“Integrative Chemical–Biological Grouping of Complex High Production Volume Substances from Lower Olefin Manufacturing Streams” as Applied to Environmental Matrices

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Sediment Management Working Group

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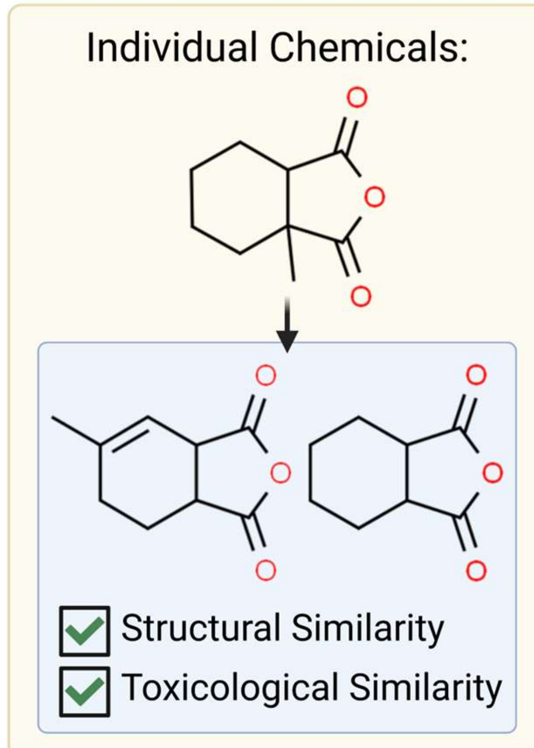
Grouping: The Status Quo

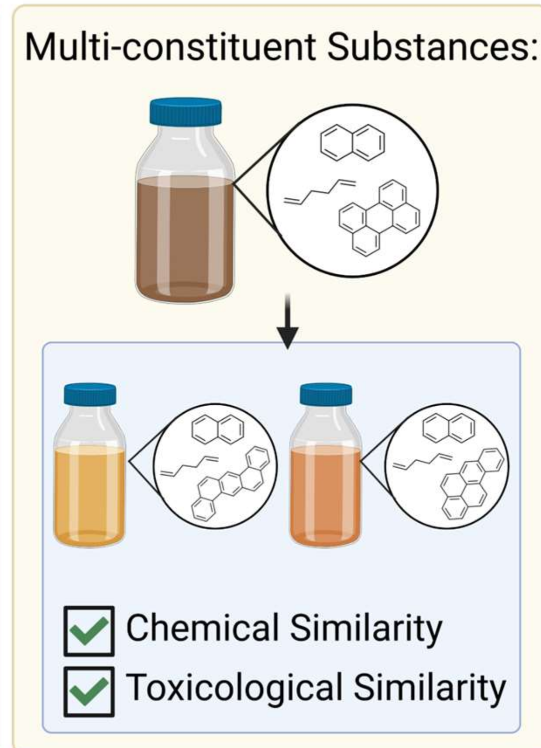
Grouping is used for various purposes:

- Filling data gaps for data-poor chemicals/substances
- Does not require additional animal testing
- Facilitates organization and prioritization of substances
- Streamlines efficiency of the chemical review process

Chemicals and substances are grouped by:

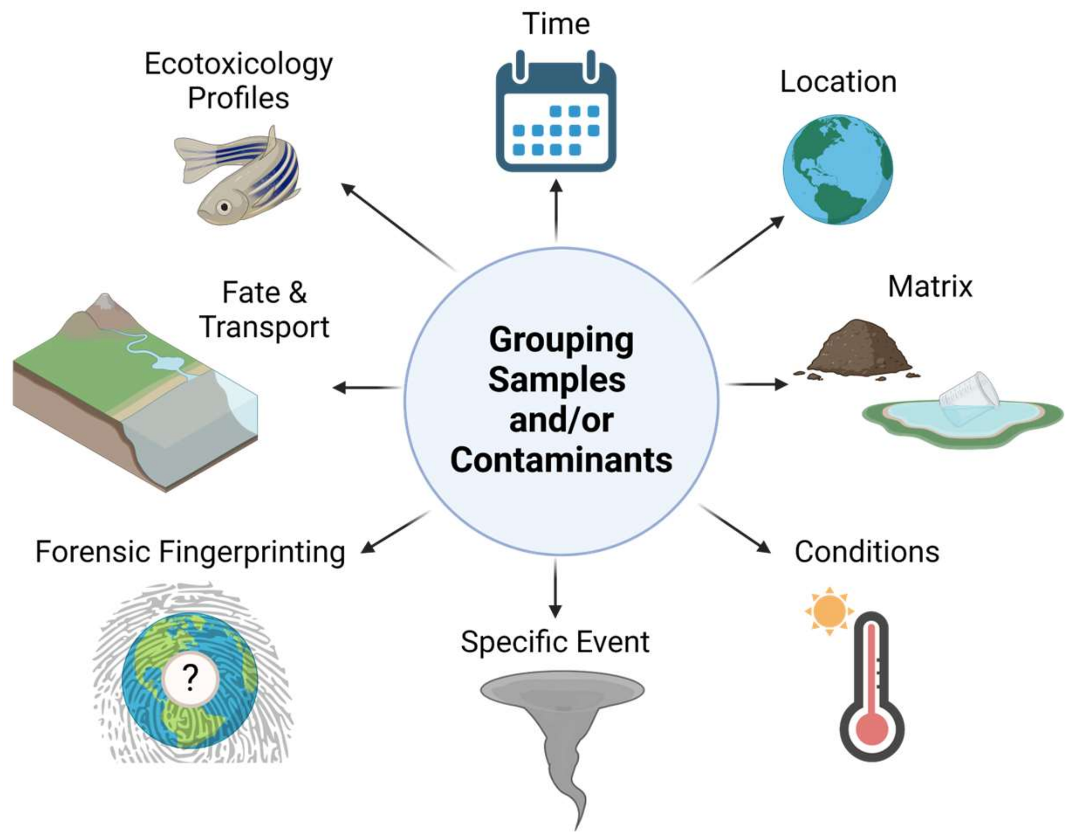
- Structural similarity
- Chemical similarity
- Physical-chemical properties
- Toxicological profiles
- Manufacturing process





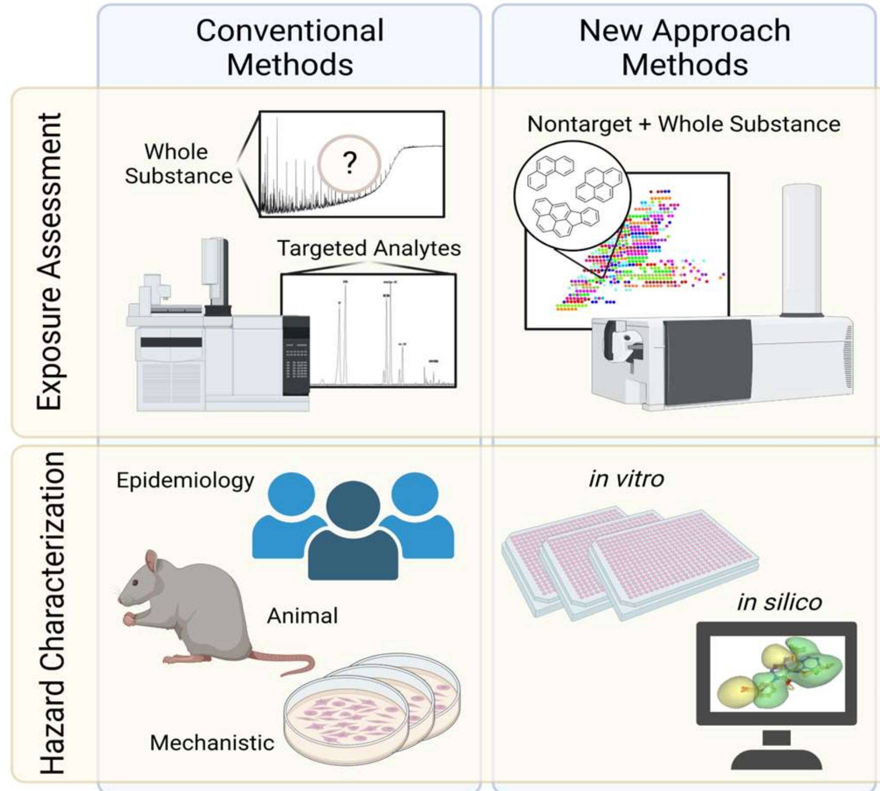
Environmental Applications

- Grouping as a concept can also be used to interpret data from environmental samples regarding several variables.
  - Ex: Samples from a disaster are grouped and evaluated by matrix
- Possible contaminants can be evaluated together, rather than individual chemicals one by one.
  - Ex: PFAS, Hydrocarbons
- Chemicals and substances can be labeled and categorized to reflect certain behavior in the environment.
  - Ex: PBT, PMT



The Problem

- Grouping complex and multi-constituent substances is challenging, especially for acceptance by regulatory agencies.
- Chemical and toxicological analyses often take either a top-down or a bottom-up approach, but not both.

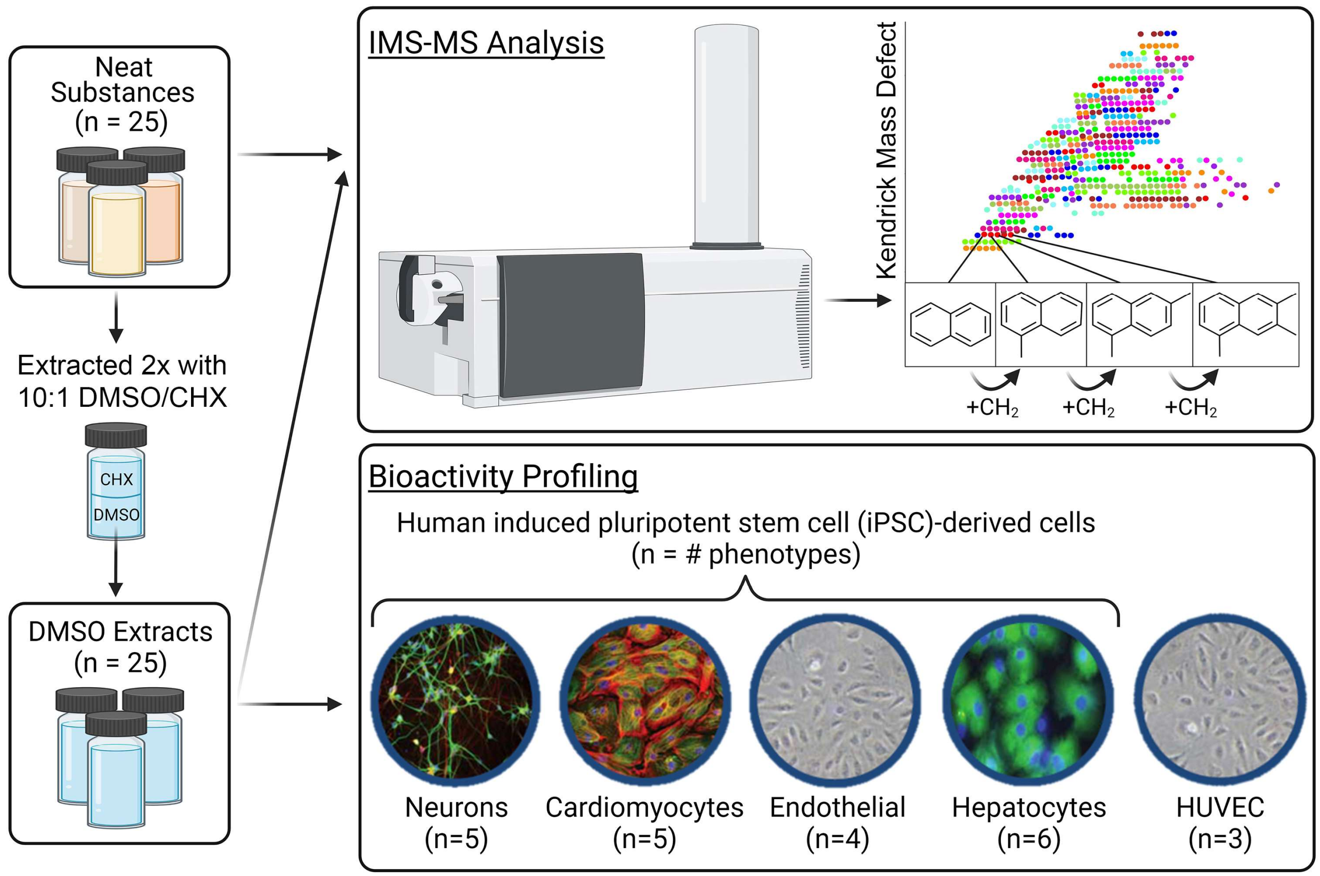


***Research Objective*:**

Develop a methodology that acts as a bridge between top-down and bottom-up approaches to evaluate complex substances.

Experimental Design

1. Can IMS-MS characterize UVCBs to meet ECHA guidelines?
2. How much *chemical* variability is to be expected within and between existing categories?
3. How much *biological* variability is to be expected within and between existing categories?
4. What constituents drive bioactivity in complex petroleum UVCBs?



Figures produced using BioRender

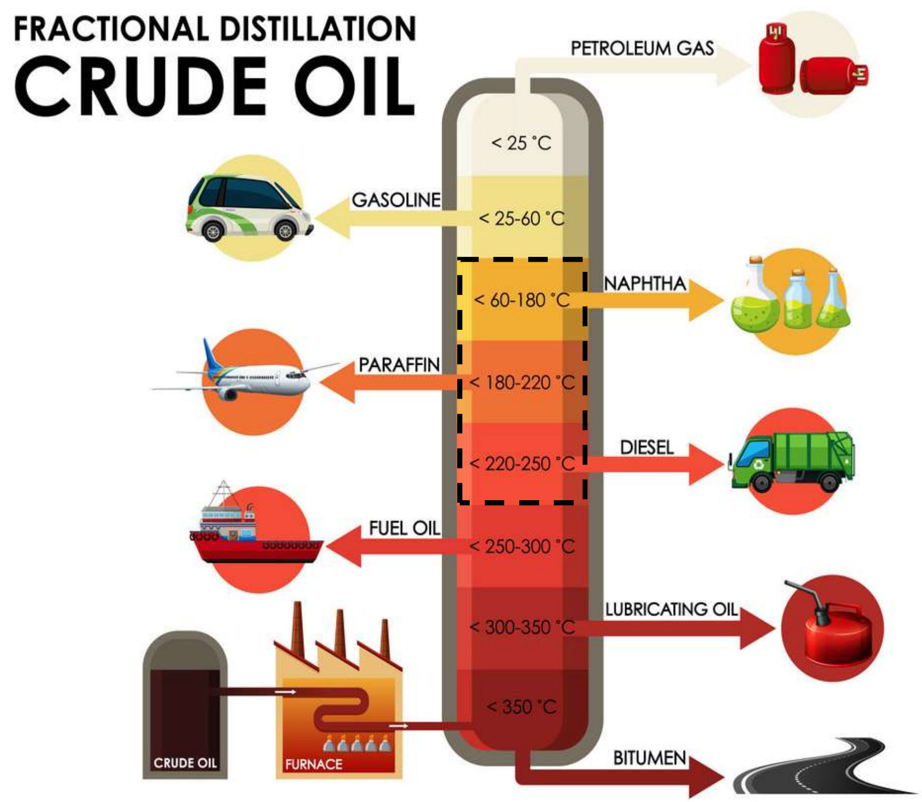
Substances Used in This Study

Low Benzene Naphthas:

Sample ID	Human Health Hazard Group
83757	Group I
83806	
83946	
84070	
84003	
84075	Group II
83979	
84024	
83984	Group III
83683	
83758	Group V
83931	Not Defined Properly

Resin Oils:

Sample ID	Human Health Hazard Group
83981	Group I
84023	
83949	
83980	Group II
84012	
84074	
83879	Not Defined Properly
83955	
83618	
83956	
83985	
83998	
84543	



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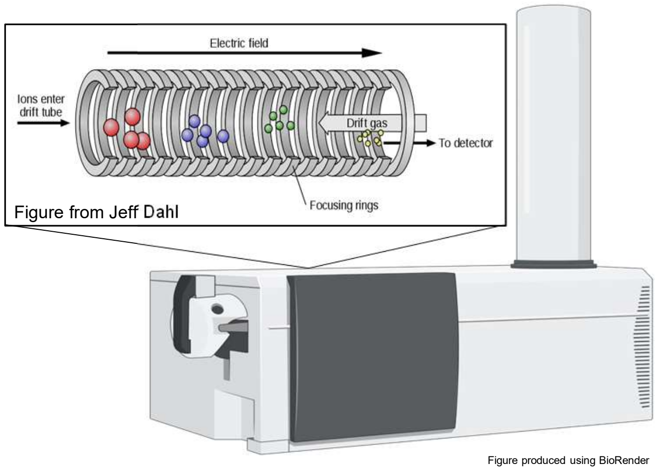
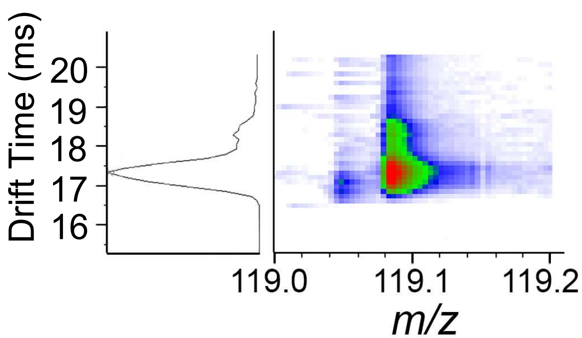
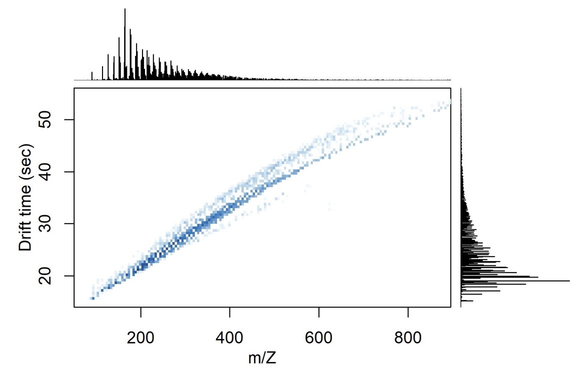
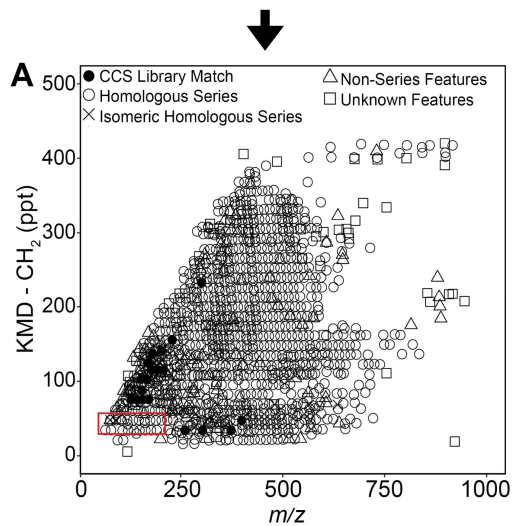
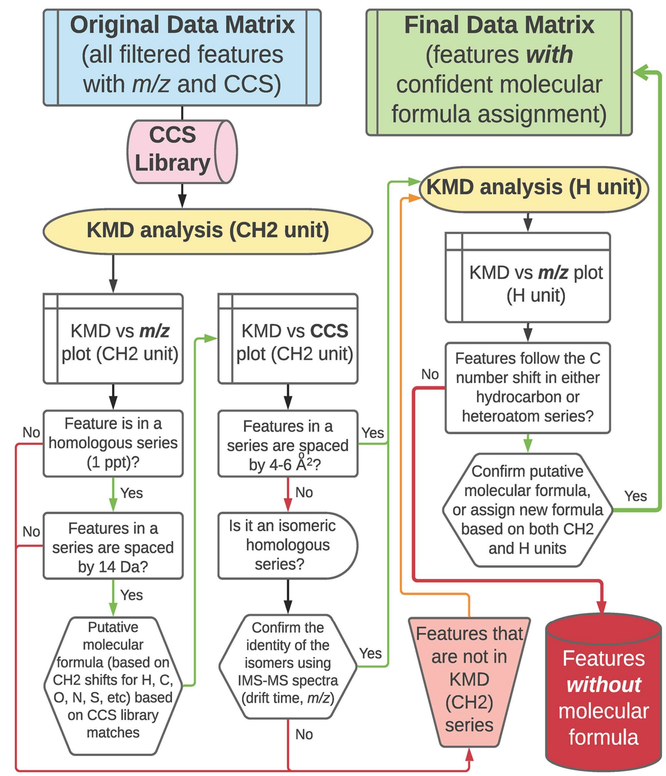
1. Chemical Characterization











Figures adapted from: Roman-Hubers, A. T., Cordova, A. C., Aly, N. A., McDonald, T. J., Lloyd, D. T., Wright, F. A., Baker, E. S., Chiu, W. A., & Rusyn, I. (2021). Data Processing Workflow to Identify Structurally Related Compounds in Petroleum Substances Using Ion Mobility Spectrometry-Mass Spectrometry. *Energy & fuels : an American Chemical Society journal*, *35*(13), 10529–10539. https://doi.org/10.1021/acs.energyfuels.1c00892

2. Grouping & Variability by Chemistry

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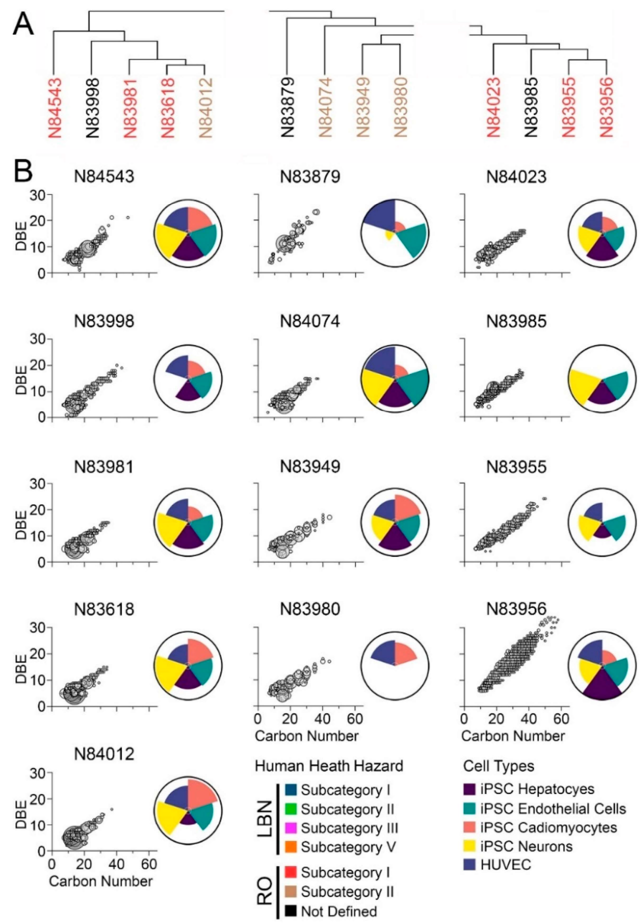

<u>Our Analysis</u>:

- Determined how representative DMSO extracts were of neat substances
- Characterized chemical composition to the extent necessary by ECHA guidance
- Evaluated the concordance of assigned categories & health hazard subcategories based on expected constituents

<u>In Environmental Analyses</u>:

- Determine how well *in vitro*-compatible extracts represent original samples
- Characterize chemical composition to the extent necessary to determine temporal, spatial trends
- Evaluate the presence of expected substances and constituents in a group of samples (e.g., several substances spill in a disaster)

2. Are expected constituents observed?

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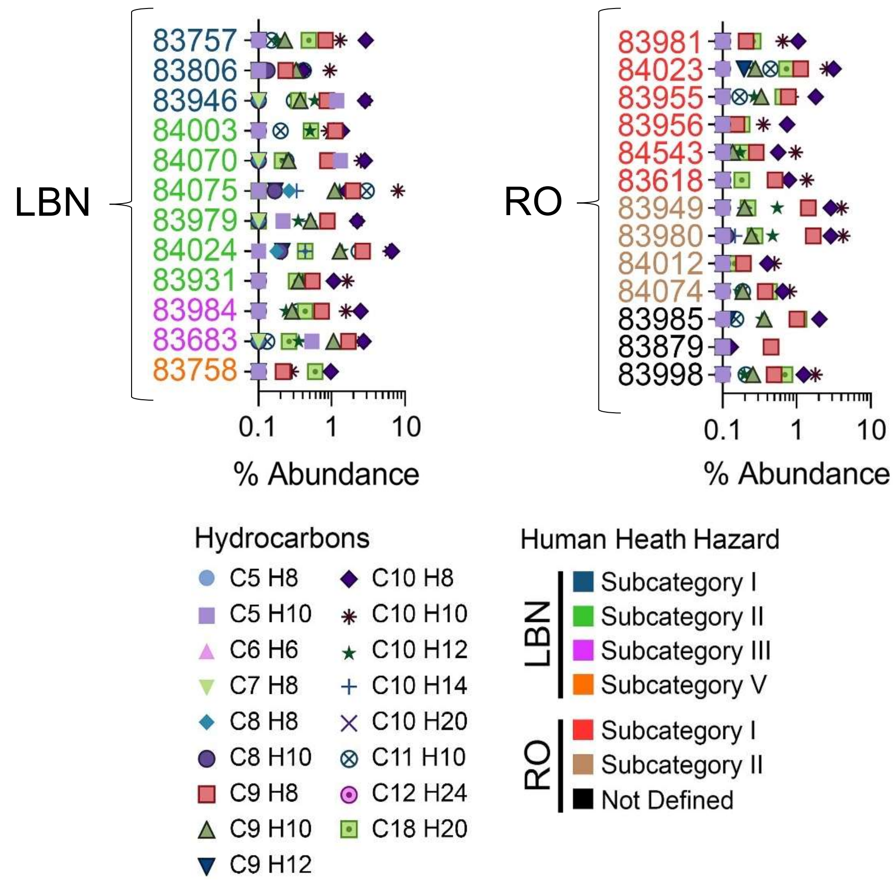
Expected Compositions

- <u>Low Benzene Naphthas</u>:
  *"…**C7 to C12 aromatic and cycloaliphatic hydrocarbons**."*
- <u>Resin Oils</u>:
  *"…**C8 to C12 aliphatic cycloalkenes, and aromatic hydrocarbons** of which dicyclopentadiene (DCPD) is a key chemical constituent in the majority of streams."*

Observed Compositions

- Subcategories exhibited comparable profiles of expected constituents.
- Expected constituents are observed within predefined concentration ranges.

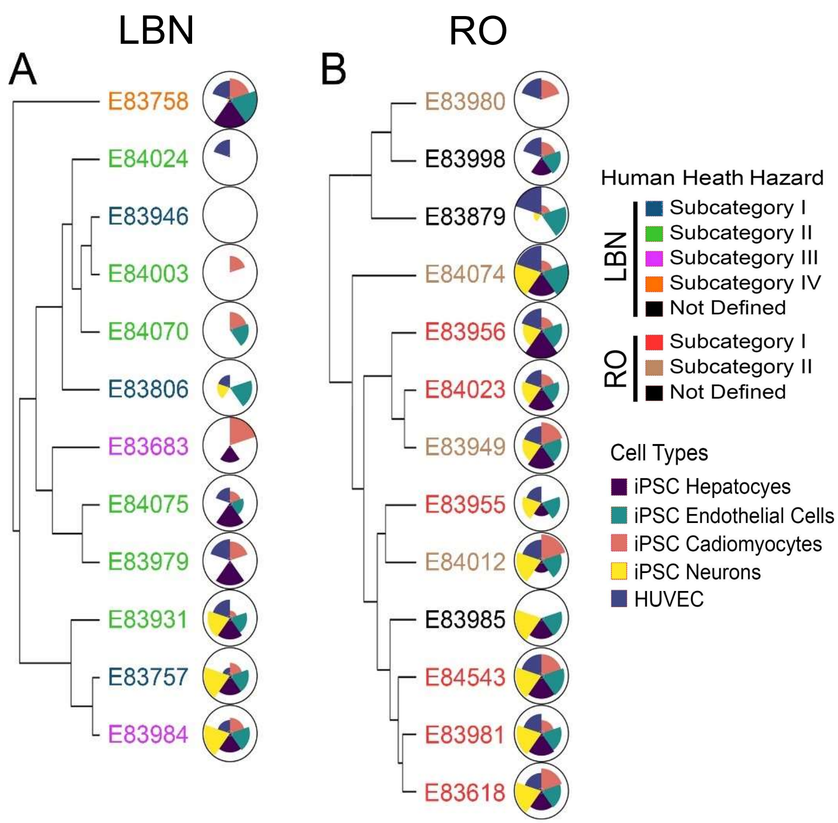


Reference Material: US EPA Screening-Level Hazard Characterizations for Low Benzene Naphthas & Resin Oils and Cyclodiene Dimer Concentrates Categories

3. Grouping & Variability by Bioactivity

<u>In Our Analysis:</u>

- Determined the bioactivity of each substance tested with each cell type
- Determined the concordance of bioactivity profiles within assigned groups
- Compared the extent of bioactivity between groups
- Compared bioactivity profiles with expected bioactivity based on chemistry



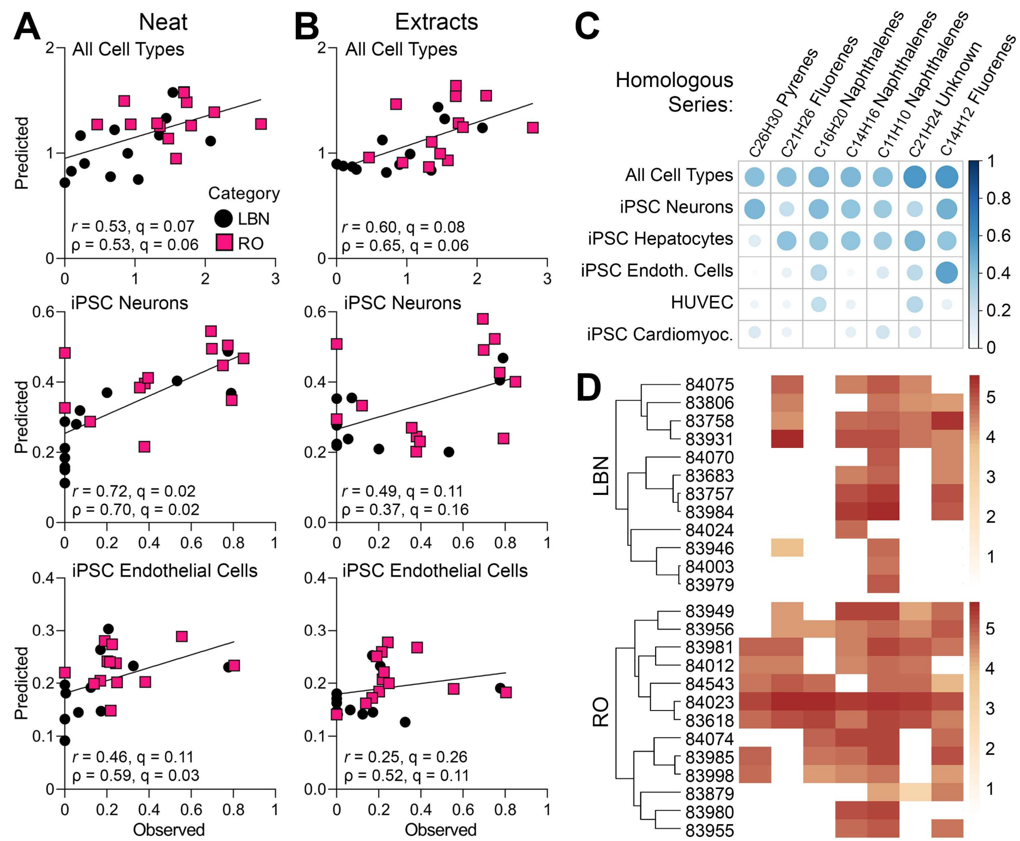
<u>In Environmental Analyses:</u>

- Determine the bioactivity of individual samples for various cell types
- Group samples by bioactivity
- Determine the concordance of bioactivity profiles depending on variables of interest (time, location, matrix)
- Use bioactivity trends to inform interpretation of results in the context of the experiment/problem

4. *Determine constituents that are potential drivers of bioactivity*

- Determined which cell types are most informative or sensitive for assessing bioactivity
- Identified which constituents were most significantly predictive of the overall ToxPi score
- Compared the abundance of most predictive features in each sample and within and between groups

Also applicable to environmental analyses & matrices!



Conclusions

1. To what extent can petroleum UVCBs be characterized using IMS-MS to meet ECHA guidelines for read-across?
2. How much *chemical* variability is to be expected within categories?
3. How much *biological* variability is to be expected within categories?
4. What constituents are potential drivers of bioactivity in complex petroleum UVCBs?

In Environmental Analyses…

1. What contaminants are present in various samples?
2. How much of the contaminant(s) is present in water, soil, sediment, etc.?
3. What hazards do humans and the environment face from the contaminant(s)?
4. From what constituents do humans and the environment face the greatest risk?

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- Erin Baker & Lab

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