The Problem of PFAS Contamination: Characterizing Toxicity Using Computational Toxicology

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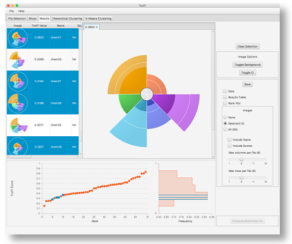
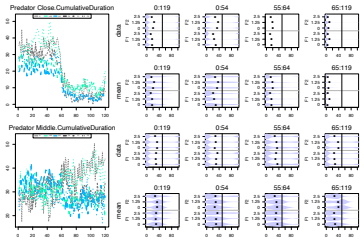
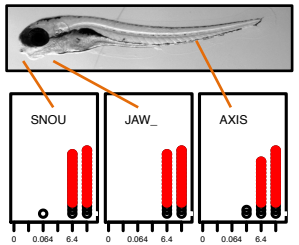
Analytics



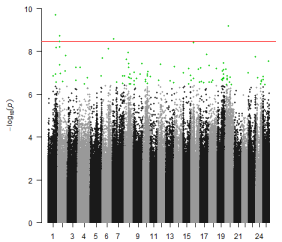
Behavior



Development

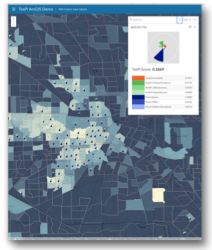


Genetics



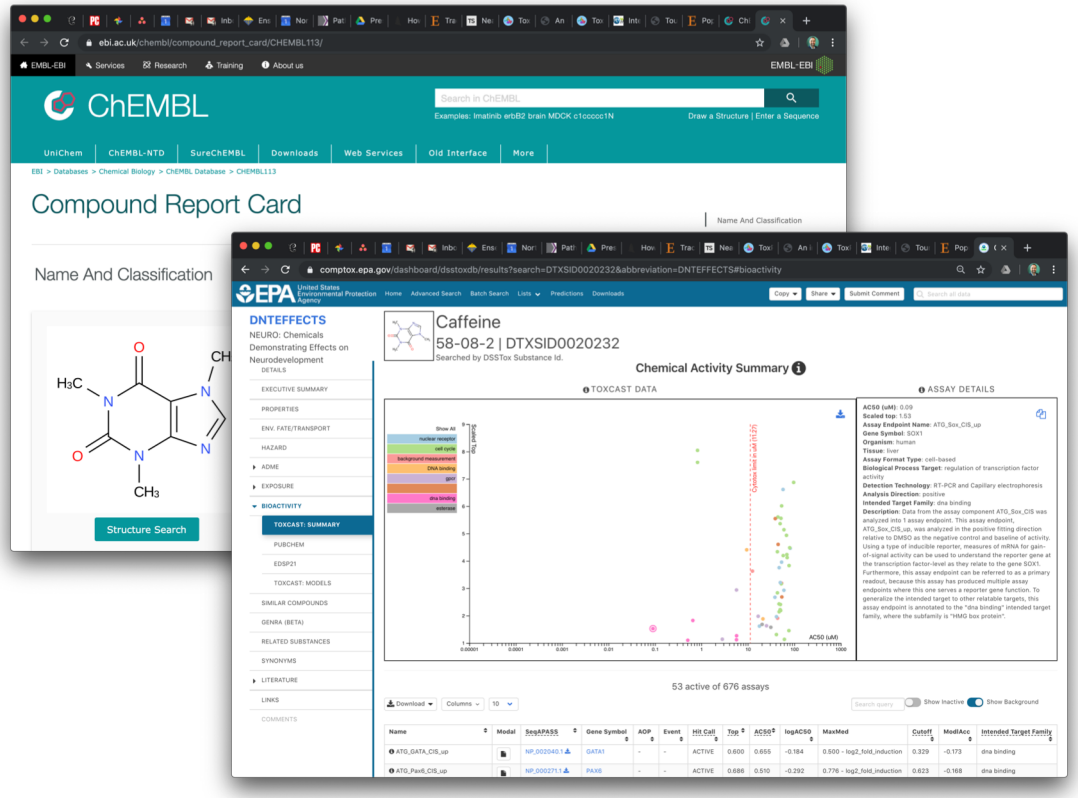
Integration

Translation



Overarching theme of this session: Computational Toxicology enables integrative, multiscale approaches to characterizing toxicity

The data are out there …… now what?



EPA will host its first annual conference on the State of the Science on Development and Use of New Approach Methods (NAMs) for Chemical Safety Testing on December 17, 2019.

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This conference is one of EPA's commitments as set forth in the "Directive to Prioritize Efforts to Reduce Animal Testing" memorandum signed by Administrator Andrew Wheeler on September 10, 2019.

The Administrator's memorandum can be found at https://www.epa.gov/sites/production/files/2019-09/documents/image2019-09-09-231249.pdf

After registering, you will receive the Adobe Connect link for the webinar.

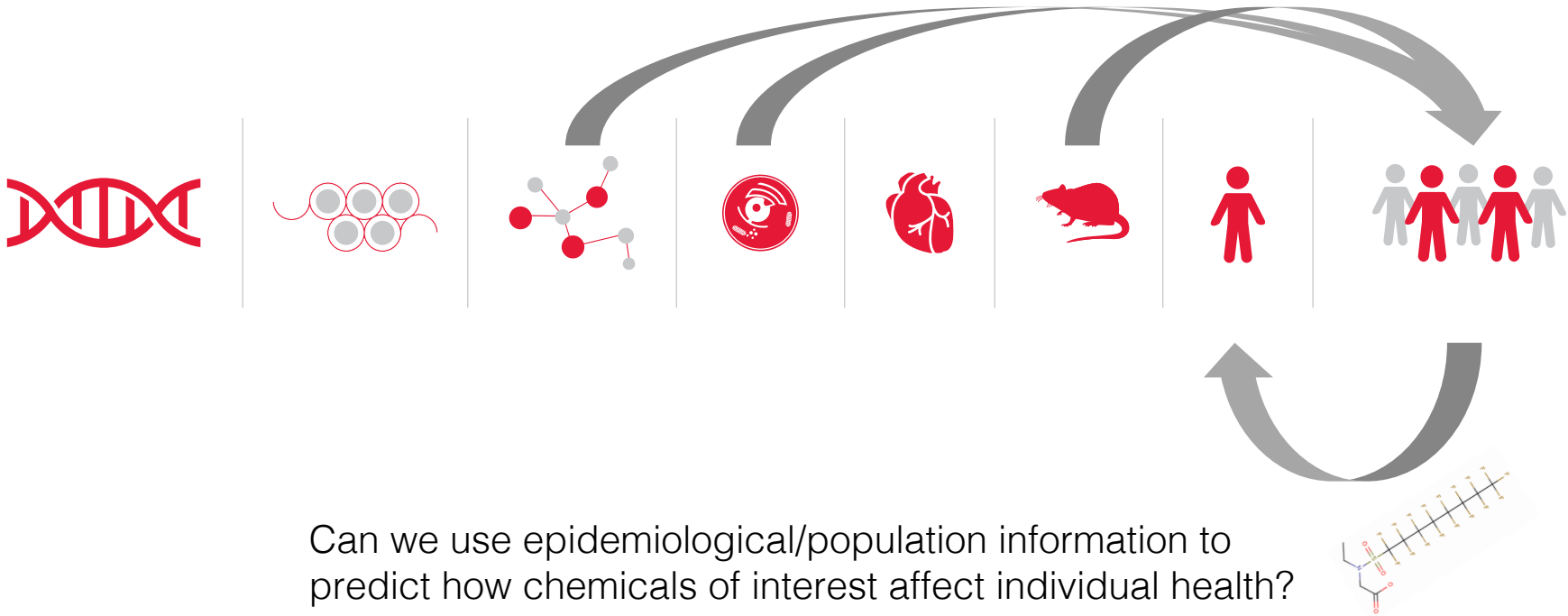
The conference agenda can be found at https://www.epa.gov/sites/production/files/2019-12/documents/first_annual_nam_conference_agenda_12092019.pdf

Location

Adobe Connect
View Map

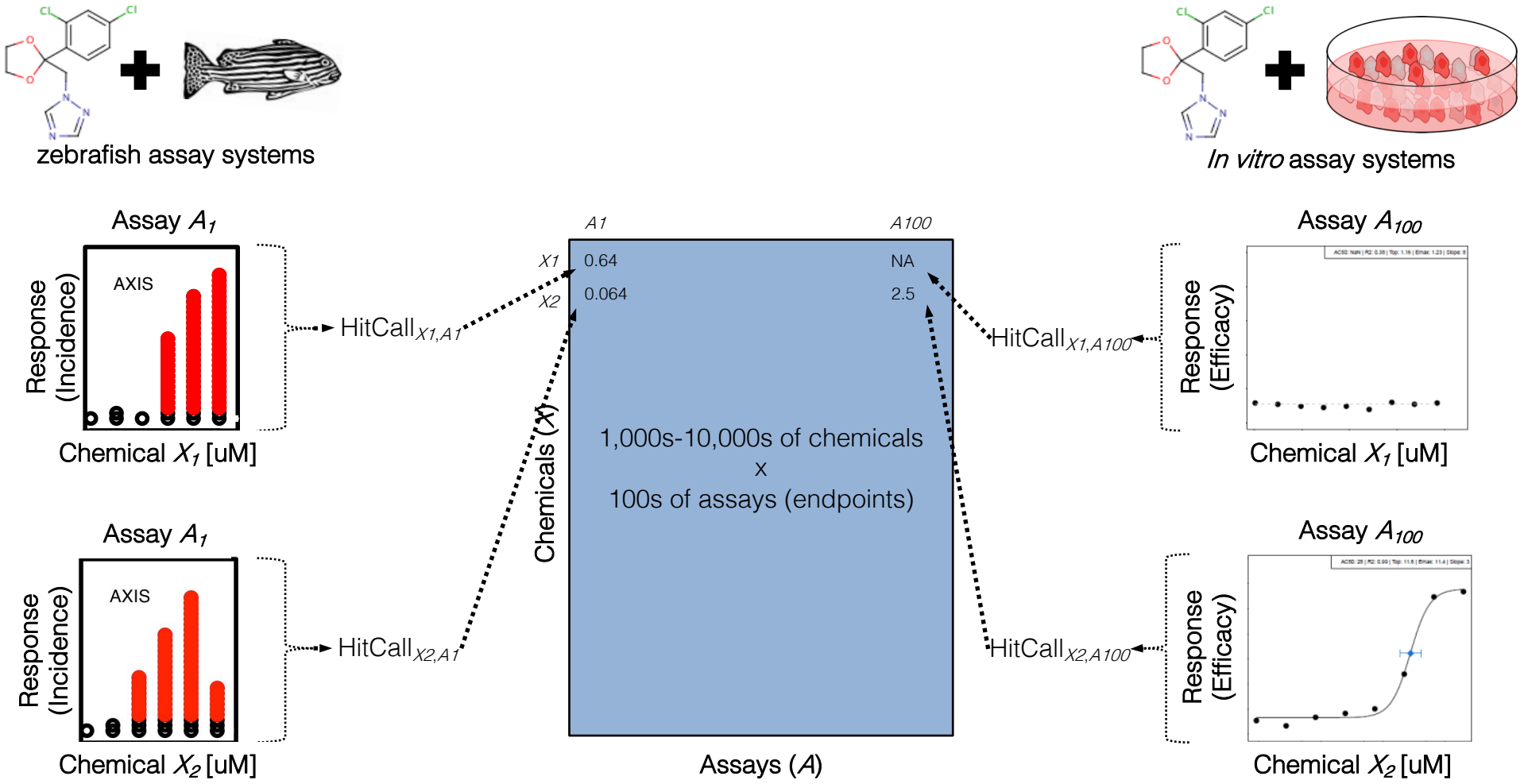
The level(s) of integration needed depend on what kinds of questions we want to address

Can we develop Integrated Approaches to Testing and Assessment (IATA) that predict population risk?

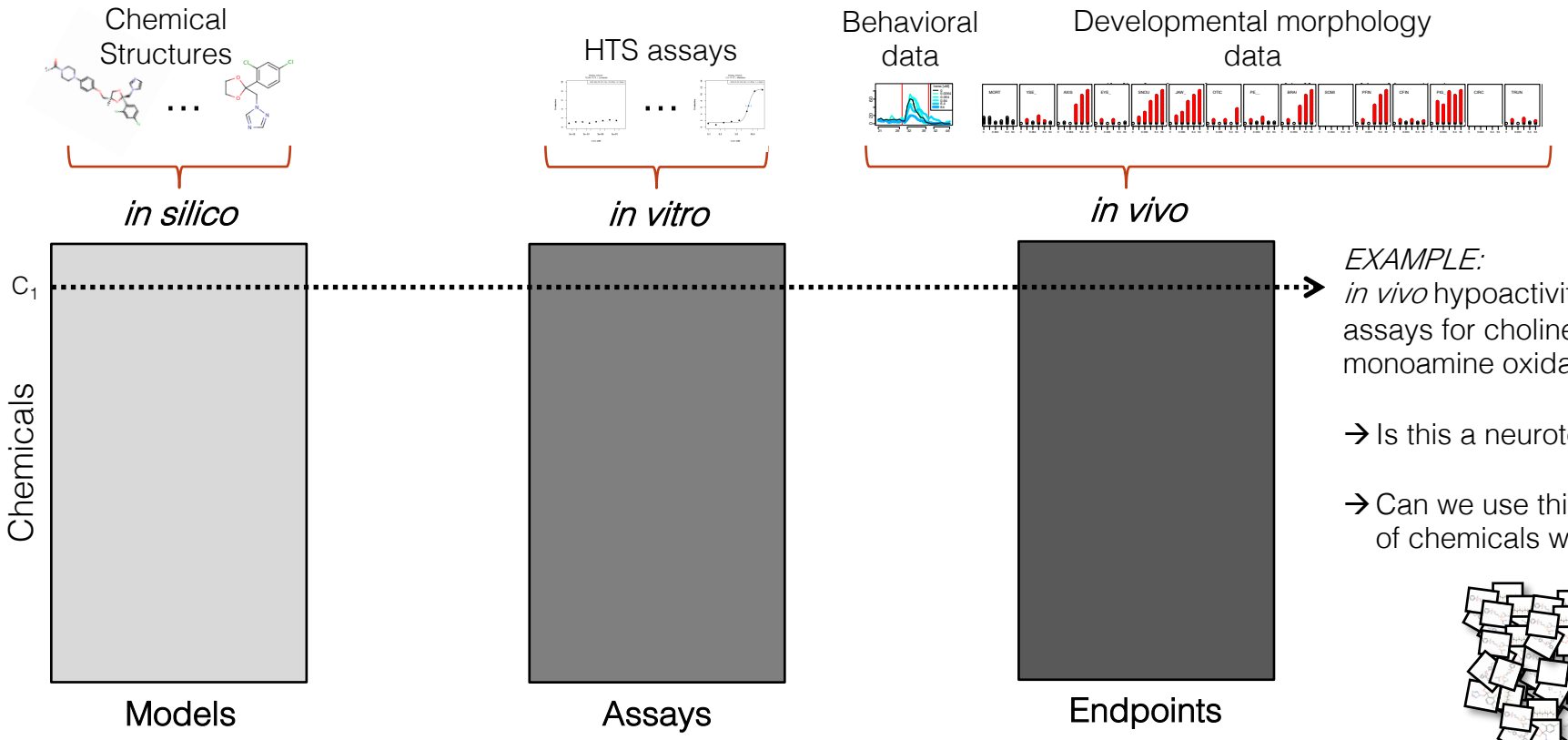


Can we use epidemiological/population information to predict how chemicals of interest affect individual health?

At a practical level, integration is about developing structures for shared data



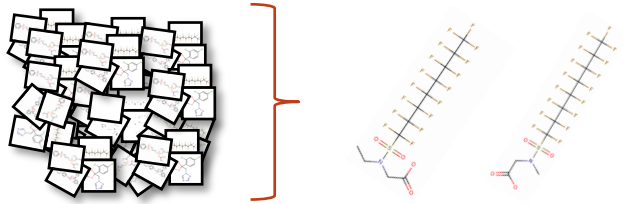
Integration allows comprehensive characterization of toxicity potential for single chemicals as well comparisons amongst groups of chemicals



EXAMPLE:
in vivo hypoactivity is associated with *in vitro* hits on assays for cholinesterases, ion transporters, monoamine oxidases

→ Is this a neurotoxic AOP?

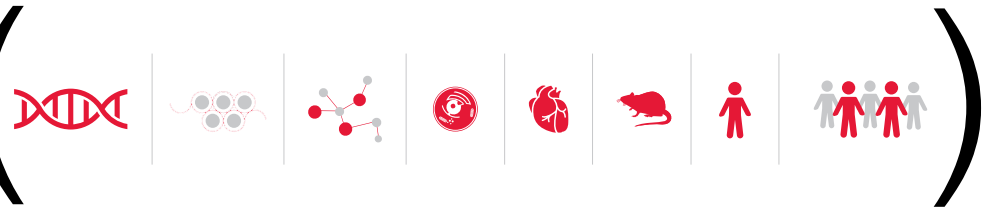
→ Can we use this an an anchor for read-across to sets of chemicals with similar assay response profiles?



Software and methods exist for integration of multiscale data

10s-10000s of chemicals

x



Multiple sources for data on hazard testing, exposure, chemical structure, etc.

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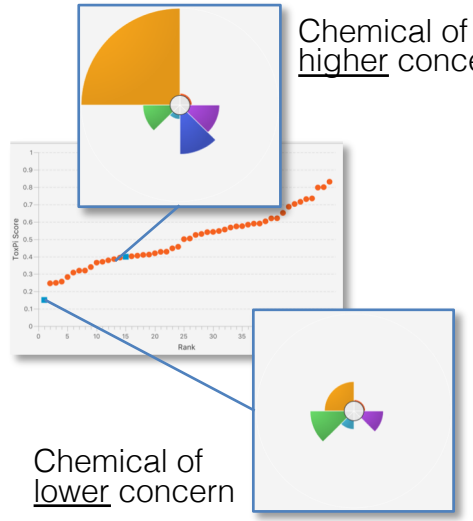
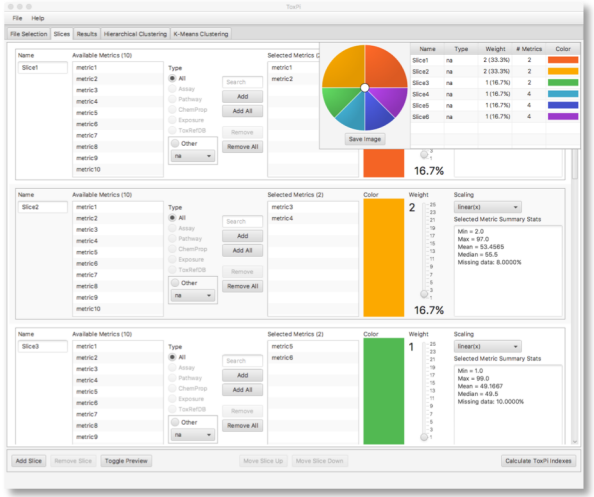
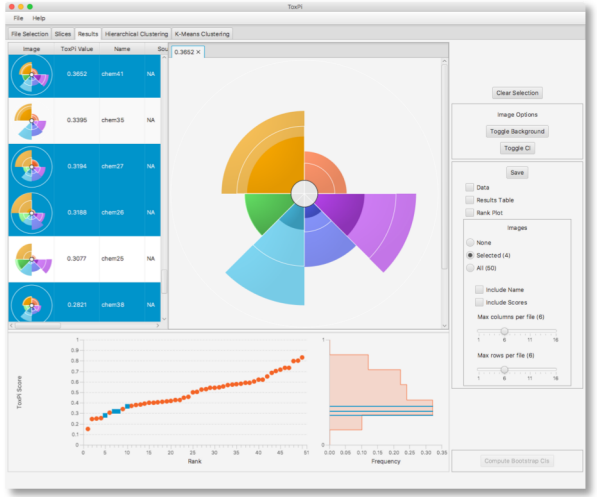
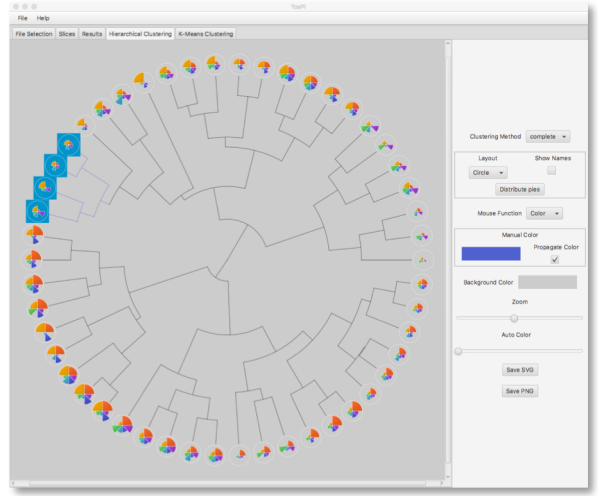




Build data models



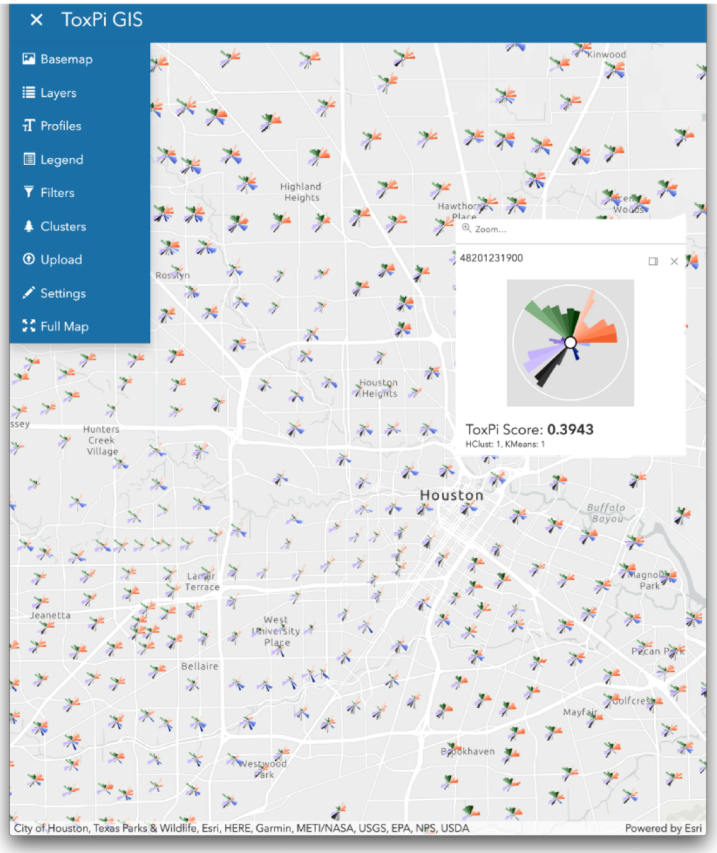
Examine priority (rank) distribution



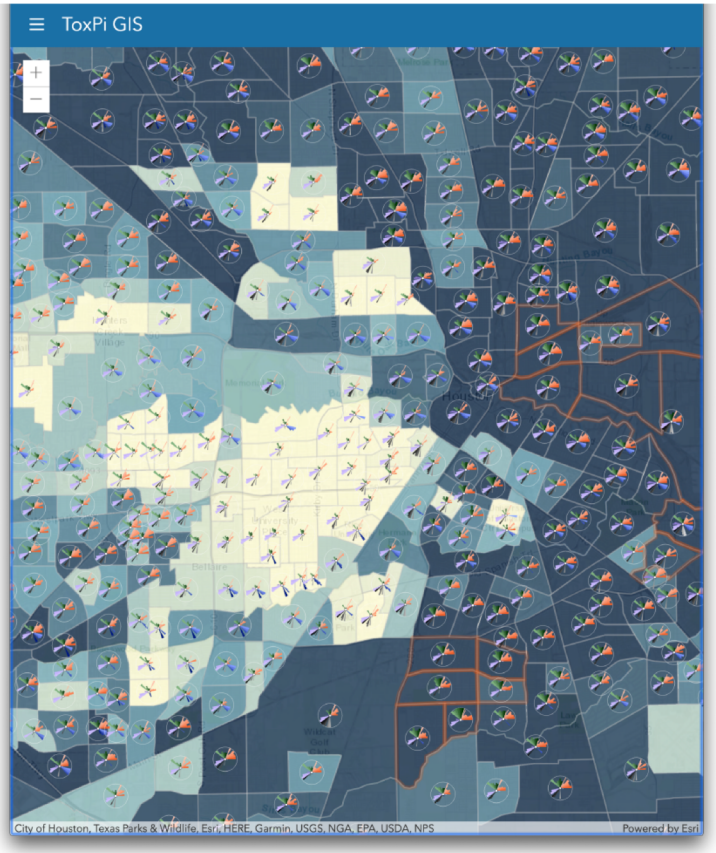
Examine profile similarity via clustering

Integrating GIS data can help address questions on persistence and mobility

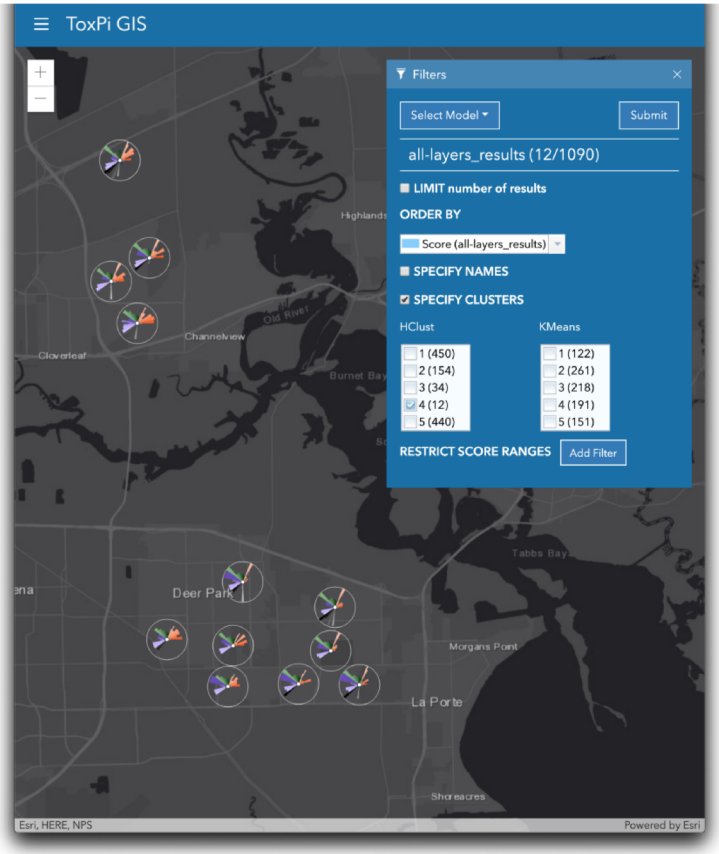
For example: Given information on PFAS exposure, persistence and mobility, can we prioritize at-risk communities?



ToxPi profiles vary by neighborhood atop "plain" basemap layer



ToxPi profiles atop layer colored by overall model score (darker = higher score)



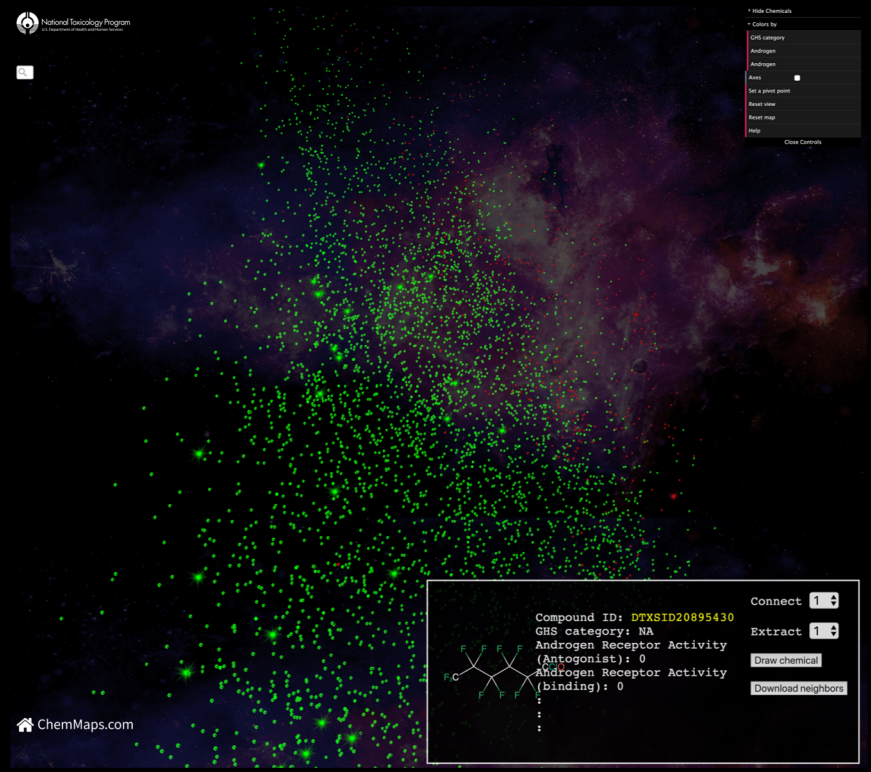
Filtering by ToxPi profile shape clusters reveals geographic clusters

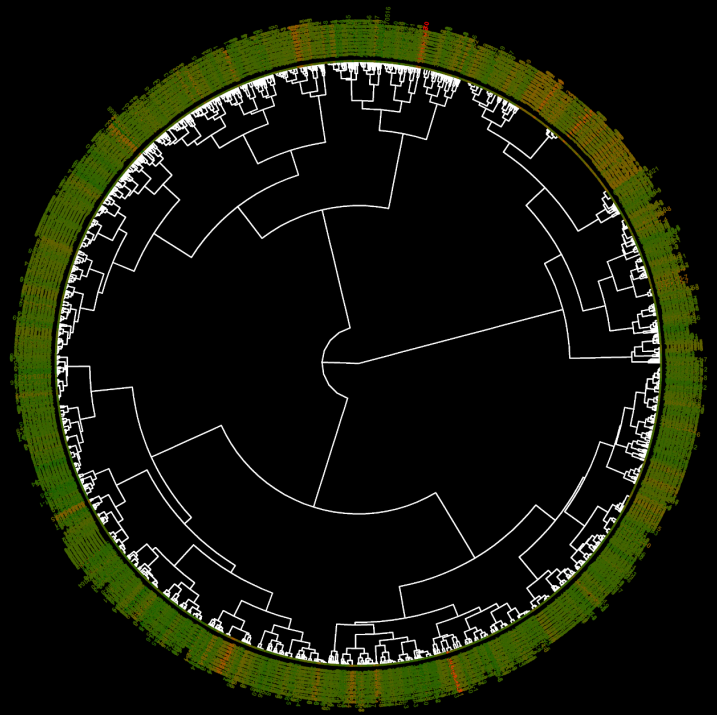
[Marvel, Bhandari, Wright, Rusyn, Chiu, Reif. *in prep*]

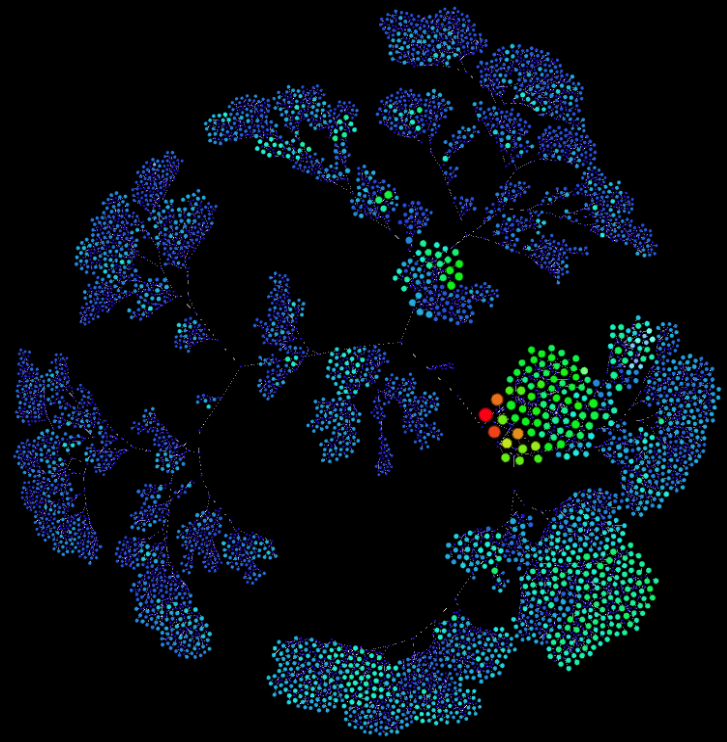
How do we prioritize where in the PFAS universe to start?

There are many options for how to apportion the thousands of compounds in the PFAS universe in chemical space and/or decorate it with biological knowledge

→ How can we integrate across data sources/scales/types to derive an objective priority list?







Acknowledgements & Funding

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