Progress in High-Throughput Exposure Assessment for Prioritizing Human Exposure to Environmental Chemicals

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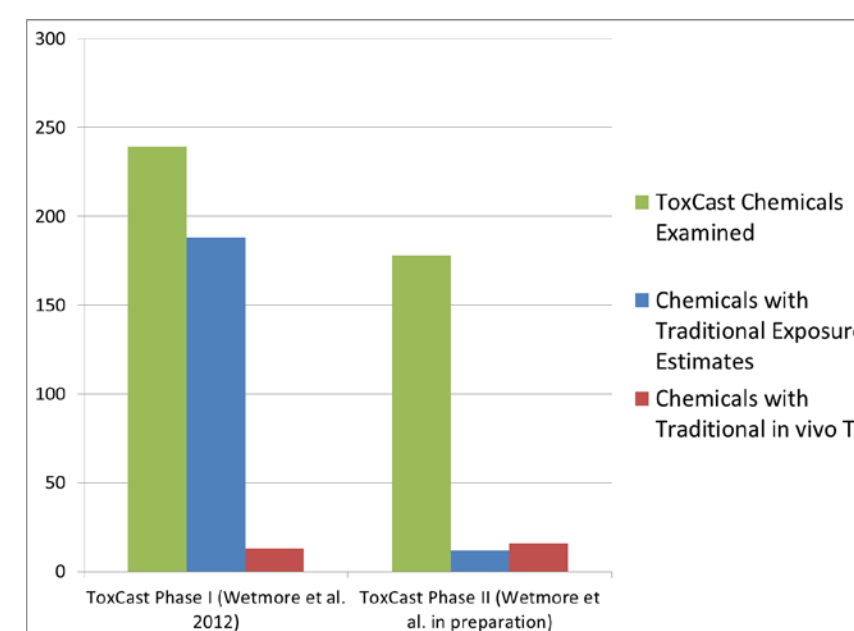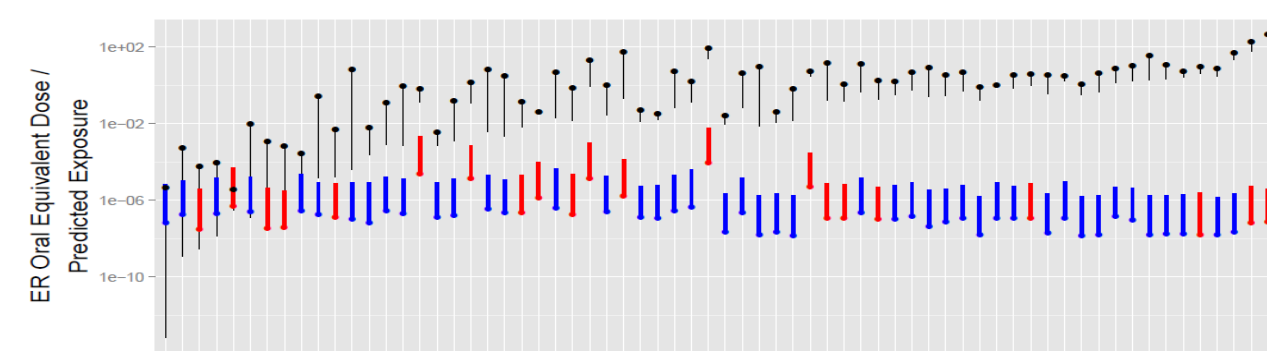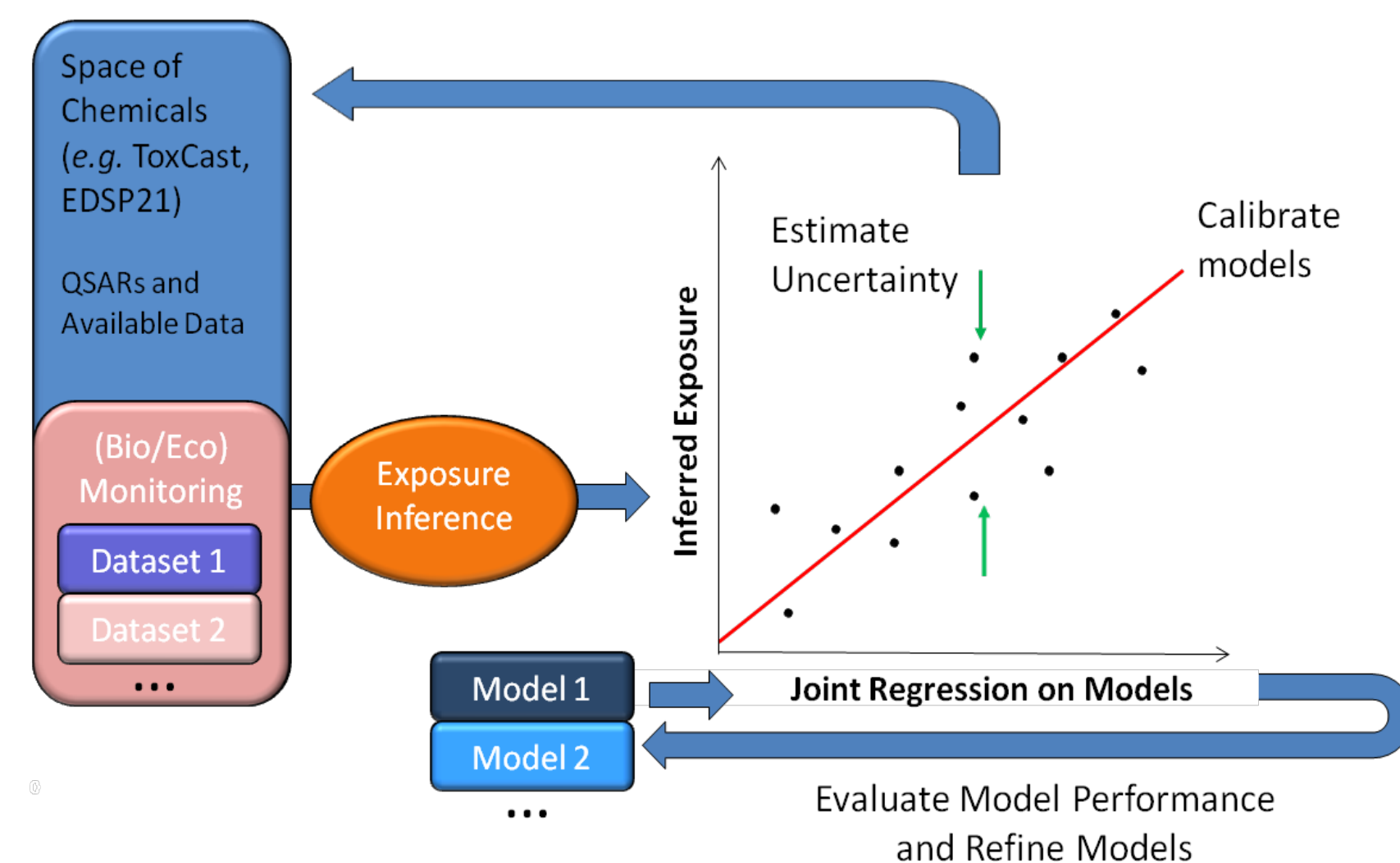[2]National Exposure Research Laboratory

Introduction

(1) The Endocrine Disrupter Screening Program (EDSP) is mandated to examine thousands of chemicals in drinking water and pesticides for potential to alter human and ecological endocrine function
(2) EDSP21 is developing the data and tools to generate rapid and scientifically-defensible exposure predictions for the full universe of existing and proposed commercial EDSP chemicals
(3) We must develop the data and tools required to convert both biomonitoring data and bioactive in-vitro concentrations to predicted real world exposure or doses
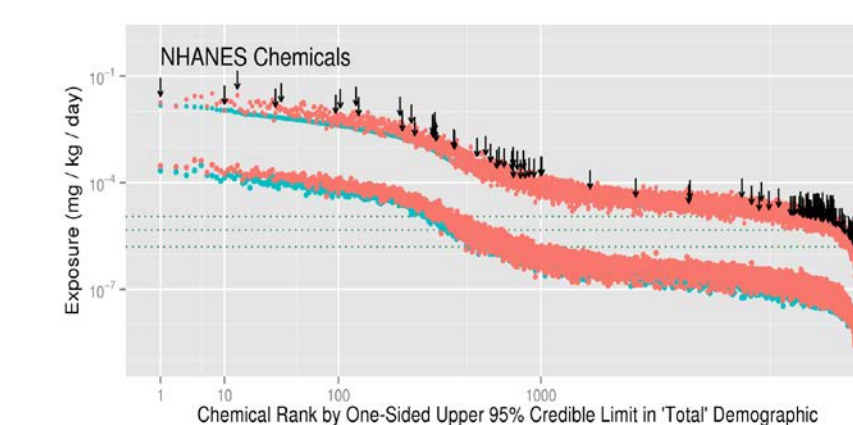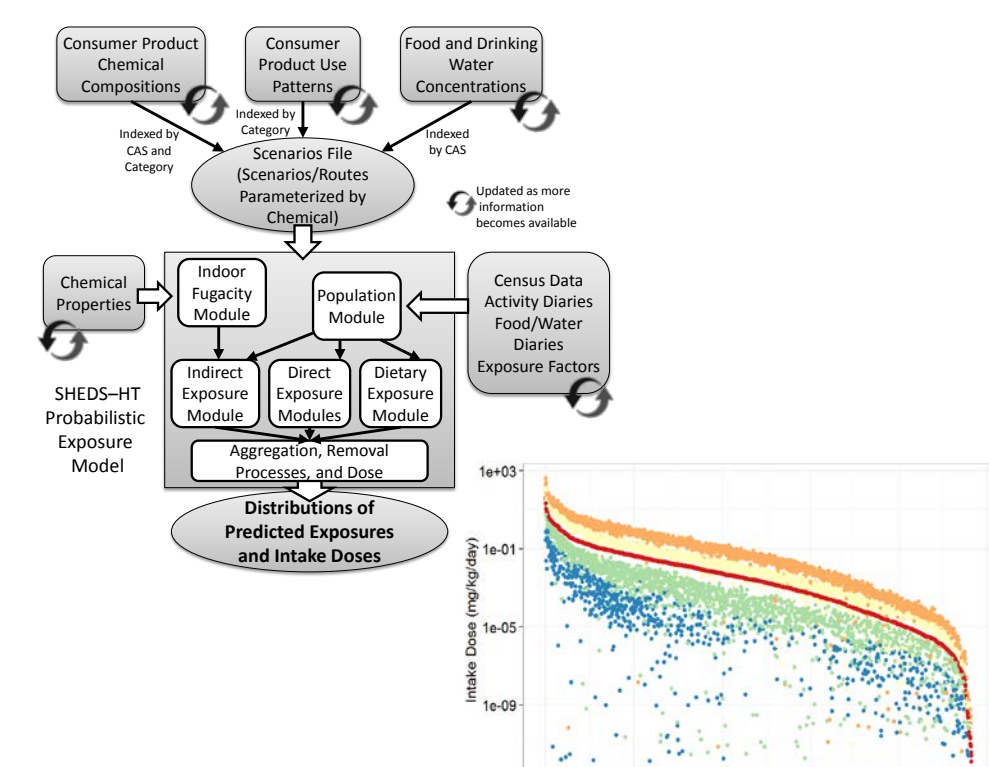(4) We must evaluate predictions against available data in a statistically robust manner

Approach

1) Apply multiple exposure models (heuristic and mechanistic) to build consensus predictions

2) Compare with exposure estimates inferred from NHANES biomonitoring data to characterize uncertainty

3) We call this framework **Systematic Empirical Evaluation of Models** (SEEM)

4) Must robustly consider chemical domain of applicability of exposure models and pharmacokinetic models for exposure inferences

1) At present, the risk prioritization method proposed for the Endocrine Disrupter Screening Program (EDSP) compares exposure and bioactivity for each chemical individually

2) However, people are exposed to chemicals in complex mixtures, both from products and environments containing mixtures of chemicals
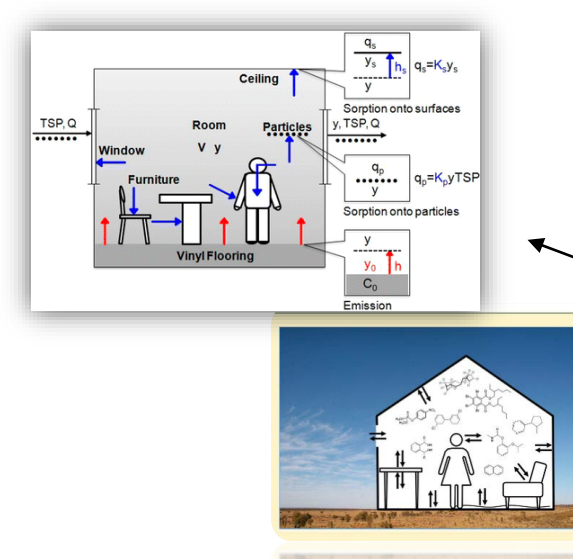

Chemicals

December, 2015 Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel: "Scientific Issues Associated with Integrated Endocrine Bioactivity and Exposure-Based Prioritization and Screening"

Domain-specific Application of SEEM Methods for EDSP21 chemicals

Mechanistic exposure models for consumer products chemicals and pesticides

Heuristic-based exposure models appropriate for application to all chemicals having simple use and property descriptors

Existing far-field literature models for industrial chemicals

Pesticide or Food Contact Substance registration exposure assessments

New or existing near-field models for emission from articles
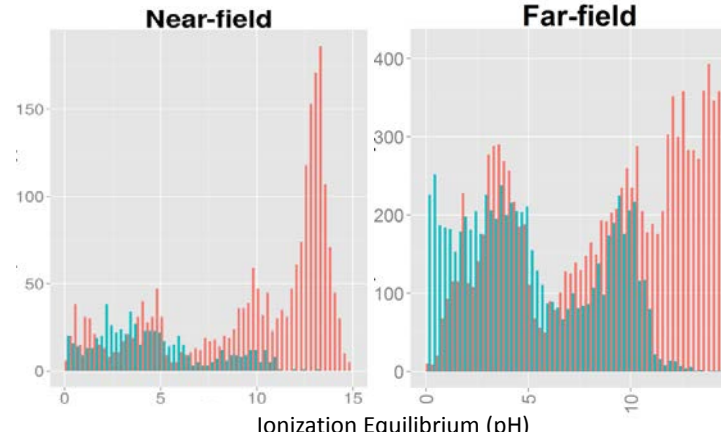
Functional use heuristics
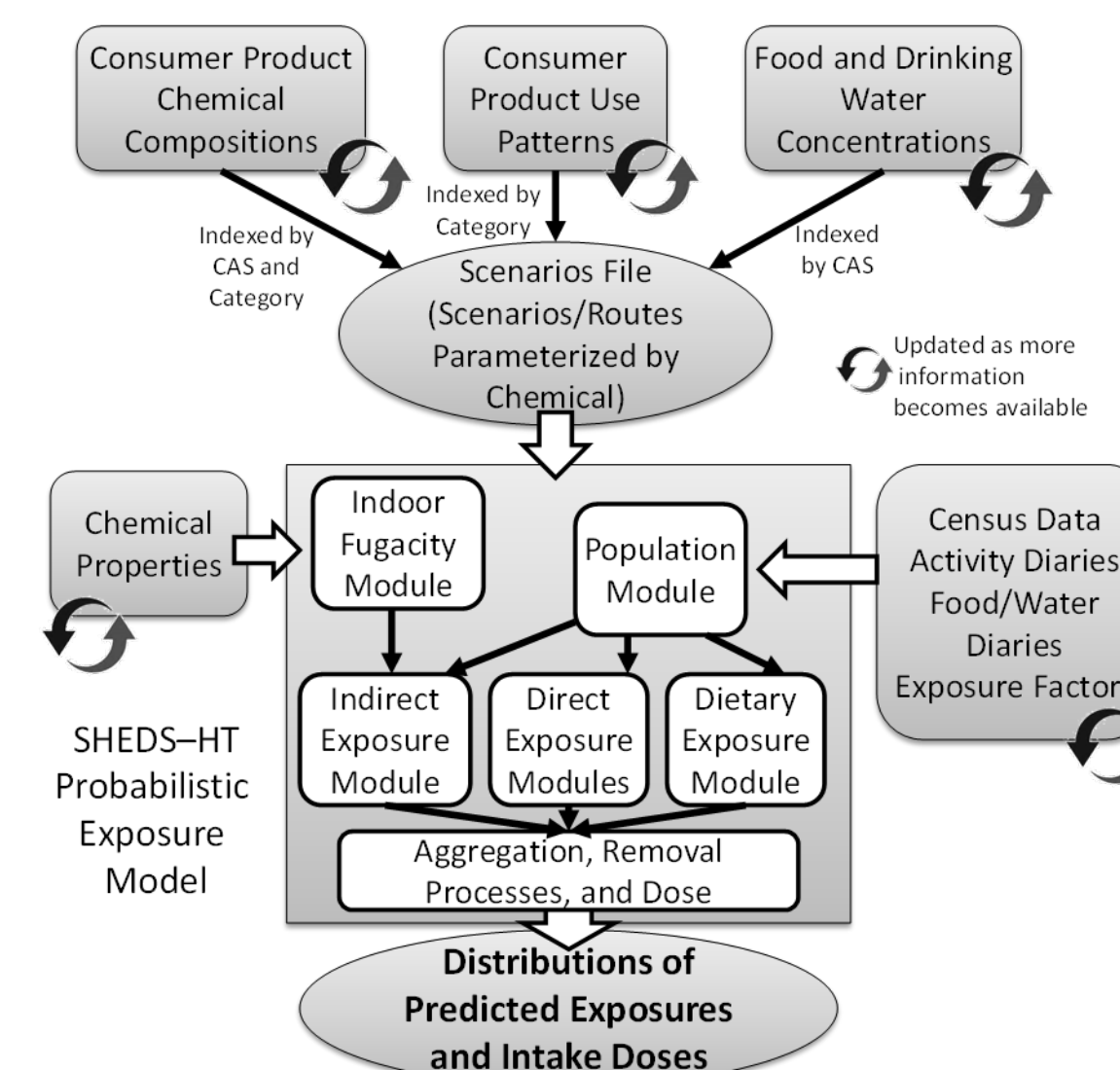
Determining Appropriate Domain for HTPK Models

• White lines indicate residuals
• Residuals can be predicted as a function of properties
• Chemicals with low predicted residuals are within the domain of applicability of HTPK approaches
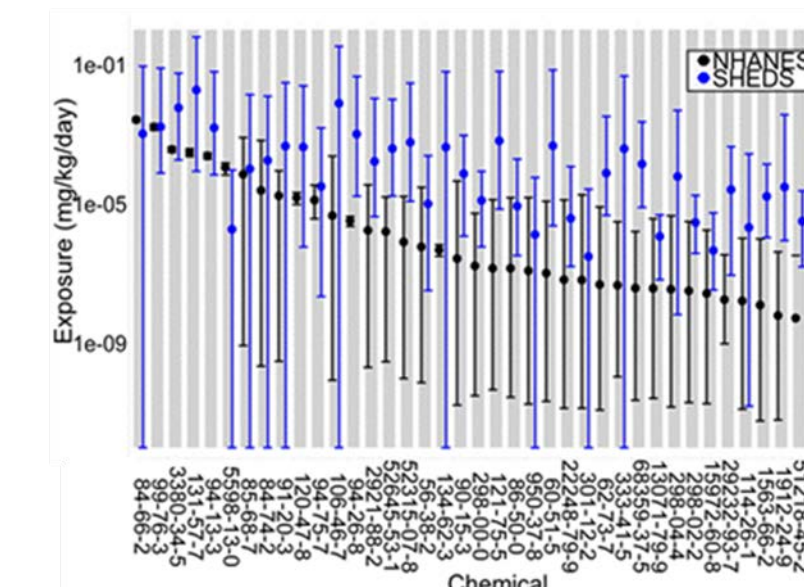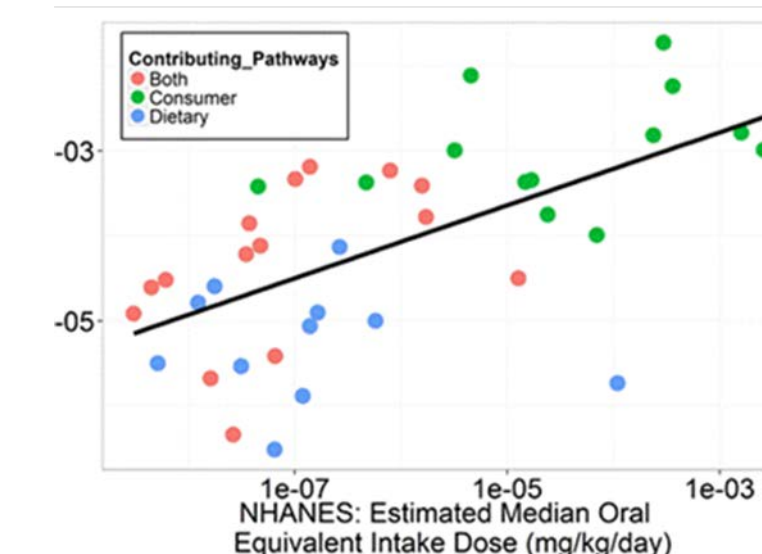
Prediction of Ionization

• Neutral and ionized species of the same molecule will partition differently into environmental and biological media
• Better models are needed for predicting pKa at different pH for chemicals

SHEDS-HT, a High-Throughput Mechanistic Exposure Model

Mechanistic-based exposure model appropriate for application to chemicals with 'near-field' exposures and requiring estimates of product composition.

SHEDS-HT predicted chemical intake doses compared to oral equivalent intake doses inferred from NHANES biomarker data for 39 chemicals (Wambaugh et al., ES & T, 2013). Top: SHEDS median intake dose versus biomonitoring-based predicted median intakes. Bottom: SHEDS 5th,50th ,95th percentile predictions compared to median inferred predictions using NHANES with uncertainties.

Conclusion

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• Consensus predictions for EDSP21 chemicals make use of available exposure estimates across multiple domains to reduce uncertainty
• When combined with HT hazard information from the HTT Project, will inform screening and prioritization of ESDP21 chemicals

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