Air Pollution, the Aging Brain and Alzheimer's Disease

ACT-AP; Co-funded by NIEHS and NIA

Principal Investigators

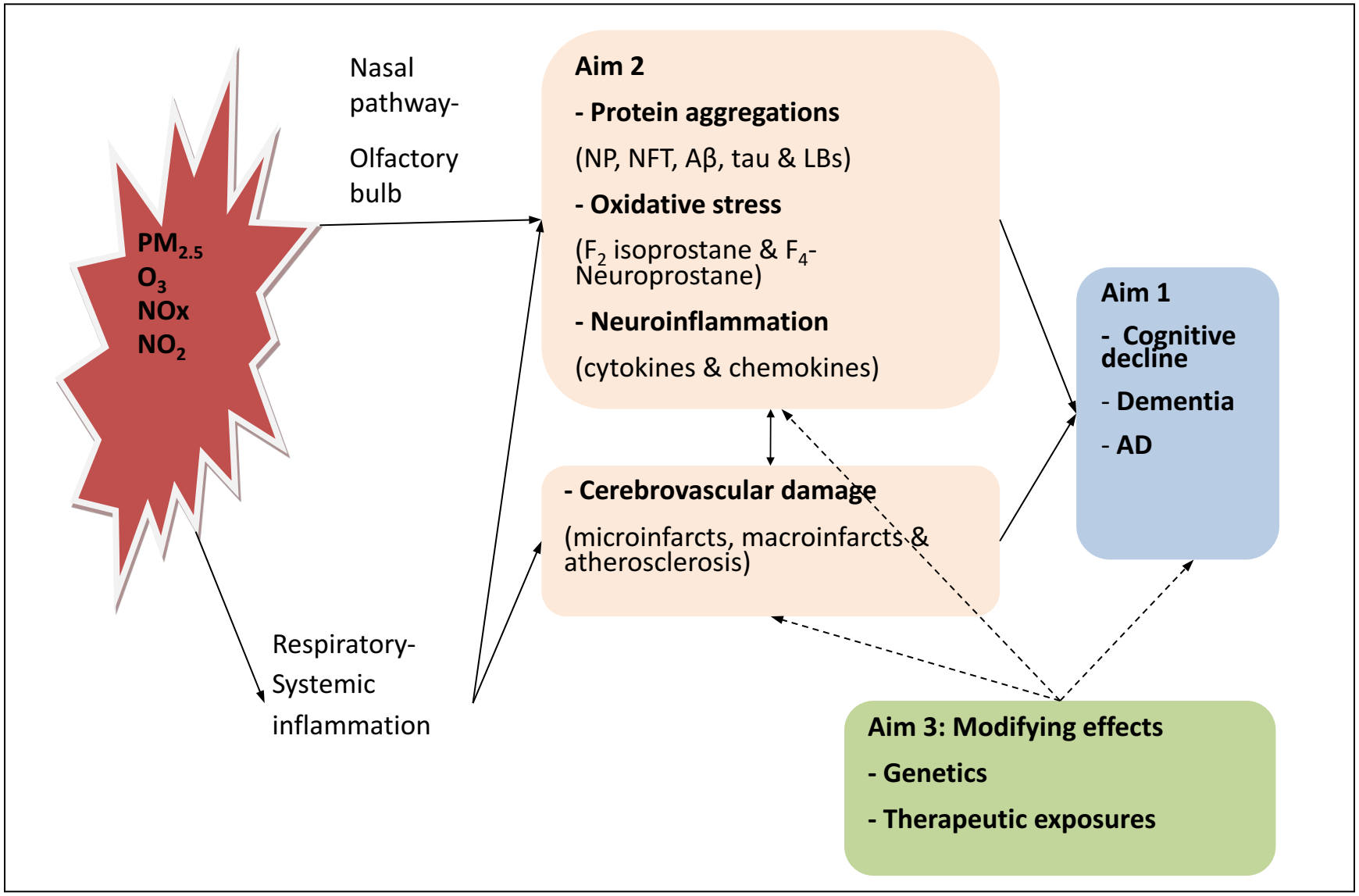
Ge (Gail) Li, MD, PhD

Elizabeth A (Lianne) Sheppard, PhD

Background

- Ambient air pollution (AP):
  - Complex mixture of particles and gases
  - Much respiratory & cardiovascular health effect evidence (e.g., Dockery et al 1993, Miller et al 2007)
  - Recent evidence of cognitive effects (Weuve et al 2012, Power et al 2011)
- Particulate matter (PM), may
  - Have important neurotoxic effects
  - Enter the circulation from the olfactory system and cross the blood-brain barrier (Block et al 2009 & 2012)
- Neurotoxic mechanisms of AP unknown. Possibly (Block et al 2009)
  - Neuroinflammation
  - Oxidative stress

Impact of AP on the Brain



Specific Aim 1

To determine in the entire ACT cohort the association of long-term average individual-level AP exposure with

- (**Aim 1a**) the rate of cognitive decline, and
- (**Aim 1b**) the risk of AD and all-cause dementia.

Specific Aims 2 & 3

Aim 2. To determine the effect of AP exposures on pathophysiologies of the brain, using autopsy data:

- Standard qualitative measures including presence of neuropathological AD and Lewy body disease, and cerebrovascular damage;
- Novel quantitative measures including Histelide measurements of amyloid beta (Aβ) and tau; and
- Biomarkers of oxidative stress in fresh frozen brain samples

Aim 3. To explore the interactive effects of AP with genetic variants (GxE) and therapeutic exposures (ExE) on rate of cognitive decline, AD and dementia risk, and pathological changes in brain

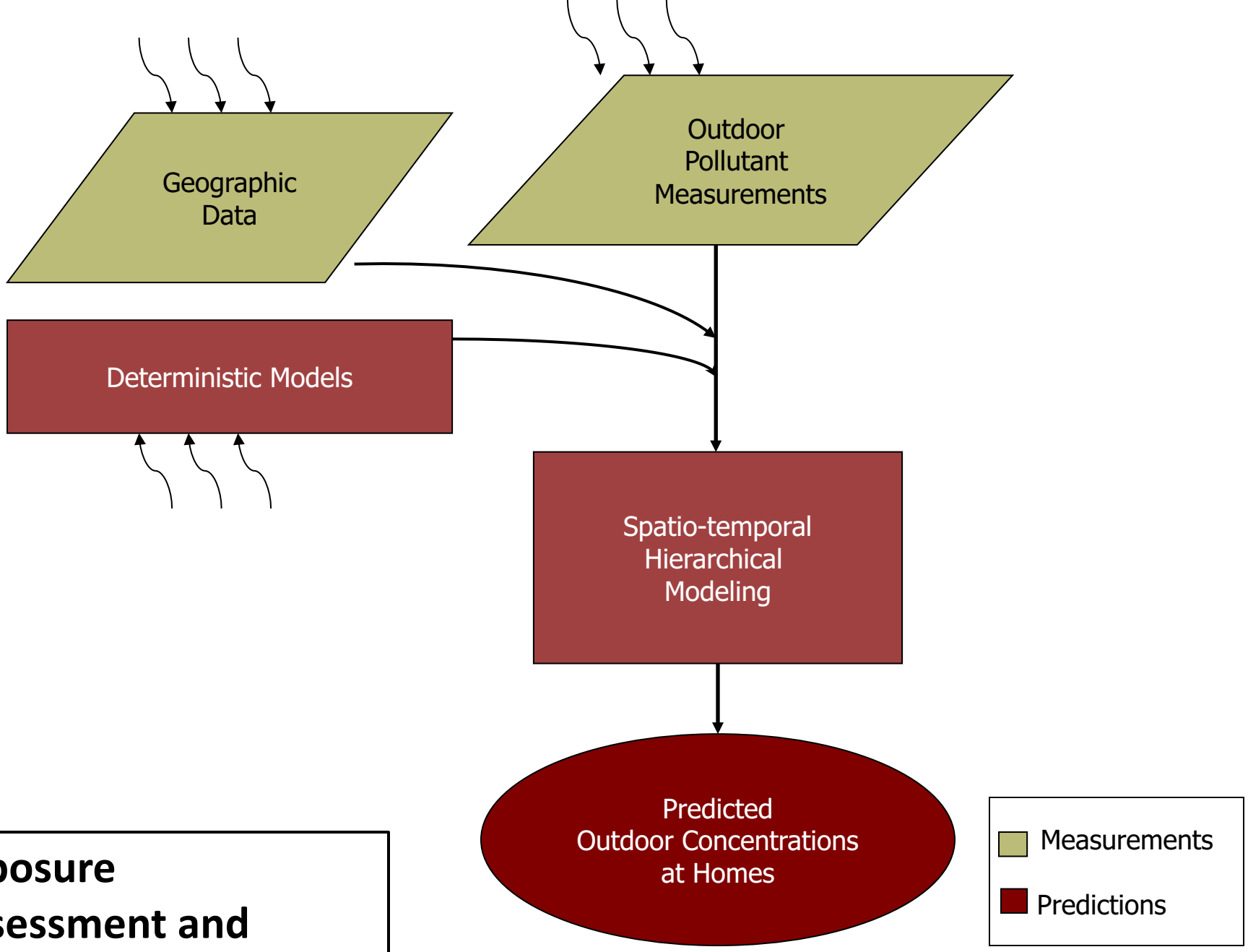
ACT-AP Approach

Combine state-of-the-art AP exposure modeling with the well-established and well-characterized NIA-funded large cohort of elderly participants in the Adult Changes in Thought (ACT) study:

- Study samples
  - 5,088 ACT subjects with an average of 7 (2-22) years follow-up
  - Incident dementia cases: 1,068 (859 AD)
  - Autopsy: 633 (303 fresh frozen brains)
    - New neuropathological measures in fresh frozen brains

Air Pollution Exposure Assessment & Modeling Plans

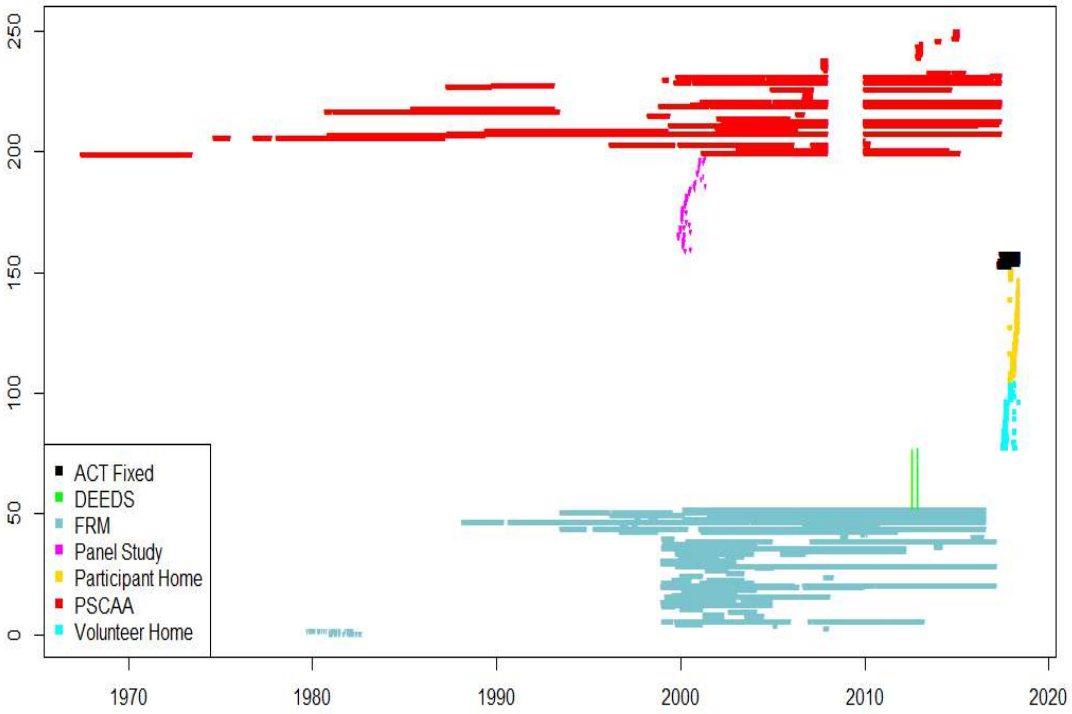
- **Add existing monitoring data to our database**
  - Data from local agencies
  - Previous research studies in the Puget Sound
- **Collect new monitoring data**
  - Low-cost sensors for PM, NO, NO_2, CO, O_3 (25 monitors)
    - Co-locations + ACT participant homes and similar locations
  - 3 snapshot campaigns for NO_X, NO_2, and O_3 using 110 Ogawa samplers
    - 17 roadway gradient clusters + 7 locations representative of ACT participants
- **Evaluate sensor data quality & calibrate data**
- **Geocode & calculate geocovariates**
  - Geocode ACT participant addresses (current & historical)
  - Calculate up to 800 geocovariates at each ACT participant address + monitor locations
- **Predict AP at ACT participant addresses**
  - Fit spatio-temporal exposure models using monitoring data since 1970's
  - Predict 2-week averages at ACT participant addresses; average to long time periods



Exposure Assessment and Modeling Paradigm

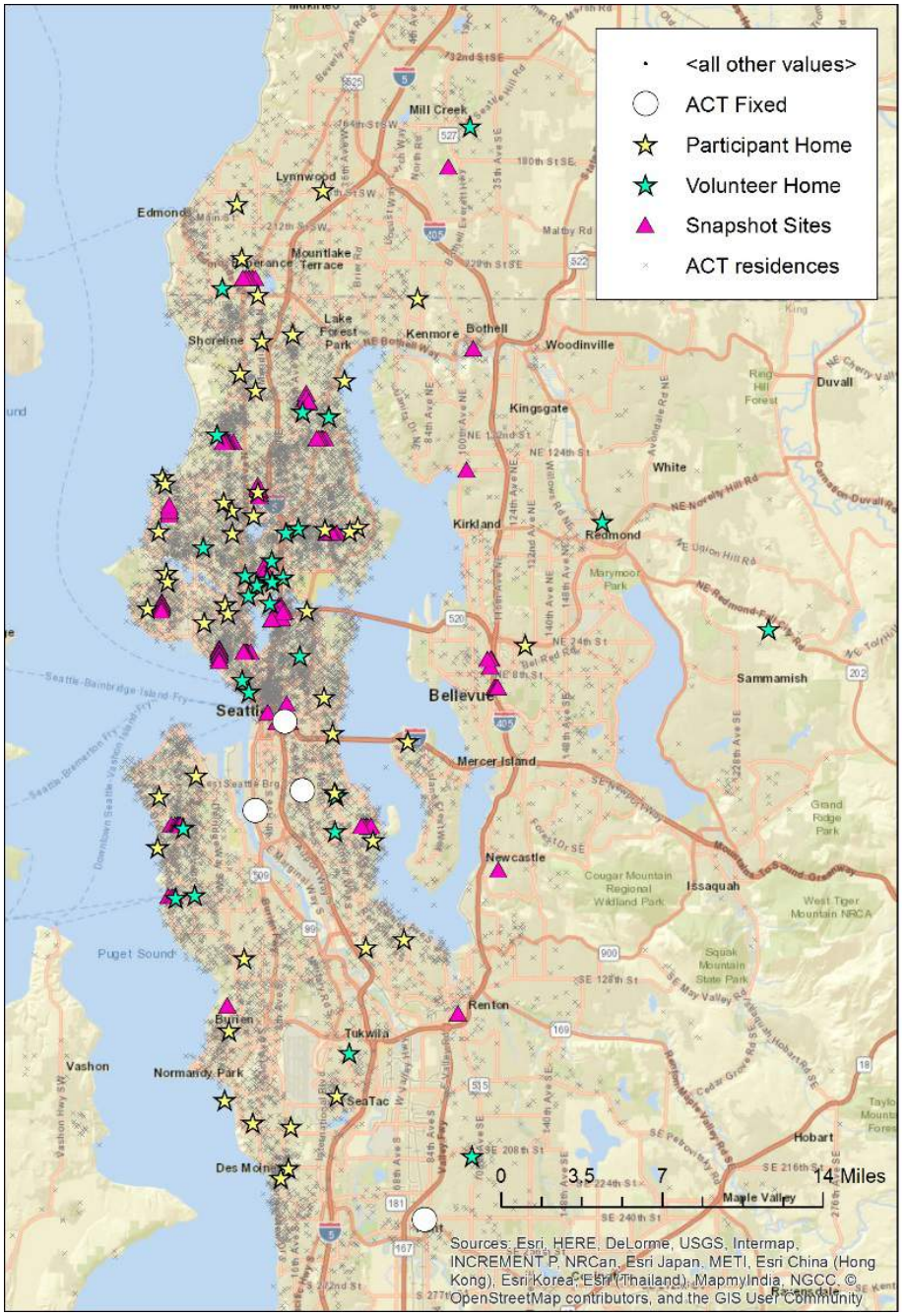
$PM_{2.5}$ Monitoring in Puget Sound

Data Density by Study or Source

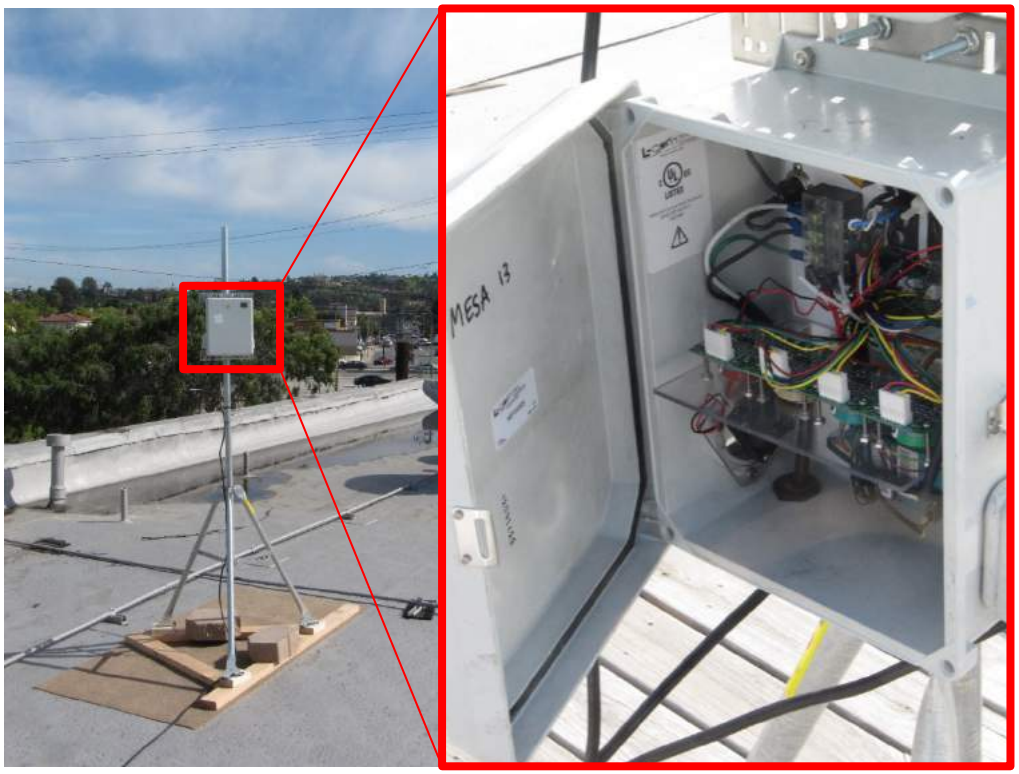


Monitor Locations

ACT-Specific Monitoring and ACT Participants



Low Cost Monitor Technology: QC & Calibration are Necessary!



Pollutant	Method
$PM_{2.5}$	Light scattering: *2 Plantower (lasers), 2 Shinyei (LED)*
NO, NO_2, O_3, CO	Chemical reaction produces an electrical current that is linearly proportional to the fractional volume (i.e. measures parts per volume, rather than mass): *Alphasense*
	Additionally measure temperature & RH inside the box

Co-location for Calibration

Sensor QC

Challenge: Identify and replace broken sensors quickly to limit bad data

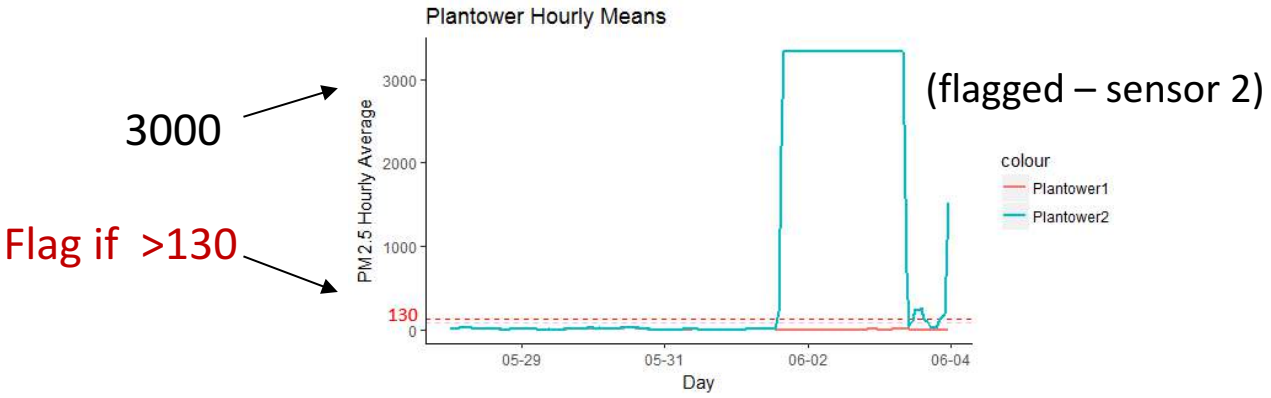
Solution:

- Automated weekly report in R / Rmarkdown (code on Github*)
- Flag sensor quality issues with multiple criteria and levels of severity

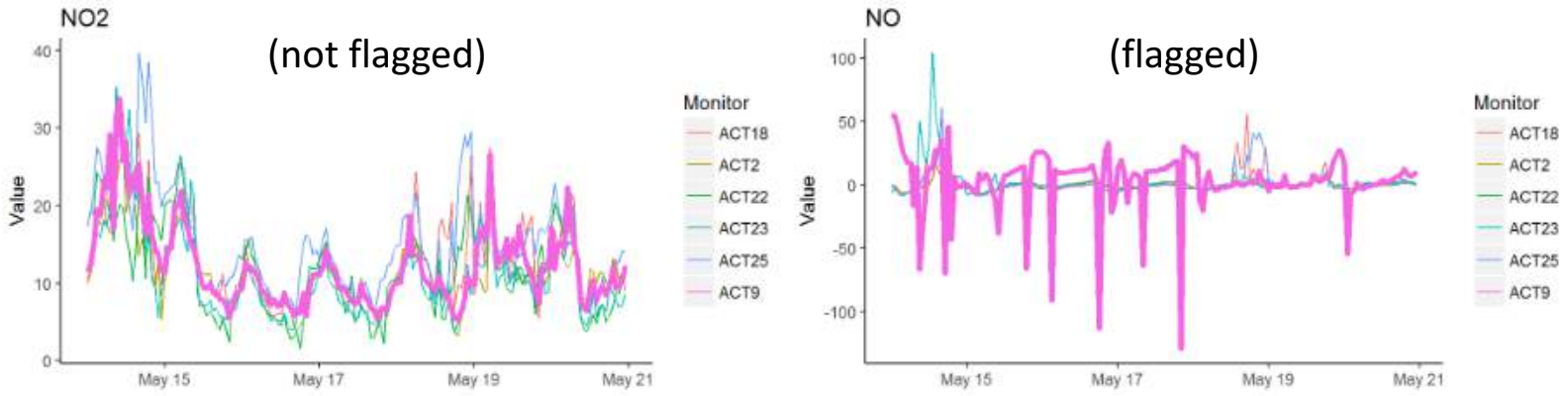
*https://github.com/kaufman-lab/uw-radical/tree/master/Sensor_QC

Sensor QC: Quality Flags

- Data completeness
- Correlation of duplicate sensors in the same box
- Sensible pollutant values/variation



- Network Correlations of geographically close sensors



Sensor QC Report Format

Challenge: Distill massive amounts of data into a readable report

Solution: Design a report with 2 main purposes:

1. Immediately identify the biggest problems.
2. Easily navigate to further details (but avoid the complete picture for monitors without issues).

1) Table of Contents

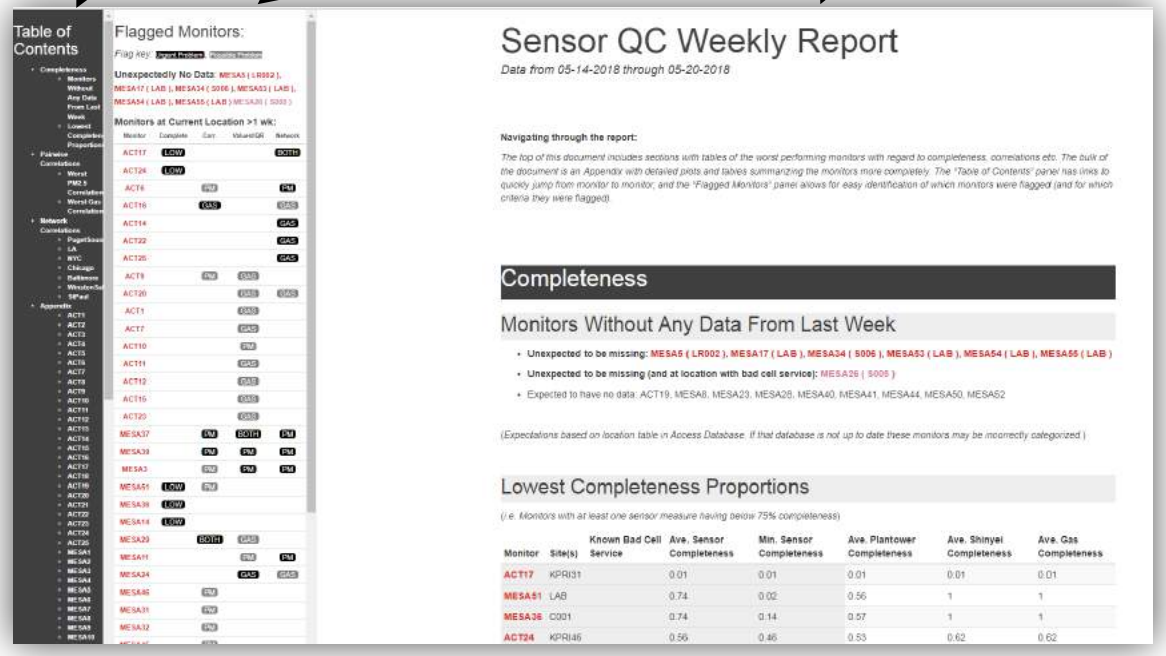
- Easy navigation to further details on any monitor

2) Flag Table

- Summary of quality flags and prioritization of issues.

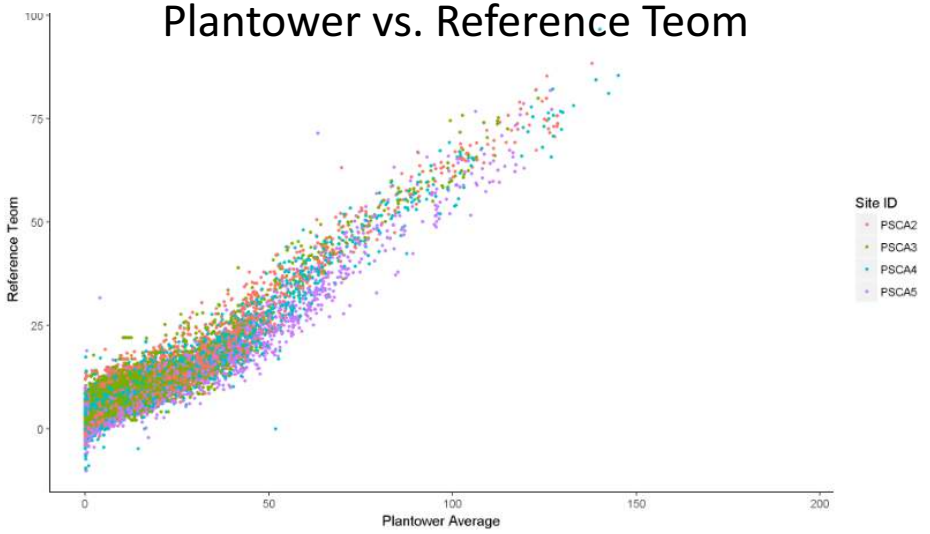
3) Body

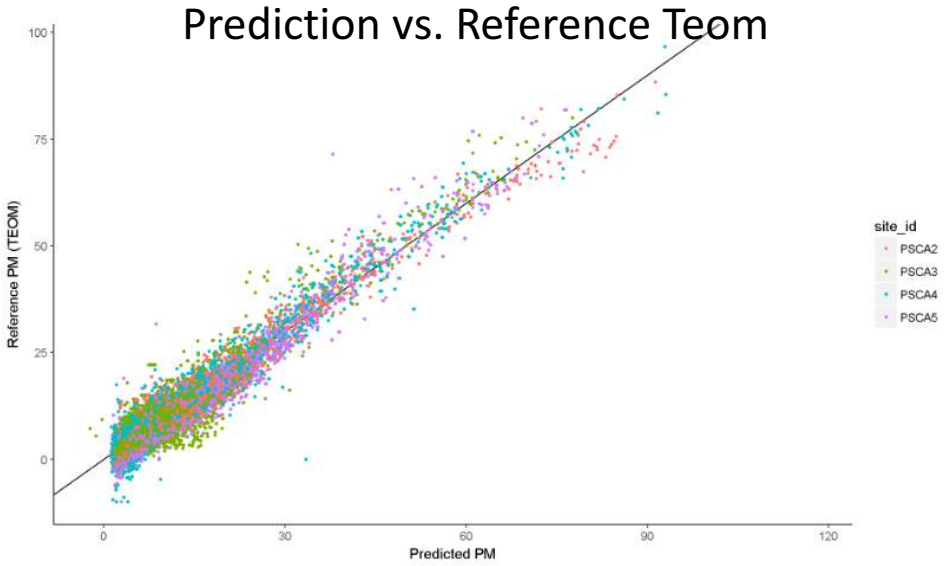
- Sections for each quality criteria and for each monitor



PM2.5 Calibration

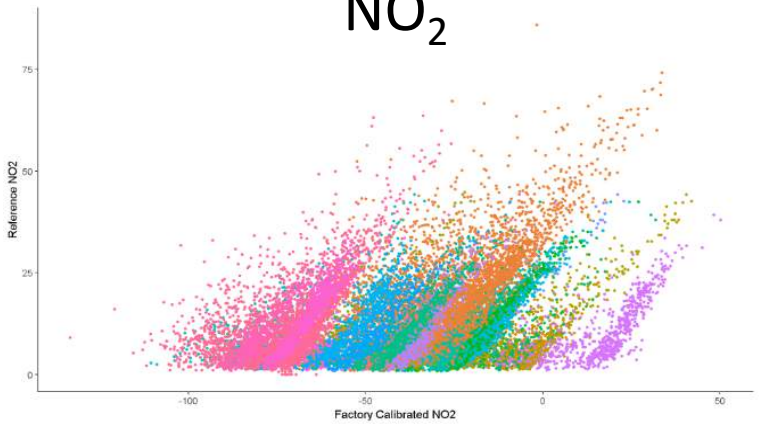
- Co-location at 4 PSCAA locations with TEOMs
  - Beacon Hill, Kent, Tacoma, Marysville
  - Excluded co-located data at Duwamish
- Calibrated Plantower $PM_{2.5}$ measurements to reference TEOM; hourly time scale; 10-fold cross-validation
  - Shinyei PM2.5 data not used
- Model Performance
  - Predictors: Plantower_avg, Plantower_avg^2, Plantower bin counts, Temp, RH
  - CV R^2 = .911
  - RMSE = 2.13 $\mu g/m^3$



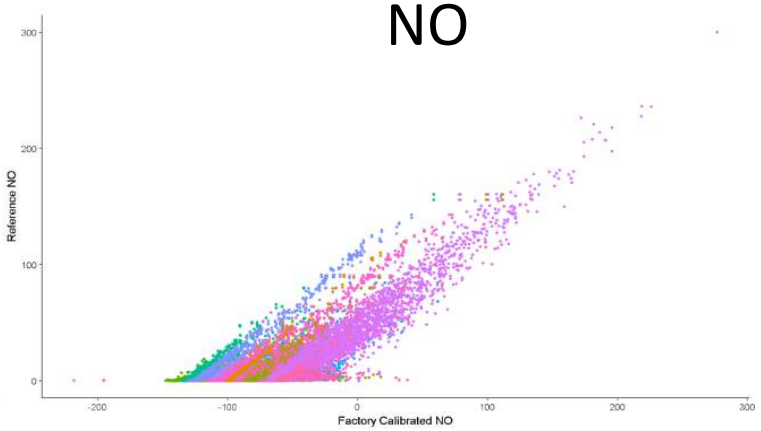


Gas Calibration: Alphasense Factory Calibrations vs. PSCAA Reference

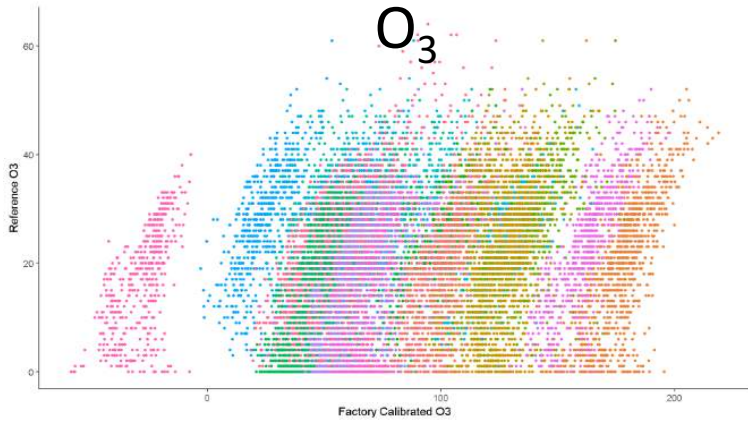
NO_2



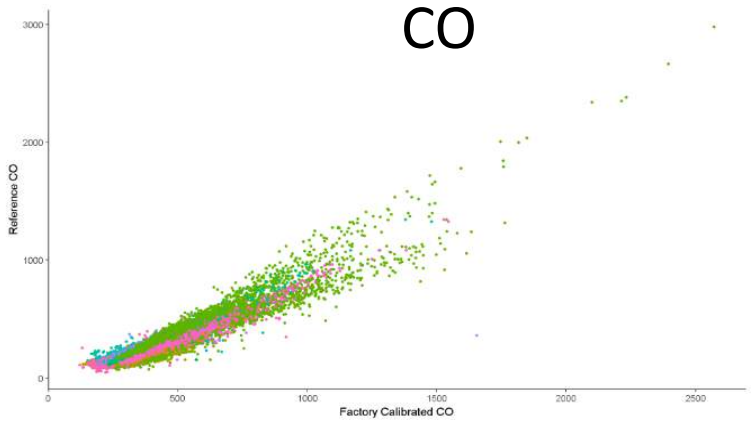
NO



O_3



CO



Gas Calibration

- Leveraged two sensors for each gas
  - Active (WE)
  - Encased/Auxiliary (AUX)
- Current Model Performance
  - Co-location at 2 PSCAA locations
  - Hourly time scale; 10-fold cross-validation
  - Included sensor ID covariate to account for sensor offsets

Station	NO2	NO	O3	CO
Beacon Hill	x	x	x	x
10th/Weller	x	x		x

Gas	CV R^2	RMSE (ppb)	Model Predictors
NO_2	.891	2.97	NO2_aux, NO2_we, NO2_we², NO2_we³, Temp, Temp², RH, RH², SensorID
NO	.953	4.41	NO_aux, NO_we, NO_we², NO_we³, Temp, Temp², RH, RH², SensorID
O_3	.966	2.26	O3_aux, O3_we, O3_we², O3_we³, NO2_we, Temp, Temp², RH, RH², SensorID
CO	.947	37.41	CO_aux, CO_we, CO_we², CO_we³, Temp, Temp², RH, RH², SensorID

Spatio-Temporal Exposure Model

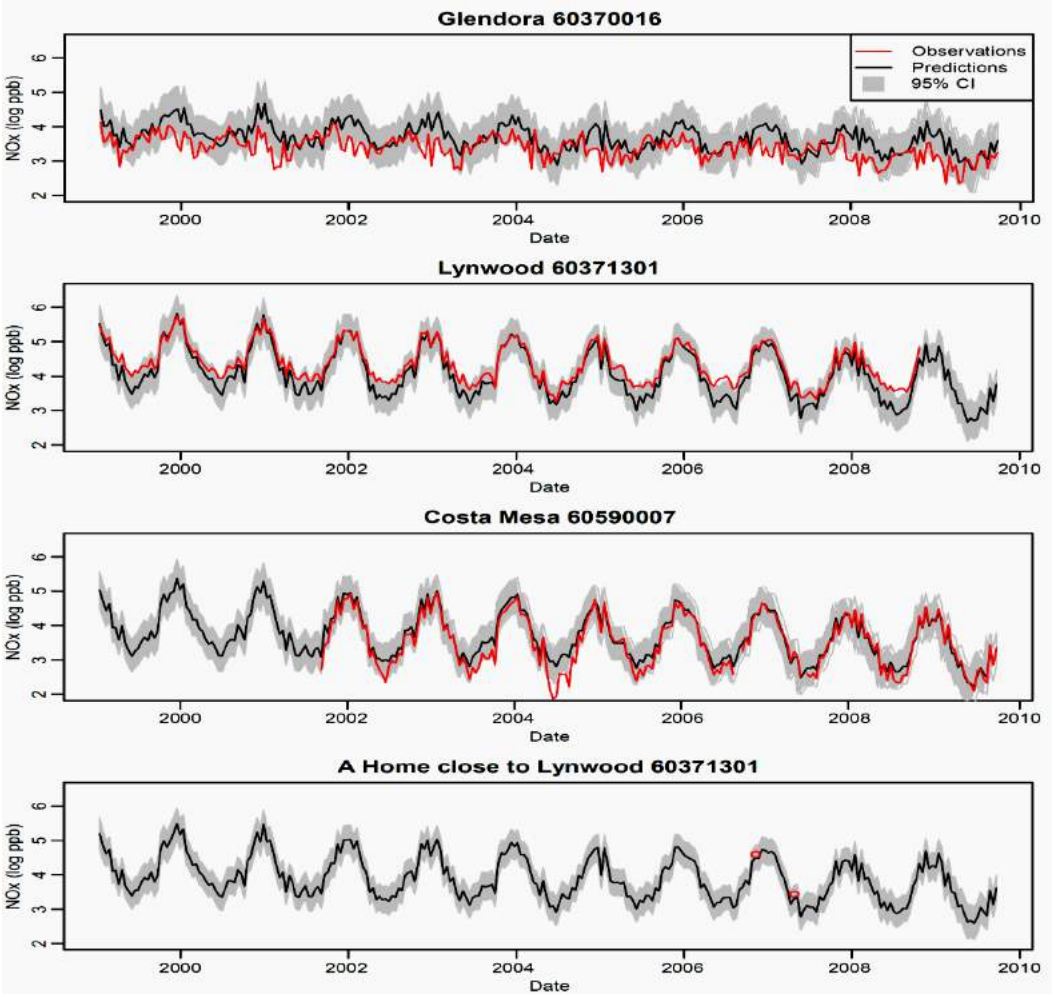
- $C_{s,t} = \mu_{s,t} + \nu_{s,t}$ ← measured concentrations on log scale
- $\mu_{s,t} = \beta_{0,s} + \sum_{i=1,K,m} \beta_{i,s} f_i(t) + \gamma M(s,t)$ ← temporal trends at location *s* + space-time covariate
  - $f_i(t)$ smooth temporal basis functions derived from data
  - $\beta_{i,s}$ spatial random fields distributed as $N\left(X_i \alpha_i, \Sigma(\phi_i, \sigma_i^2)\right)$
    - Geostatistical covariance structure with "land use regression" covariates for population, traffic, land use, etc.
  - $M(s,t)$ space-time covariate
- $\nu_{s,t}$ ← variation from temporal trend (mean 0)
  - Geostatistical spatial structure with simple temporal correlation
    - Process noise + measurement error

Example GIS Covariates

Predictor Variable	Symbol	Units	Buffer radii	Functional Form
Land Use				
Population	Pop	Total people within buffer (m)	500,1000,1500,2000, 2500,3000,5000, 10000,15000	scaled by 1/10000
Intense Use Land	Int	km^2	50, 100, 150, 300, 500, 750	untransformed
Open Space Land	Open	km^2	50, 100, 150, 300, 500, 750	untransformed
Distance to Coast	D2C	meters	n/a	trunc. 15km & 25km scaled by 1/1000
Distance to industrial Source (rail road, air port, etc...)	D2V	meters	n/a	untransformed
Industrial NO_X emissions	NOx		3000,15000,30000	untransformed
Roadway				
Distance to nearest A1, A2, or A3	D2R	meters	n/a	Log10
Distance to nearest A1	D2A1	meters	n/a	Log10
Distance to nearest A2	D2A2	meters	n/a	Log10
Distance to nearest A3	D2A3	meters	n/a	Log10
Length of A1roads within buffer	A1	meters	50, 100, 150, 300, 500, 750, 1000, 5000 10000, 15000	scaled by 1/1000
Length of A2 roads within buffer	A2	meters	50, 100, 150, 300, 500, 750, 1000, 5000 10000, 15000	scaled by 1/1000
Length of A3 roads within buffer	A3	meters	50, 100, 150, 300, 500, 750, 1000, 5000 10000, 15000	scaled by 1/1000

Example: NO_x Model Performance in Los Angeles

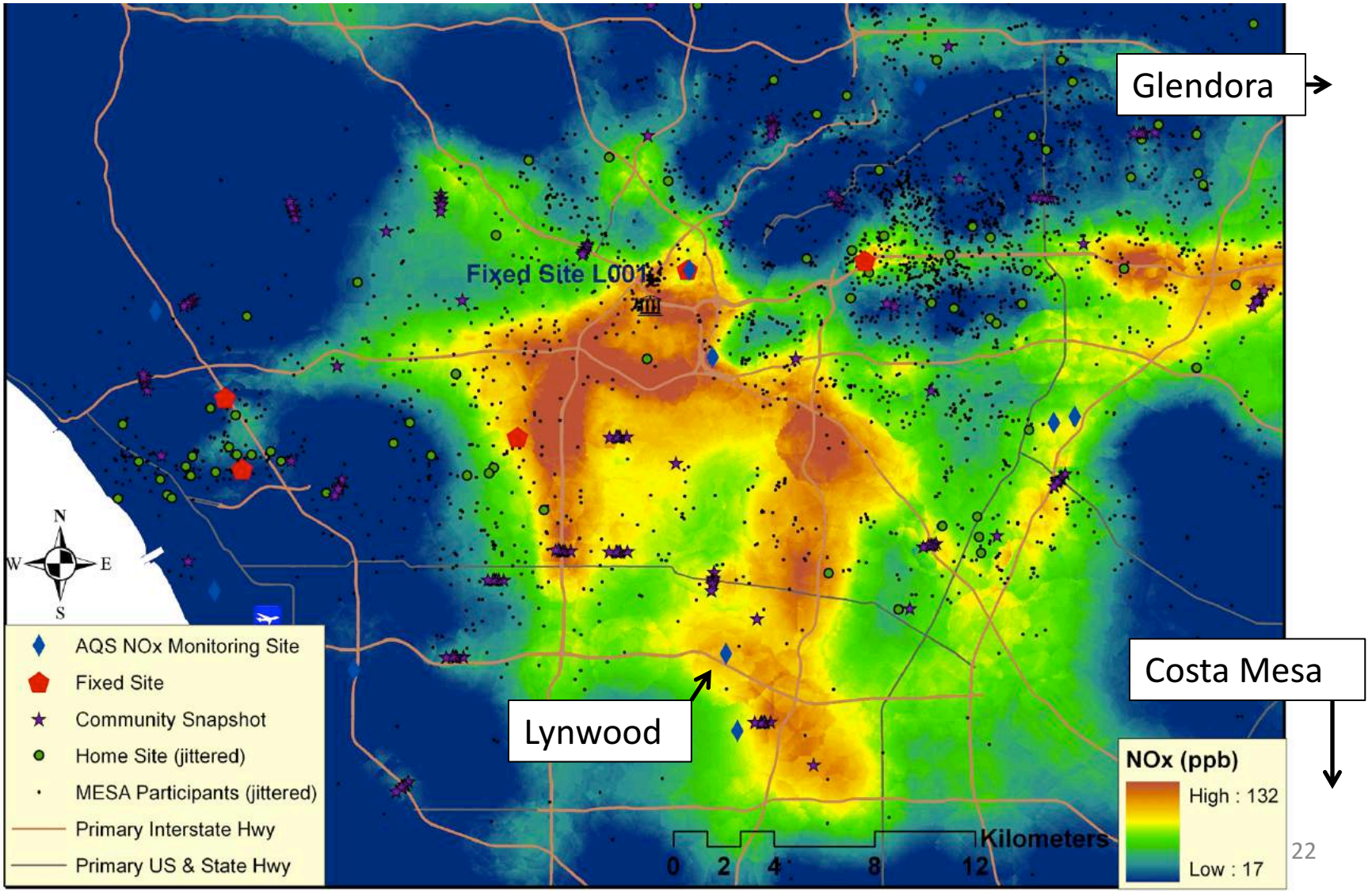
Predictions* are similar to observations:



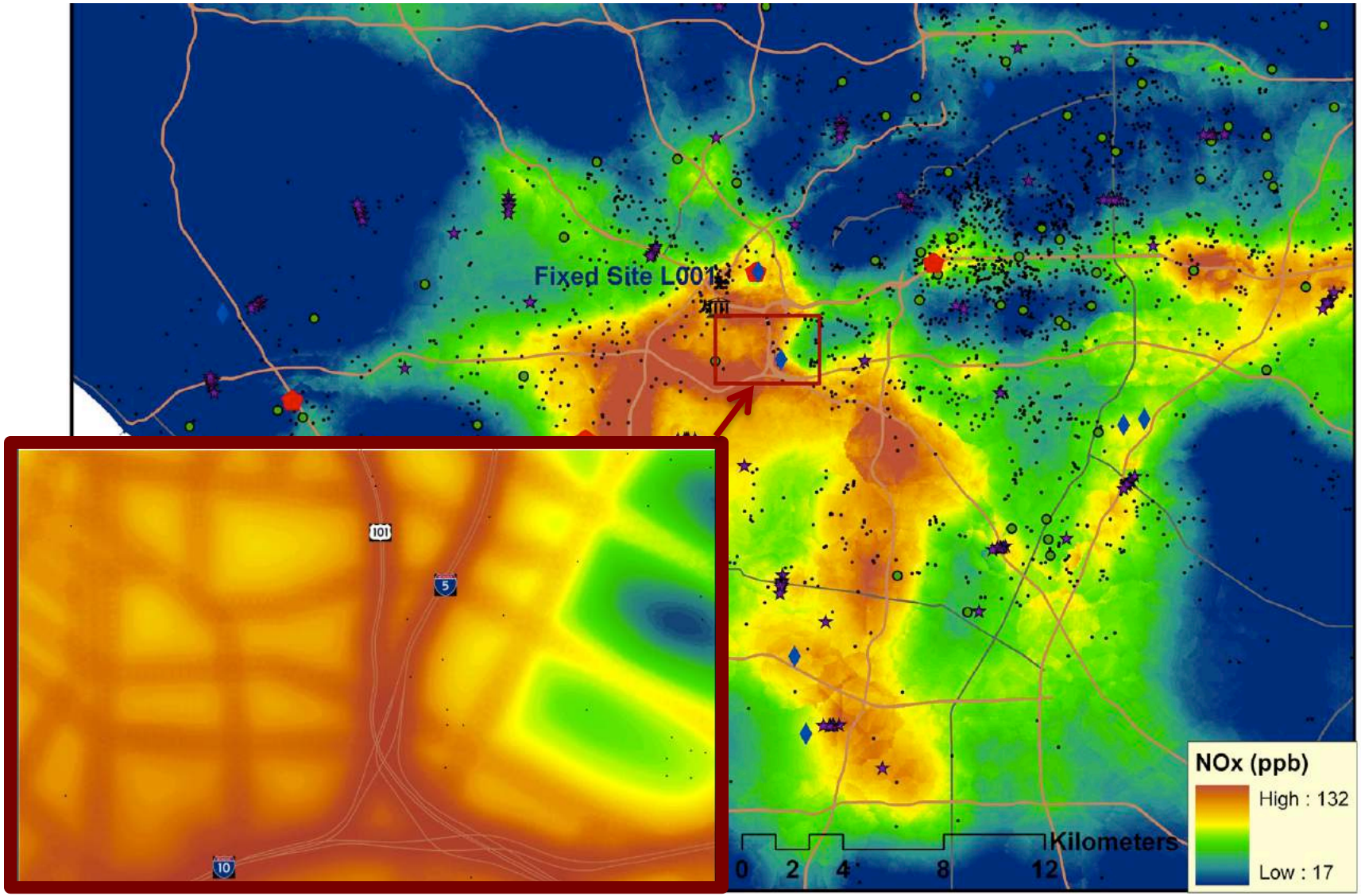
and available at all times:

*Cross-validated

Example: Predicted NO_x Concentrations in Los Angeles, California



Example: Predicted NO_x Concentrations in Los Angeles, California



Questions?

Acknowledgements & Resources

ACT: NIA U01 AG006781
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Principal Investigators
- Ge (Gail) Li, MD, PhD gli@uw.edu
- Elizabeth A (Lianne) Sheppard, PhD sheppard@uw.edu

Exposure Assessment Co-Investigators
- Edmund Seto, PhD eseto@uw.edu
- Tim Larson, PhD tlarson@uw.edu

Links
Sensor QC tools: https://github.com/kaufman-lab/uw-radical/tree/master/Sensor_QC
View current sensor data: https://shiny.deohs.washington.edu/app/act-dashboard
ACT-AP study: http://deohs.washington.edu/act-ap
CAMPS (Community Air Monitoring in Puget Sound): http://deohs.washington.edu/camps