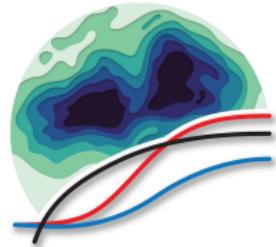


Geospatial Methodologies in Toxicology

Linking exposure, toxicity, and disease profiles to identify U.S.
regions at elevated health risks

Kyle P Messier, PhD

National Institute of Environmental Health Sciences - Division of Translational
Toxicology - Predictive Toxicology Branch



Spatiotemporal Exposures
and Toxicology (SET) Group

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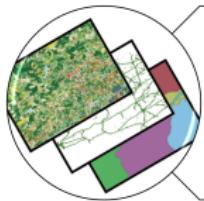
About Us

Spatiotemporal Exposures and Toxicology {SET} group

- Spatiotemporal Exposure Mapping
 - Chemical and Stressor Mixtures Prediction
 - Mechanistically Informed Geospatial Risk Assessment

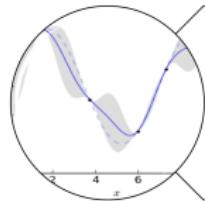


Geospatial Methods



Translational

- Maps
 - Integrative



Predictive

- Interpolation
 - Uncertainty

Objective

- Provide an overview of geospatial methods, data, applications, and future directions in toxicology and risk assessment

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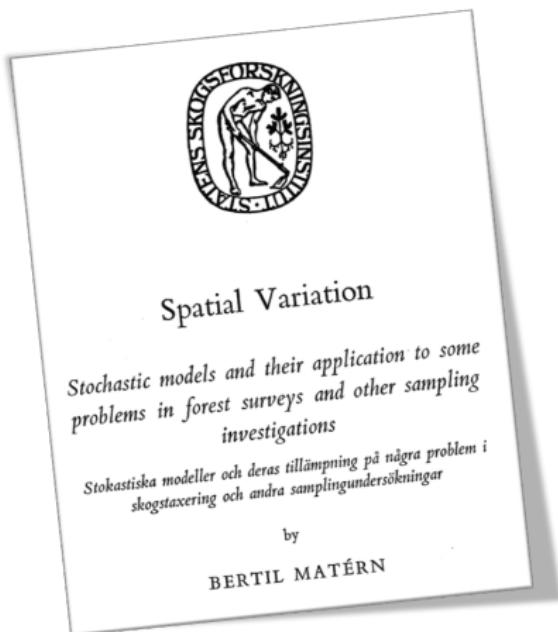
History

Mining



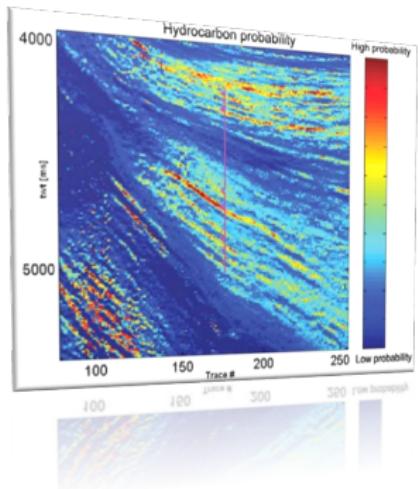
- Matheron and Krige developed geostatistical methods to predict ore content from core samples
- Matheron coined the term “Kriging” after Krige
- “Nugget” is a term used to random noise because predicting where gold nuggets were was so difficult

Forestry



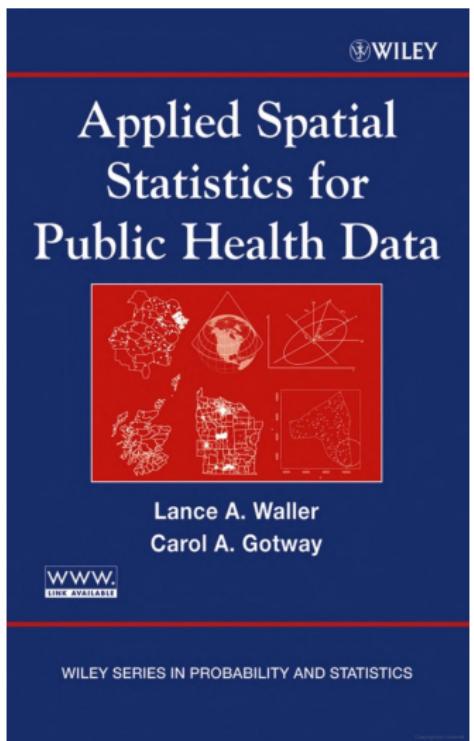
- Matérn developed correlation models for spatial variation for applications in Forestry
- To this day, we use the “Matérn” covariance function

Petroleum Engineering



- Used to evaluate the oil and gas field reservoirs
- Uses geology and seismic data

Public Health



- Cressie, 1990: Statistics for Spatial Data
- Waller and Gotway, 2004: Applied Statistics for Public Health Data
- Wide scale adoption for statisticians and engineers in ecological and human exposure and risk applications

Toxicology



- **Toxicology is a new frontier for geospatial methods**
- Aggregate Exposure Pathways
- Adverse Outcome Pathway
- GeoTox
- Source-to-Outcome

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Classical Models

Uses in Public Health

- Estimate exposure to air pollutants, water contaminants, and other environmental stressors
- Geocode patient addresses to link to environmental exposures
- Estimate the spatial distribution of disease rates
- Estimate the spatial distribution of health risk factors

Land Use Regression

Linear regression for spatial data

$$Y(s) = X(s)\beta + \varepsilon$$

where $Y(s)$ is the response variable, $X(s)$ are the predictor variables, β are the regression coefficients, ε is the iid error term, and (s) denotes the spatial location.

Not a terrible idea for spatial data, but it directly violates the assumption of independence of observations.

Kriging

Kriging and spatial models provide an explicit term for spatial correlation. A reasonable approach is a random-effect model:

$$Y(s) = \mu(s) + \varepsilon + \eta(s)$$

where $\eta \sim N_n(0, \Sigma_\theta)$

and Σ_θ is a covariance matrix with parameters, θ , that accounts for correlation between spatial and temporal locations

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Data Sources

Common Data Sources and Types

- U.S. Census Bureau
- U.S. Environmental Protection Agency
- U.S. Geological Survey
- National Aeronautics and Space Administration
- National Oceanic and Atmospheric Administration
- U.S. Department of Agriculture
- Land cover data
- Health statistics
- Population characteristics
- Infrastructure data
- Air quality data
- Water quality data
- Satellite imagery

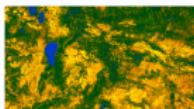
Satellite Imagery



Sentinel-2 Level-2A

The Sentinel-2 program provides global imagery in thirteen spectral bands at 10m-60m resolution and a revisit time of approximately five days. This dataset contains the global Sentinel-2 archive, from 2016 to the present, processed to L2A (bottom-of-atmosphere).

[Sentinel](#) [Copernicus](#) [ESA](#) [Satellite](#) [Global](#) [Imagery](#) ...



Sentinel 1 Radiometrically Terrain Corrected (RTC)

Radiometrically terrain corrected SAR imagery derived from the Sentinel 1 Level 1 GRD product.

[ESA](#) [Copernicus](#) [Sentinel](#) [C-band](#) [SAR](#) [RTC](#)



HREA: High Resolution Electricity Access

Settlement-level measures of electricity access, reliability, and usage derived from VIIRS satellite imagery

[HREA](#) [Electricity](#) [VIIRS](#)



Planet-NICFI Basemaps (Analytic)

Planet's high-resolution, analysis-ready mosaics of the world's tropics

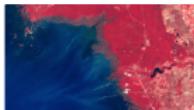
[Planet](#) [NICFI](#) [Satellite](#) [Tropics](#) [Imagery](#)



Planet-NICFI Basemaps (Visual)

Planet's high-resolution, analysis-ready mosaics of the world's tropics

[Planet](#) [NICFI](#) [Satellite](#) [Tropics](#) [Imagery](#)



Landsat Collection 2 Level-1

Landsat Collection 2 Level-1 data from the Multispectral Scanner System (MSS) onboard Landsat 1 through Landsat 5.

[Landsat](#) [USGS](#) [NASA](#) [Satellite](#) [Global](#) [Imagery](#)



MODIS Burned Area Monthly

MODIS Burned Area Monthly

[NASA](#) [MODIS](#) [Satellite](#) [Imagery](#) [Global](#) [Fire](#) ...

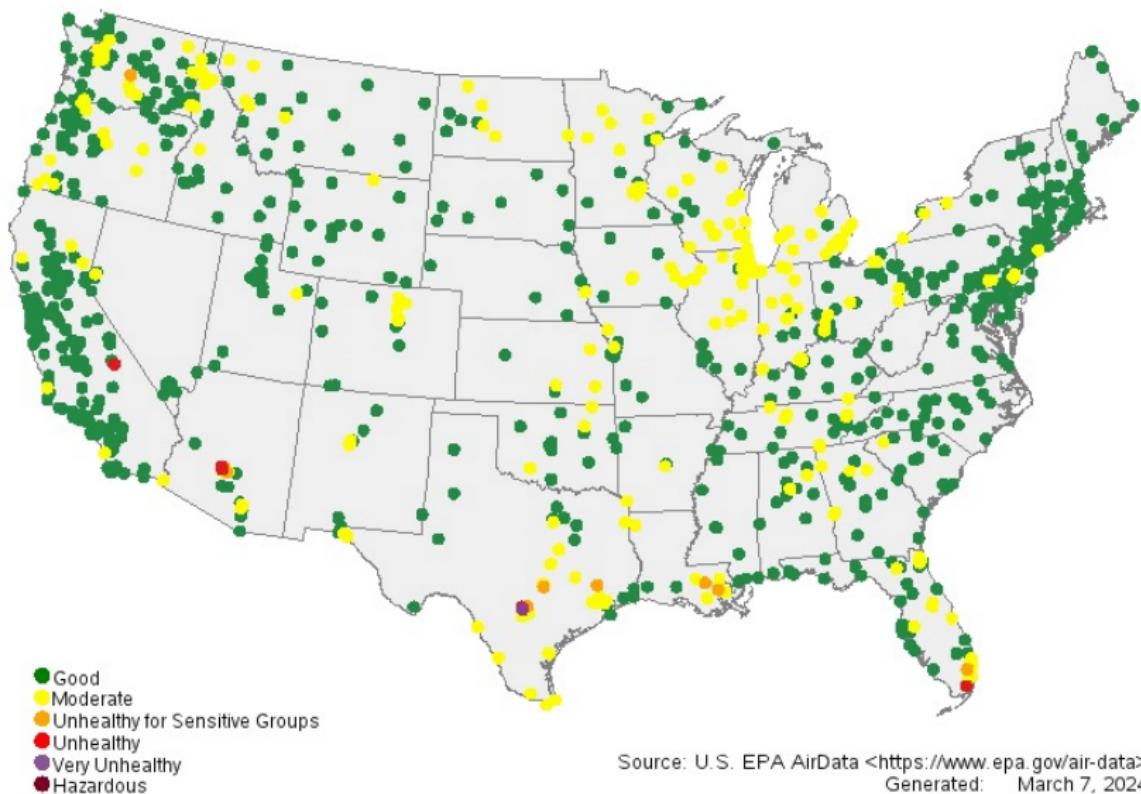


MODIS Nadir BRDF-Adjusted Reflectance (NBAR) Daily

MODIS Nadir BRDF-Adjusted Reflectance (NBAR) Daily

Air Quality Data

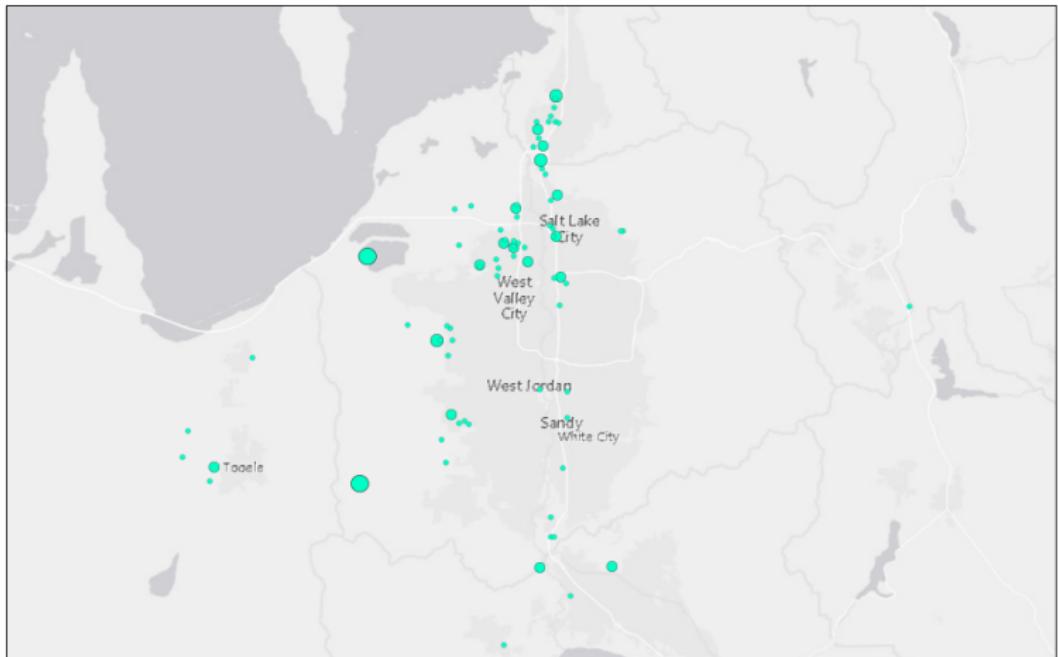
PM2.5 AQI Values by site on 01/01/2023



Source: U.S. EPA AirData <<https://www.epa.gov/air-data>>
Generated: March 7, 2024

Toxic Release Data

2021 TRI National Analysis: Where You Live



March 7, 2024

1,577,791
0 3.75 7.5 10 15 mi
0 5 10 20 km

EPA, HERE, NPS, Esri, HERE, Gamma, USGS, EPA, NPS

https://www.epa.gov/ERI/EXT

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Health Information

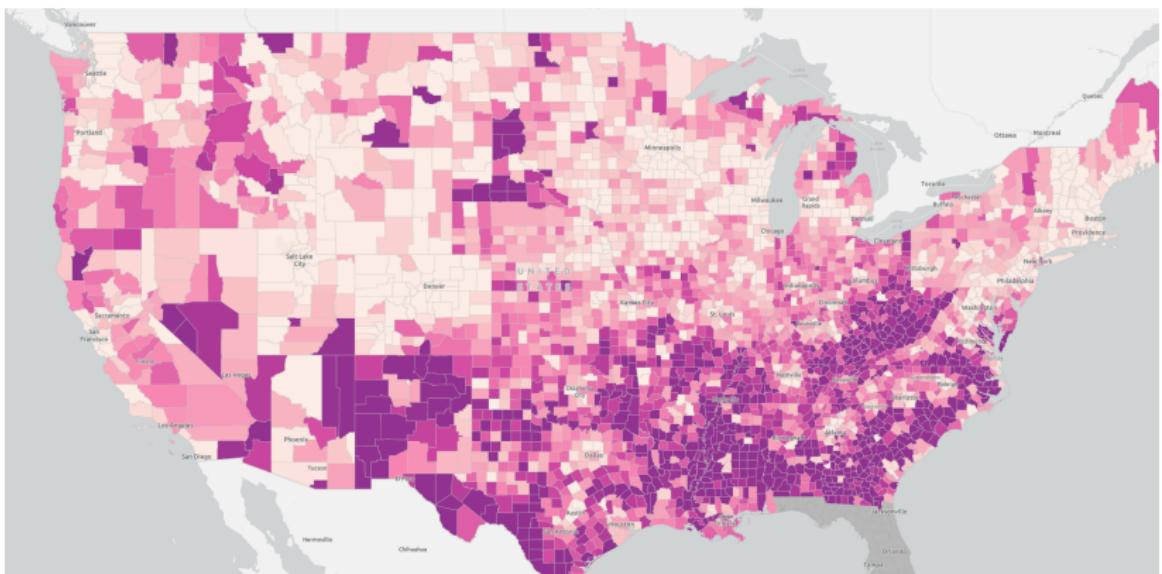


Figure 1: CDC Places Health Outcome Data: Diabetes Prevalence

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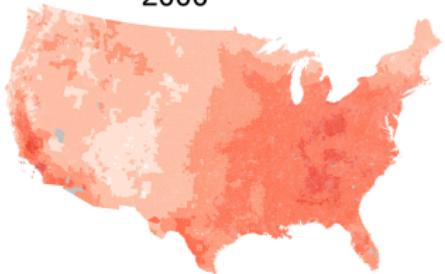
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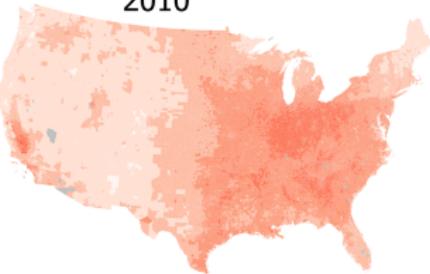
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Air Pollution Exposure Mapping

2000

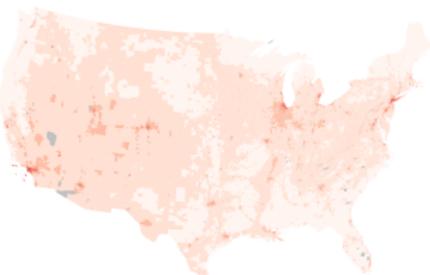
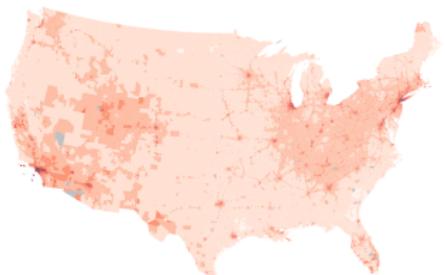


2010



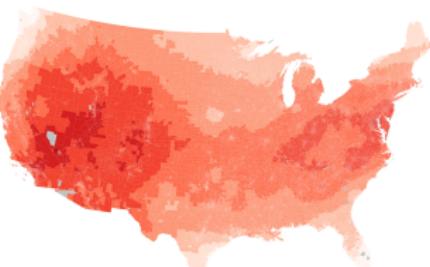
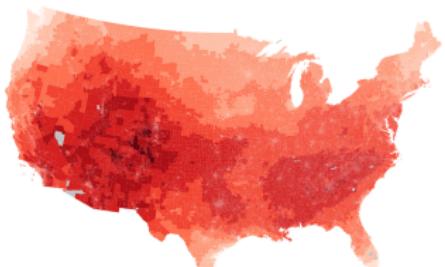
PM2.5
(µg/m³)

- < 2.5
- 2.5 - 5
- 5 - 7.5
- 7.5 - 10
- 10 - 15
- 15 - 20
- 20 - 25
- 25 - 30
- > 30
- no data



NO2
(ppb)

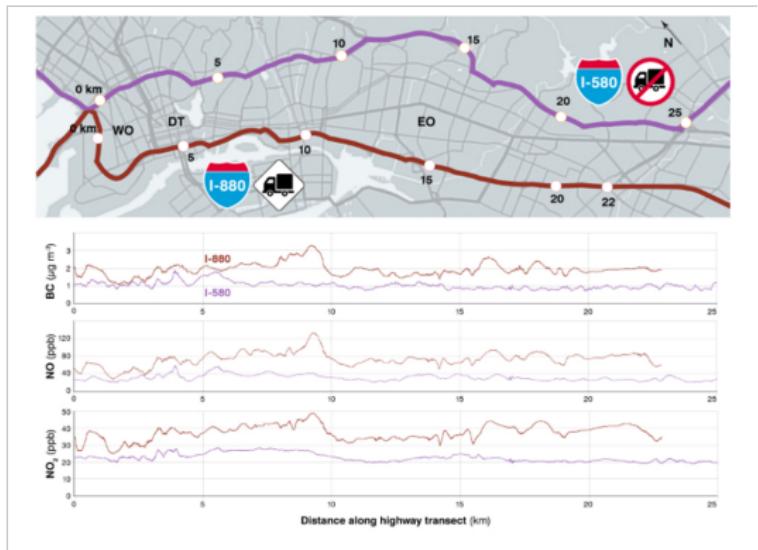
- < 3
- 3 - 6
- 6 - 9
- 9 - 12
- 12 - 15
- 15 - 20
- 20 - 25
- 25 - 30
- > 30
- no data



Ozone
(ppb)

- < 30
- 30 - 35
- 35 - 40
- 40 - 45
- 45 - 50
- 50 - 55
- 55 - 60
- 60 - 65
- > 65
- no data

Tale of Two Freeways



- All measured pollutants were consistently higher on I-880 compared to I-580
- I-580 has a heavy duty truck ban
- Heavy duty trucks are forced onto I-880 to get to the Port of Oakland

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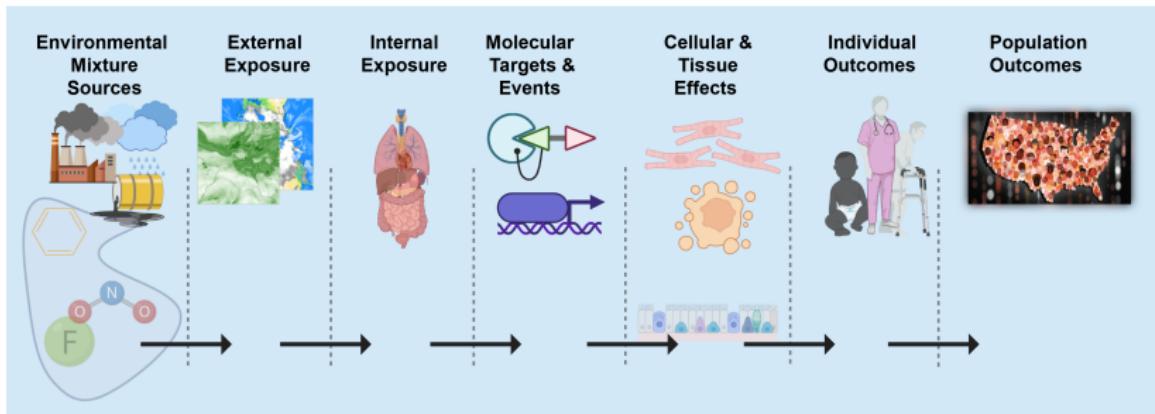
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Source-to-Outcome

Source-to-Outcome Modeling



Source-to-Outcome Modeling

- Source-to-Outcome is a framework for linking environmental sources to human health outcomes
- The framework is based on the Aggregate Exposure Pathway (AEP) and Adverse Outcome Pathway (AOP) concepts

Source-to-Outcome Modeling

- Next generation risk of cumulative and total exposomic effects on human health
- A balance between mechanistic and translational research
- A framework for integrating multiple data sources and models
- Incorporate biological and geospatial information on communities and individuals

Getting Two Frameworks to Work Together

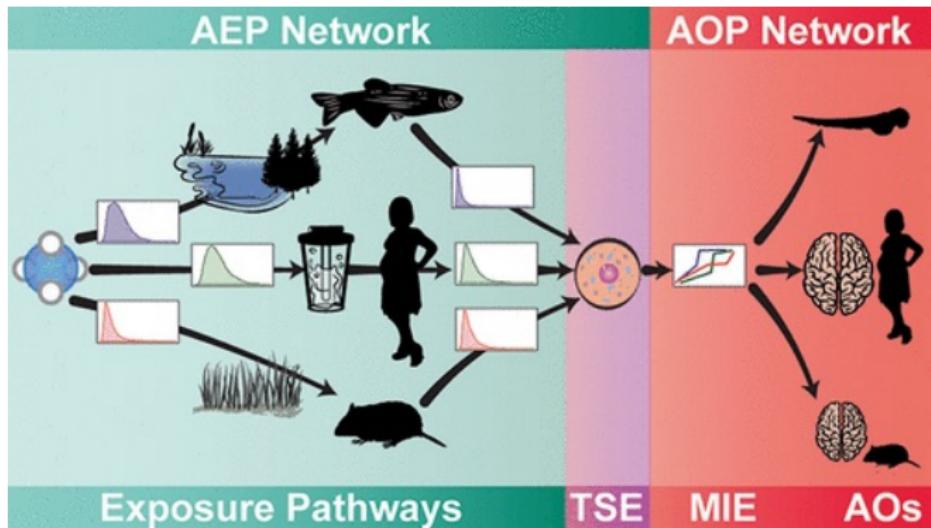
Aggregate Exposure Pathways

- AEP is a comprehensive external analysis of source, media, and transformations

Adverse Outcome Pathway

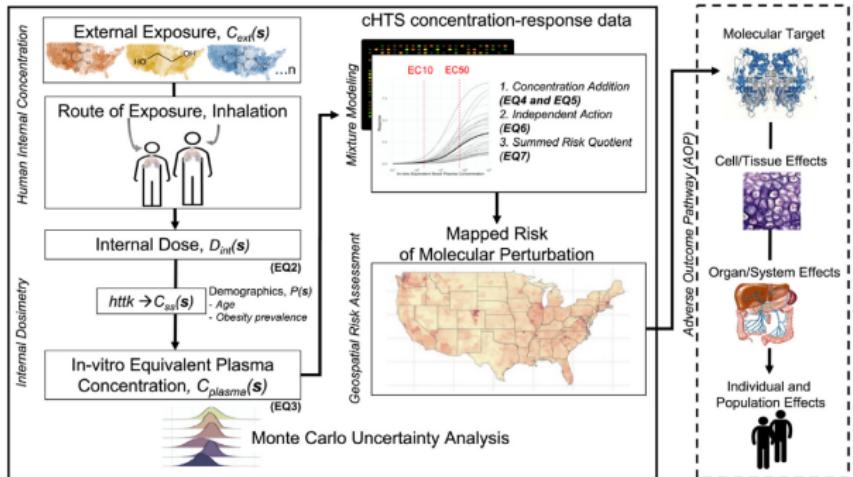
- AOPs provide a linkage specific biological target, pathway or process by a stressor and an adverse outcome(s) considered relevant to risk assessment

AEP-AOP



Hines, D. E., Conolly, R. B., & Jarabek, A. M. (2019)

GeoTox

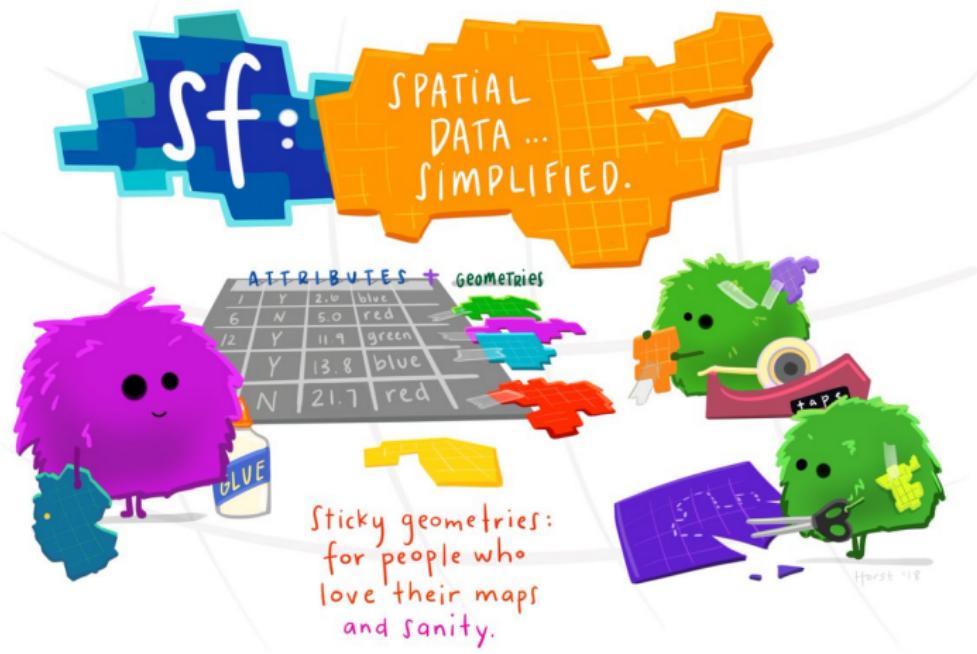


Dr. Kristin Eccles, Former Visiting Fellow in DTT
and SET, Now at Health Canada

GeoTox

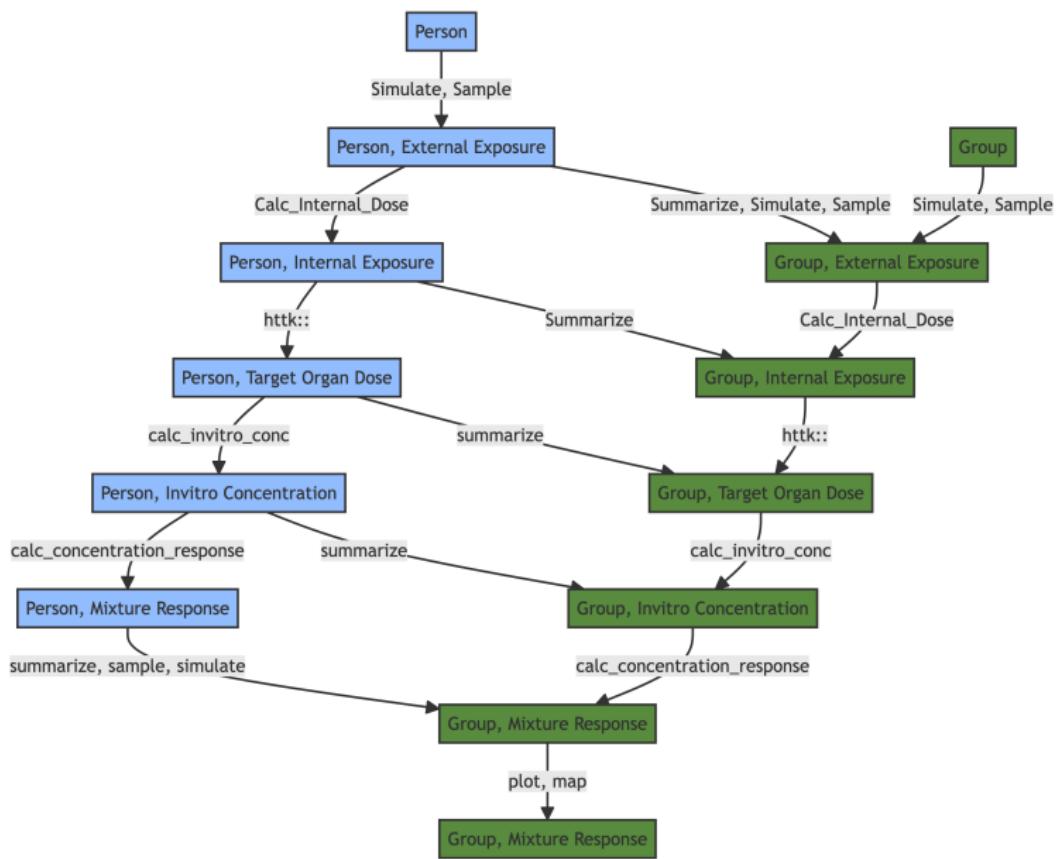
- Goal is to develop extensible, open-source software for facilitate source-to-outcome modeling (FAIR+)
- Working with Drs. David Reif and Skylar Marvel (NIEHS/DTT)
- Submitting to CRAN
- Static website hosted via {SET}group website
- Maintained, Documented, and Supported

GeoTox



sf package for spatial data in R (Edzer Pebesma and others)
(Illustration (c) 2018 by Allison Horst)

GeoTox



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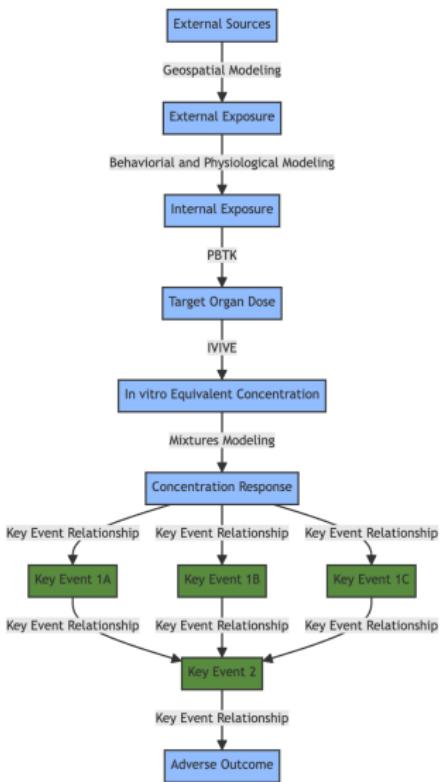
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Conclusions

Looking Forward

- The tools for each step of the source-to-outcome modeling framework are available, but the integration is still a work in progress
- The integration of these tools will allow for the development of a comprehensive source-to-outcome modeling framework that can be used to assess the risk of cumulative and total exposomic effects on human health

Multiple Assays Informing an AOP



Looking Forward

- Incorporate more refined information on individual and population-level susceptibility to environmental exposures
- It is going to be a massive code and software development challenge

Looking Forward

- Geospatial **exposures** are the foundation of a spatial, total exposome risk approach

Acknowledgements

- Daniel Zilber
 - Mitchell Manware
 - Insang Song
 - Eva Marques
 - Ranadeep Daw
 - Mariana Alifa Kassien
 - Kristin Eccles
 - Melissa Lowe
 - Taylor Potter
 - Alvin Sheng
 - John Wambaugh
 - Alison Motsinger-Reif
 - David Reif
 - Skylar Marvel
 - Nicole Kleinstreuer
 - Julia Rager
- Funding:**
- NIEHS ZIA ES103368-02
 - Patient Centered Outcome Research Trust Fund (PCOR-TF)