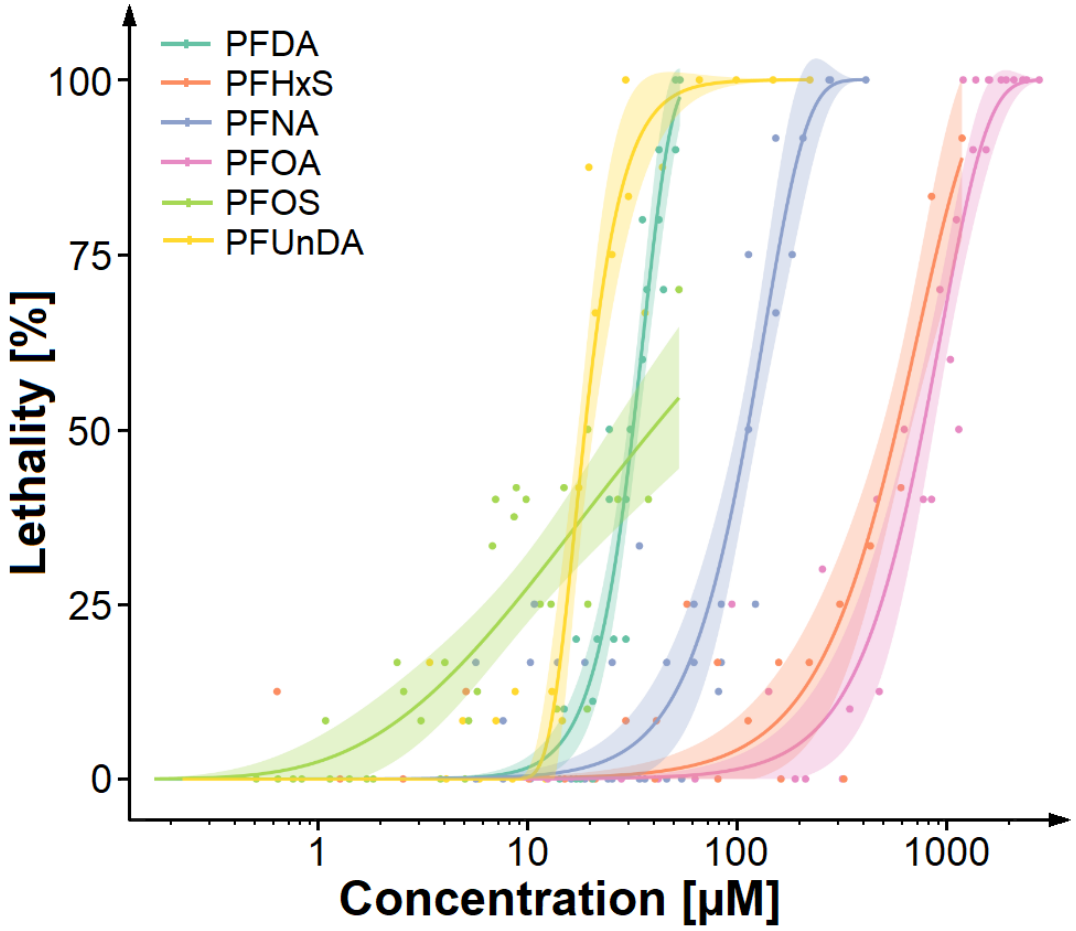
- FAIR data management
- Documentation
- Scripts and workflows
  - INTOB
  - Transcriptomics





Toxicological analysis of selected PFAS as single substances and mixtures using the zebrafish embryo acute toxicity test





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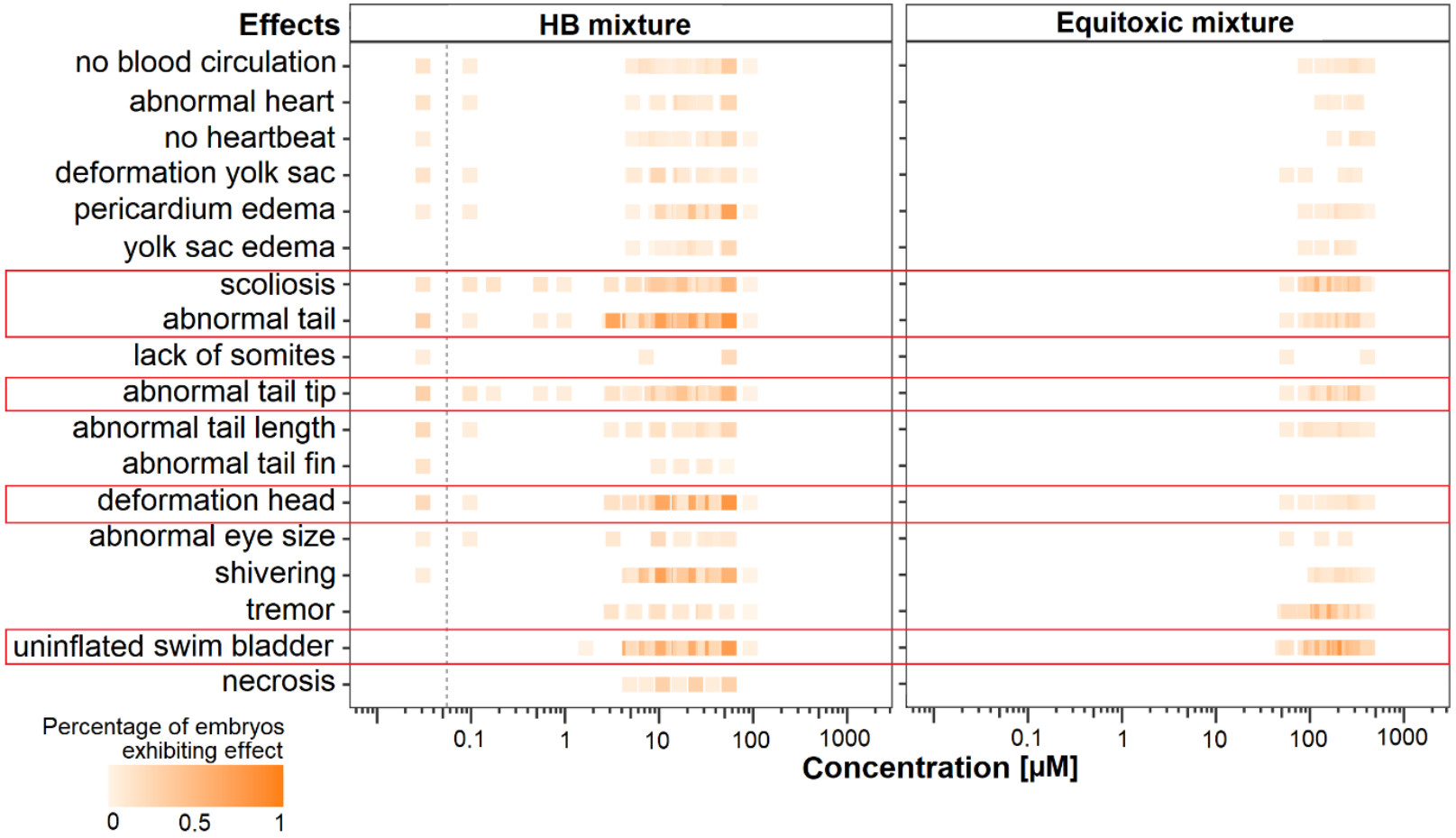

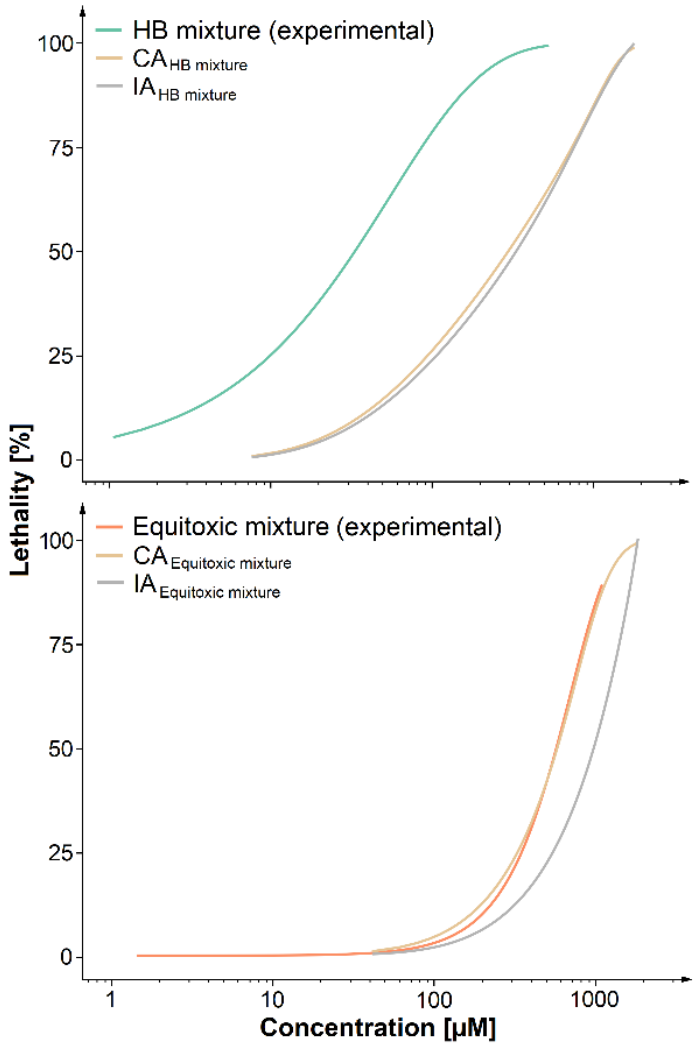

Integrative toxicology (iTOX) working group

Head: Wibke Busch

Mixture toxicology and environmental risk assessment

Data curation and mixture risk assessment with regulatory impact

scientific data

www.nature.com

OPEN

DATA DESCRIPTOR

Curated mode-of-action data and effect concentrations for chemicals relevant for the aquatic environment

Kramer et al. 2024, Sci. Data *10.5281/zenodo.7983816*

European waste water treatment plant effluent reference mixture (RefMix80)

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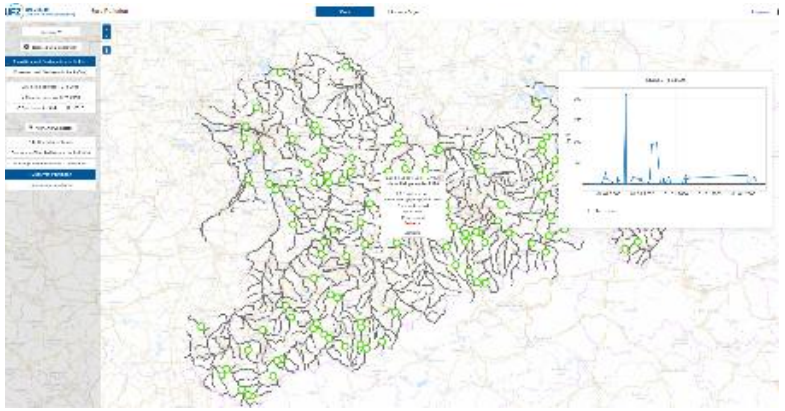
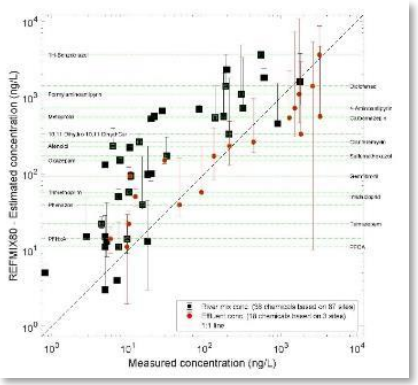
https://web.app.ufz.de/gdi/0-pollution



*Dichgans et al (2024): Dataset of **River Water Quality for Saxony**, Germany, **1985-2023** [dataset] 10.1594/PANGAEA.969111*

- **Thuringia 2017 – 2021**, 87 sites, 37 chemicals
- Predicted vs measured concentrations and impact of low water



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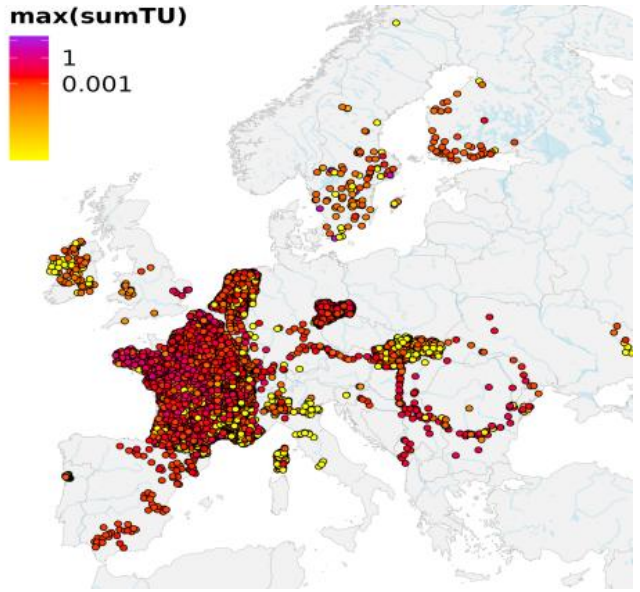
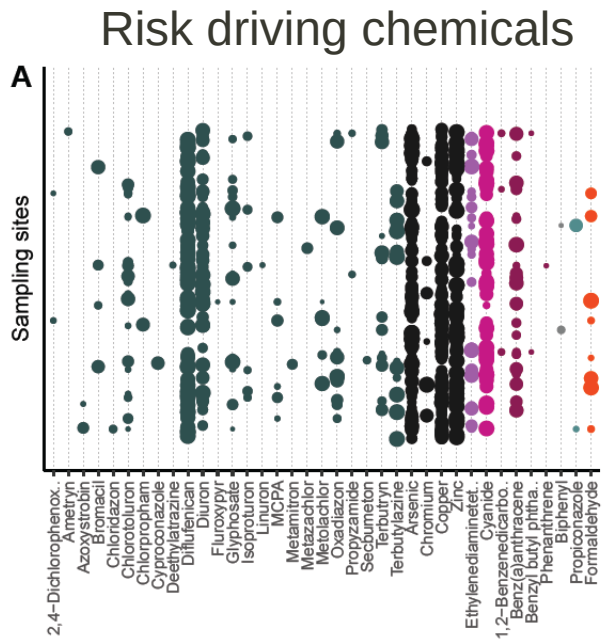
Mixture risk driver heterogeniety in Europe





Schor et al. under review

Mixture toxicology and environmental risk assessment

Data curation and mixture risk assessment with regulatory impact

scientific data

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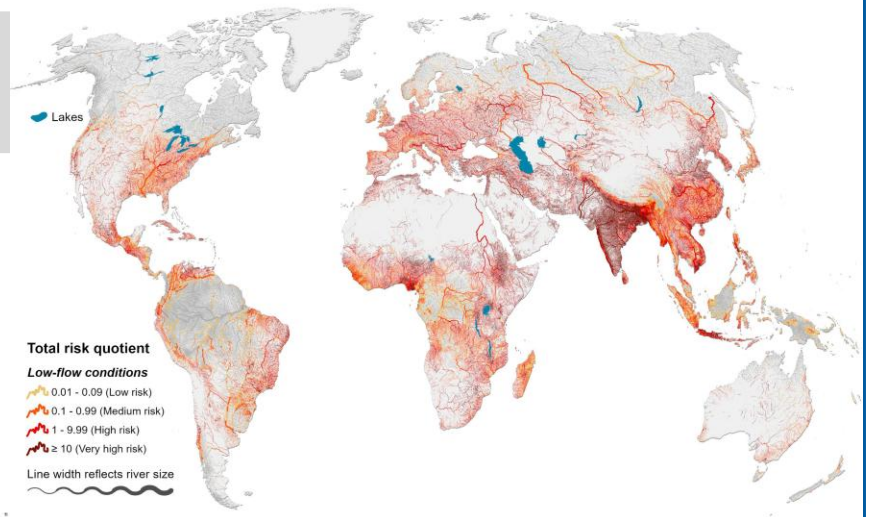
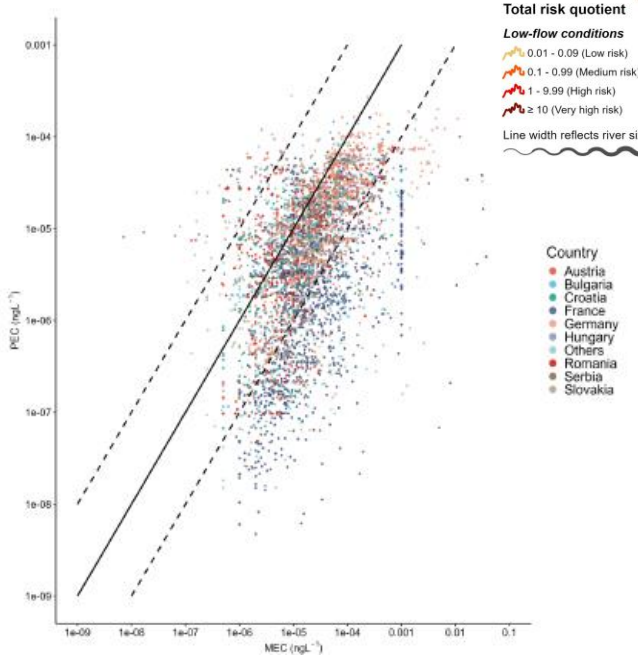
Mixture risk driver heterogeniety in Europe

Schor et al. under review

EU wide risk predictions





HydroFATE v1.1

McGill

Mixture toxicology and environmental risk assessment

Christian Weiß

Data curation and mixture risk assessment with regulatory impact

scientific data

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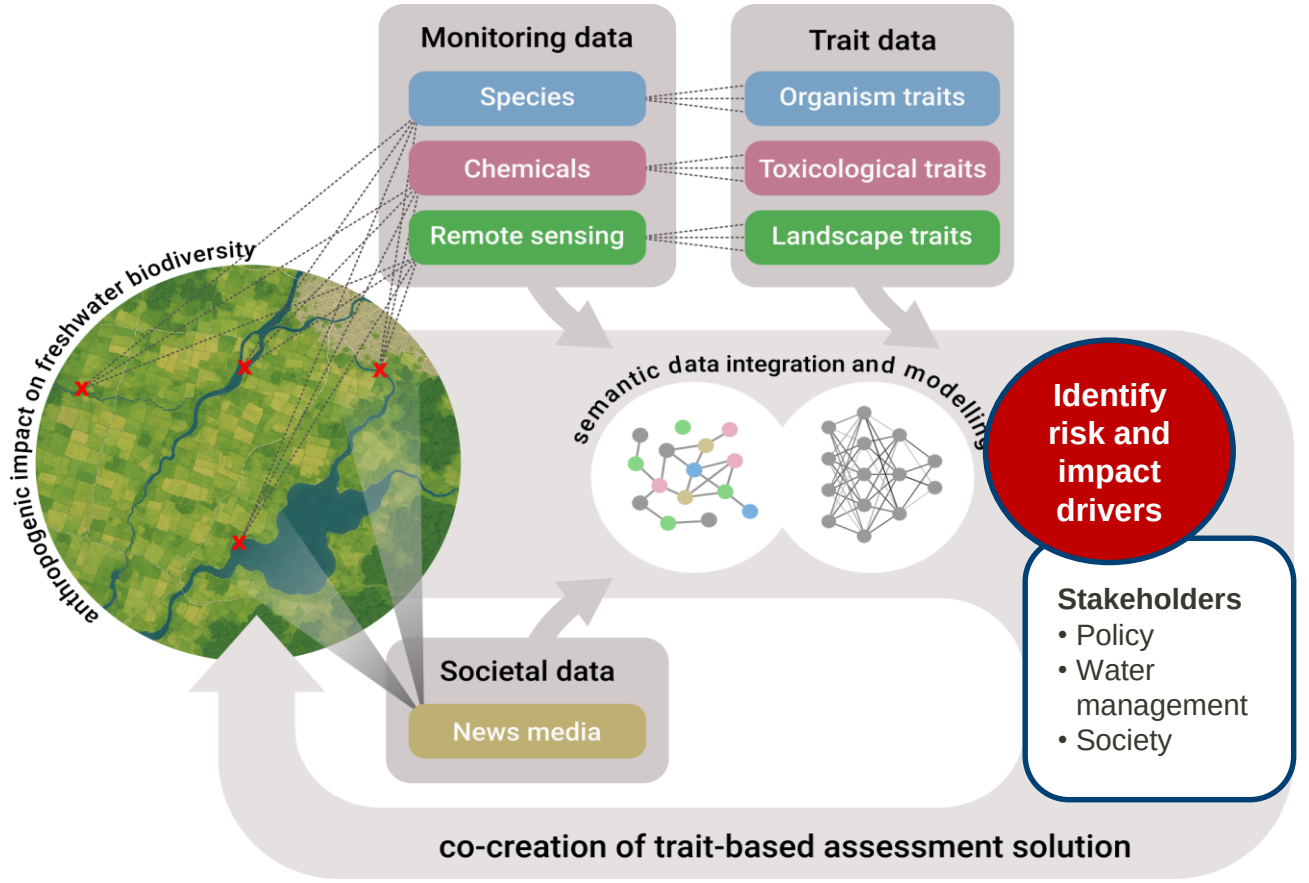
Mixture risk driver heterogeniety in Europe

Schor et al. under revision

Extend the data basis by trait data



Integrative toxicology (iTOX) working group

Head:
Wibke Busch

Toxicogenomics and data-driven toxicology with zebrafish embryos

Mixture toxicology and environmental risk assessment

Third-party funding!

Regulatory relevance!

Digitalisation in and for toxicology and risk assessment