

Air Pollution, the Aging Brain and Alzheimer's Disease

ACT-AP; Co-funded by NIEHS and NIA



Principal Investigators

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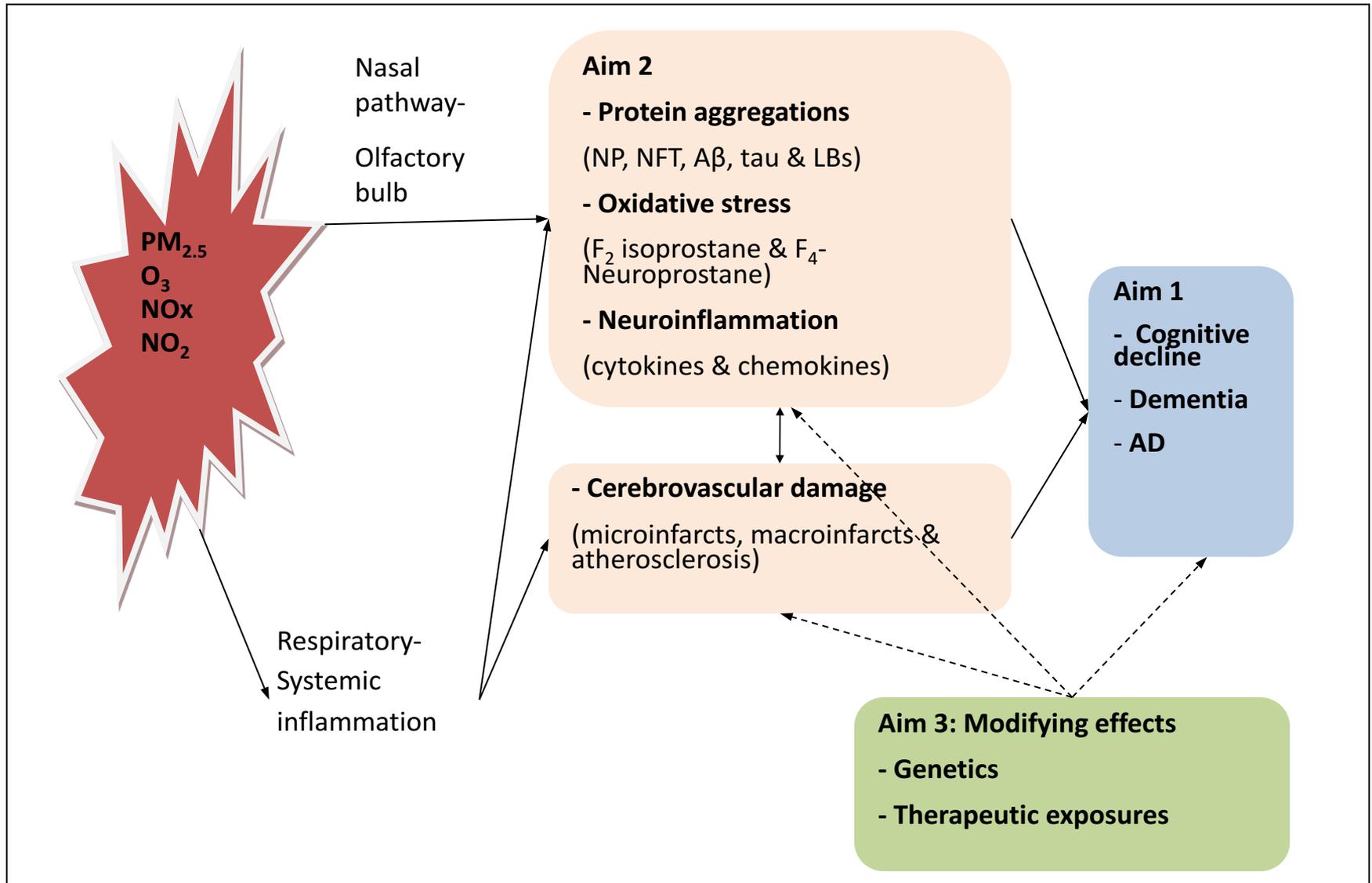
Elizabeth A (Lianne) Sheppard, PhD



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 ($A\beta$) 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

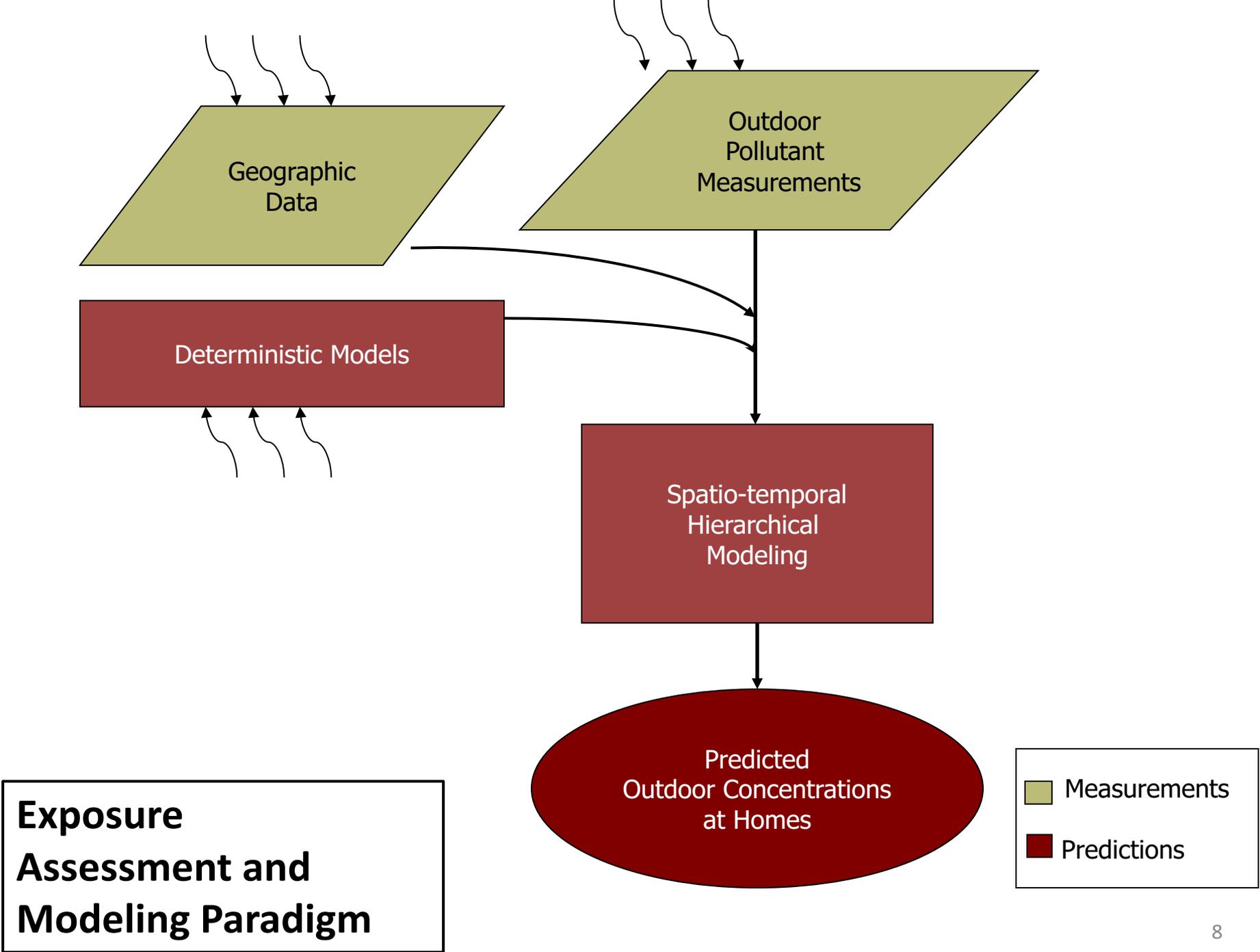
ACT-AP Approach

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

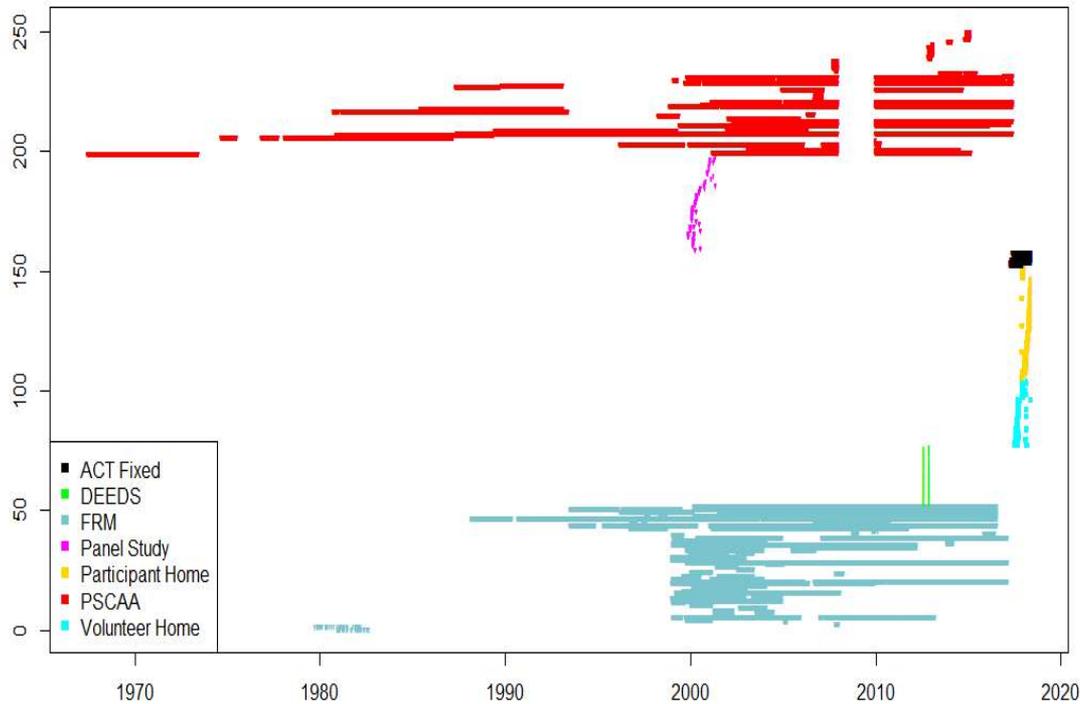
Air Pollution Exposure Assessment & Modeling Plans

- **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, NO₂, CO, O₃ (25 monitors)
 - Co-locations + ACT participant homes and similar locations
 - 3 snapshot campaigns for NO_x, NO₂, and O₃ 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



PM_{2.5} Monitoring in Puget Sound

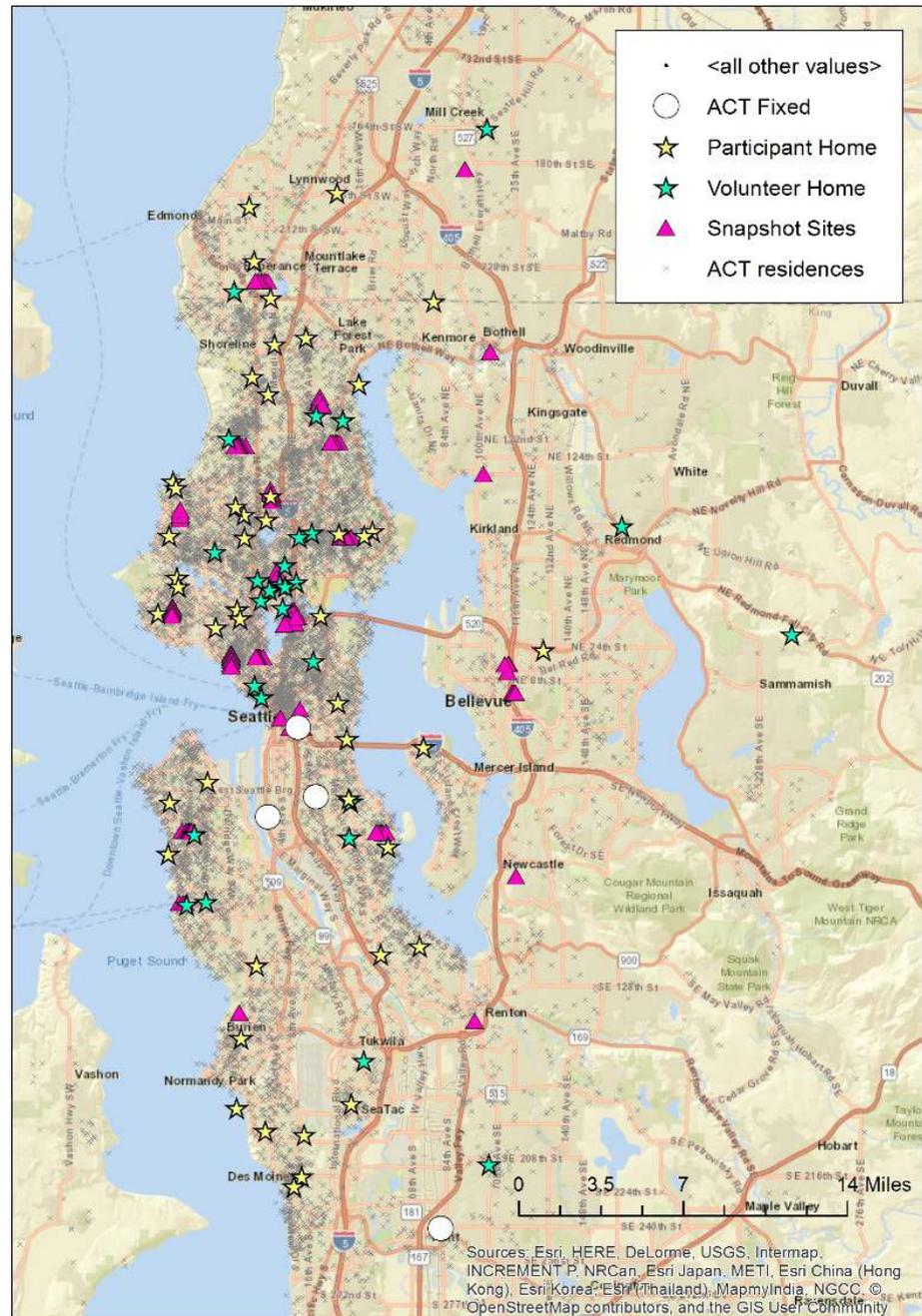
Data Density by Study or Source



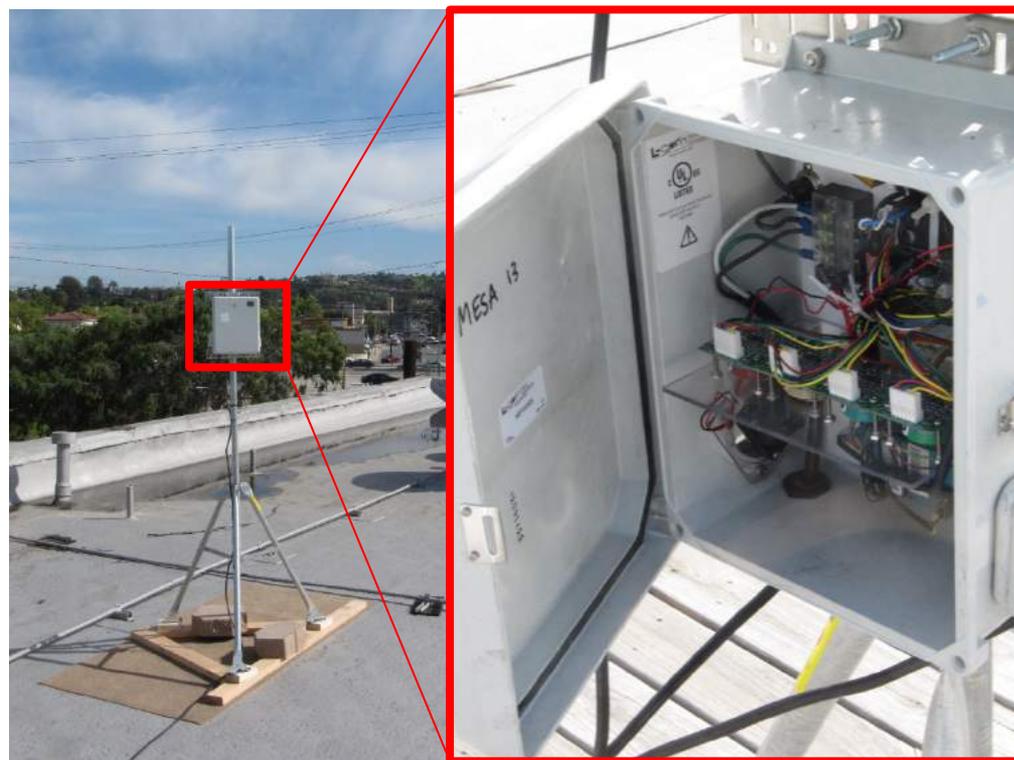
Monitor Locations



ACT-Specific Monitoring and ACT Participants



Low Cost Monitor Technology: QC & Calibration are Necessary!



Pollutant	Method
PM _{2.5}	Light scattering: <i>2 Plantower (lasers), 2 Shinyei (LED)</i>
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): <i>Alphasense</i>
	Additionally measure temperature & RH inside the box

Co-location for Calibration



Sensor QC

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

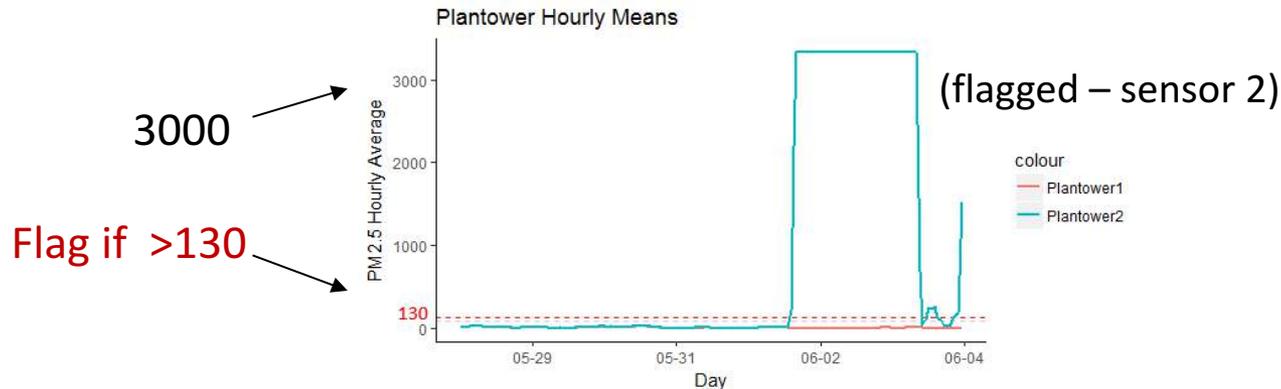
Solution:

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

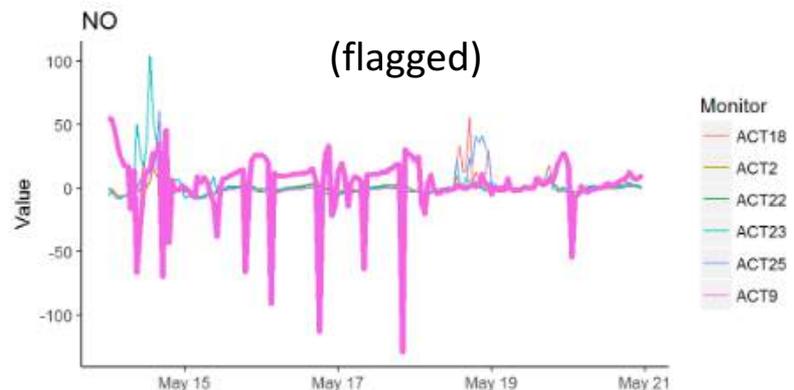
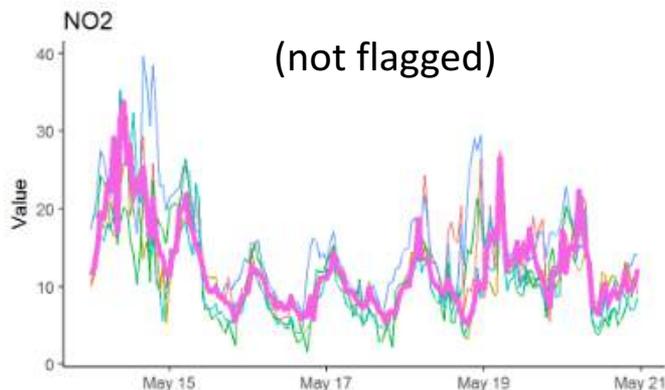
*https://github.com/kaufman-lab/uw-radical/tree/master/Sensor_QC

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

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

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).

Table of Contents

- Completeness
- Monitors
- Worst
- Any Data From Last Week
- Lowest
- Completeness Proportions
- Priority
- Considered
- Worst
- Priority
- Considered
- Worst Data
- Considered
- Monitors
- Considered
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- Worst
- Considered
- Worst Data
- Considered
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- MESA6
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- MESA98
- MESA99
- MESA100

Flagged Monitors:

Flag key: **Un** (Unexpectedly No Data) **W** (Worst) **AD** (Any Data From Last Week) **L** (Lowest) **C** (Completeness Proportions) **P** (Priority) **Co** (Considered) **WD** (Worst Data) **Mo** (Monitors) **Ca** (Considered)

Unexpectedly No Data: MESA3 (LR02), MESA10 (LAB), MESA14 (S006), MESA21 (LAB), MESA24 (LAB), MESA30 (LAB), MESA31 (S006)

Monitors at Current Location >1 wk:

Monitor	Complete	On	Value(s)	Alert(s)
ACT17	100%			Co, W
ACT24	100%			Co, W
ACT8	100%	100%		Co, W
ACT16	100%	100%		Co, W
ACT14	100%	100%		Co, W
ACT22	100%	100%		Co, W
ACT26	100%	100%		Co, W
ACT9	100%	100%		Co, W
ACT20	100%	100%		Co, W
ACT1	100%	100%		Co, W
ACT7	100%	100%		Co, W
ACT10	100%	100%		Co, W
ACT11	100%	100%		Co, W
ACT12	100%	100%		Co, W
ACT15	100%	100%		Co, W
ACT20	100%	100%		Co, W
MESA37	100%	100%	100%	Co, W
MESA33	100%	100%	100%	Co, W
MESA3	100%	100%	100%	Co, W
MESA51	100%	100%	100%	Co, W
MESA39	100%	100%	100%	Co, W
MESA18	100%	100%	100%	Co, W
MESA23	100%	100%	100%	Co, W
MESA11	100%	100%	100%	Co, W
MESA24	100%	100%	100%	Co, W
MESA46	100%	100%	100%	Co, W
MESA31	100%	100%	100%	Co, W
MESA32	100%	100%	100%	Co, W

Sensor QC Weekly Report
Data from 05-14-2018 through 05-20-2018

Completeness

Monitors Without Any Data From Last Week

- Unexpected to be missing: MESA5 (LR02), MESA17 (LAB), MESA34 (S006), MESA33 (LAB), MESA54 (LAB), MESA55 (LAB)
- Unexpected to be missing (and at location with bad cell service): MESA26 (S006)
- Expected to have no data: ACT19, MESA8, MESA23, MESA26, MESA40, MESA41, MESA44, MESA50, MESA52

(Expectations based on location table in Access Database. If that database is not up to date, these monitors may be incorrectly categorized.)

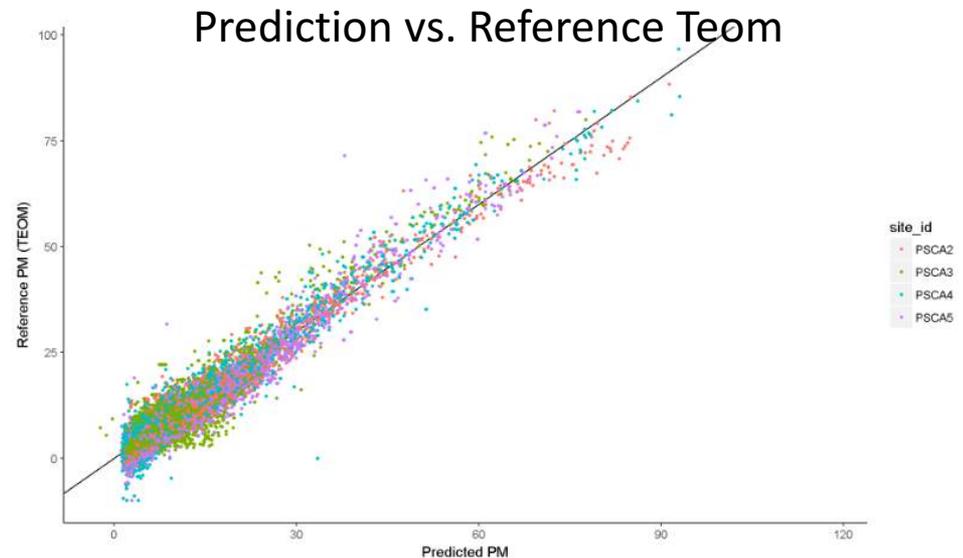
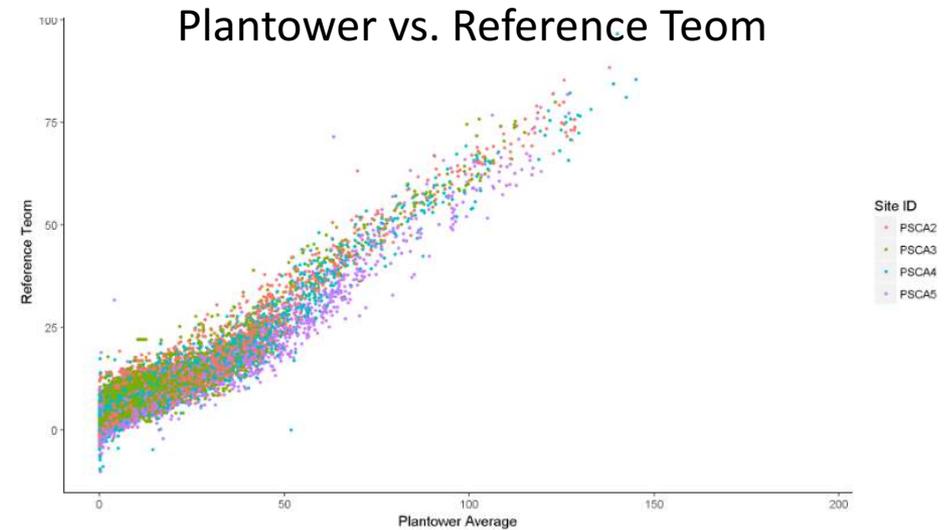
Lowest Completeness Proportions

(i.e. Monitors with at least one sensor measure having below 75% completeness)

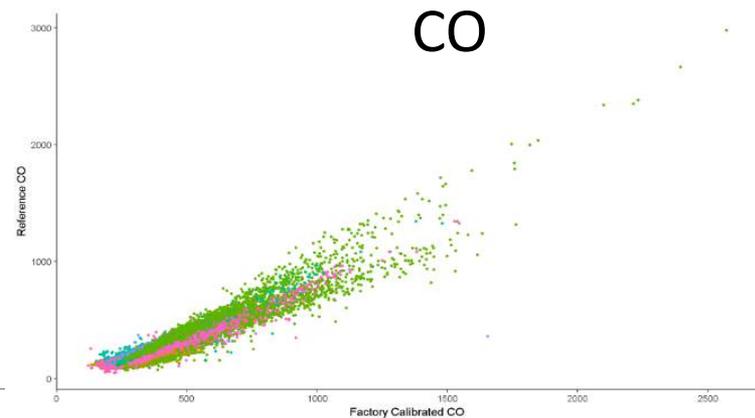
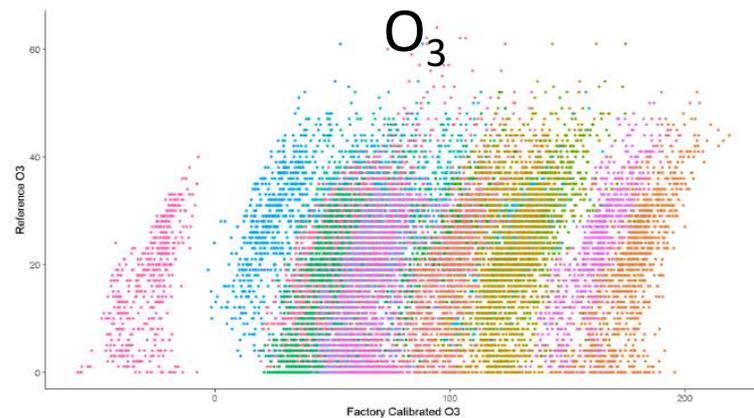
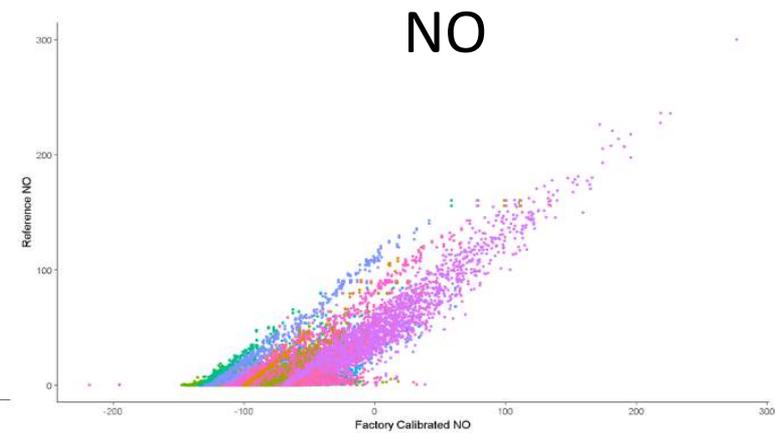
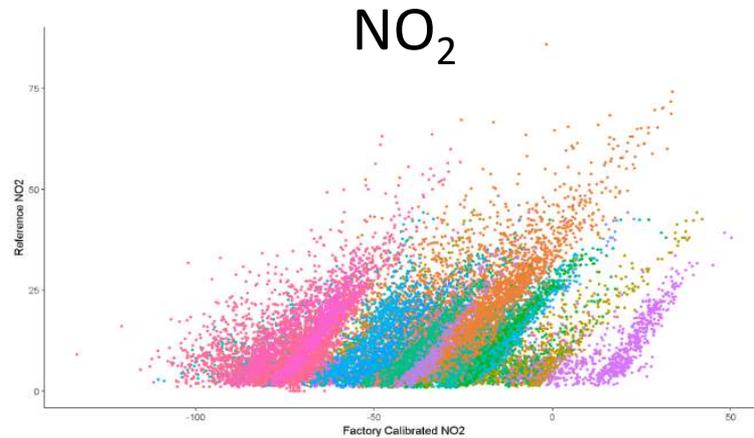
Monitor	Site(s)	Known Bad Cell Service	Ave. Sensor Completeness	Min. Sensor Completeness	Ave. Plantower Completeness	Ave. Shinyei Completeness	Ave. Gss Completeness
ACT17	KPRI31		0.01	0.01	0.01	0.01	0.01
MESA51	LAB		0.74	0.02	0.56	1	1
MESA38	C001		0.74	0.14	0.57	1	1
ACT24	KPRI45		0.56	0.46	0.53	0.62	0.62

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_avg², Plantower bin counts, Temp, RH
 - CV R² = .911
 - RMSE = 2.13 μg/m³



Gas Calibration: Alphasense Factory Calibrations vs. PSCAA Reference



Gas Calibration

- Leveraged two sensors for each gas
 - Active (WE)
 - Encased/Auxiliary (AUX)

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

- 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

Gas	CV R ²	RMSE (ppb)	Model Predictors
NO₂	.891	2.97	NO2_aux, NO2_we, NO2_we ² , NO2_we ³ , Temp, Temp ² , RH, RH ² , SensorID
NO	.953	4.41	NO_aux, NO_we, NO_we ² , NO_we ³ , Temp, Temp ² , RH, RH ² , SensorID
O₃	.966	2.26	O3_aux, O3_we, O3_we ² , O3_we ³ , NO2_we, Temp, Temp ² , RH, RH ² , SensorID
CO	.947	37.41	CO_aux, CO_we, CO_we ² , CO_we ³ , Temp, Temp ² , RH, RH ² , SensorID

Spatio-Temporal Exposure Model

- $C_{s,t} = \mu_{s,t} + v_{s,t}$ ← 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 $N(\mathbf{X}_i \alpha_i, \Sigma(\phi_i, \sigma_i^2))$

- Geostatistical covariance structure with “land use regression” covariates for population, traffic, land use, etc.

- $M(s,t)$ space-time covariate

- $v_{s,t}$ ← variation from temporal trend (mean 0)

- Geostatistical spatial structure with simple temporal correlation

- Process noise + measurement error

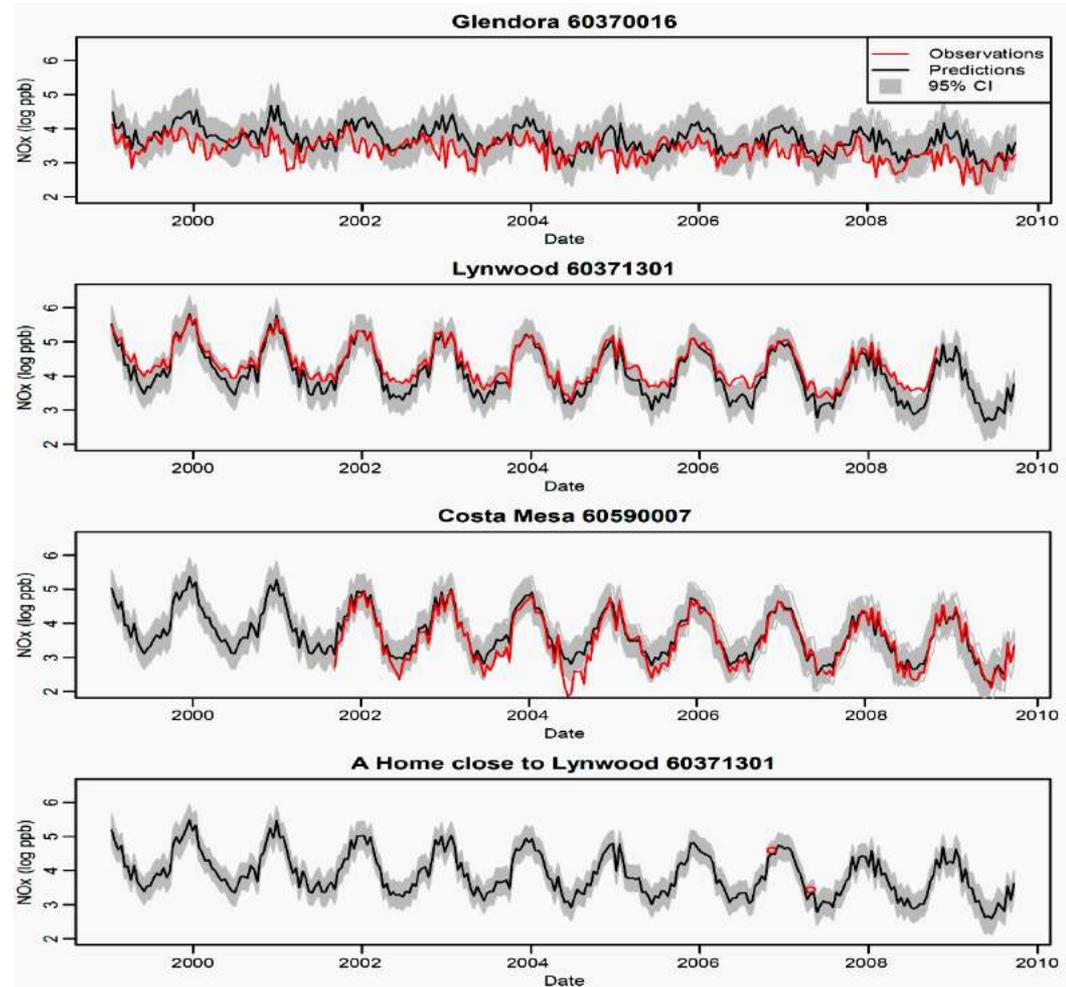
Example GIS Covariates

Predictor Variable	Symbol	Units	Buffer radii	Functional Form
<u>Land Use</u>				
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	NO _x		3000,15000,30000	untransformed
<u>Roadway</u>				
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 A1 roads 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

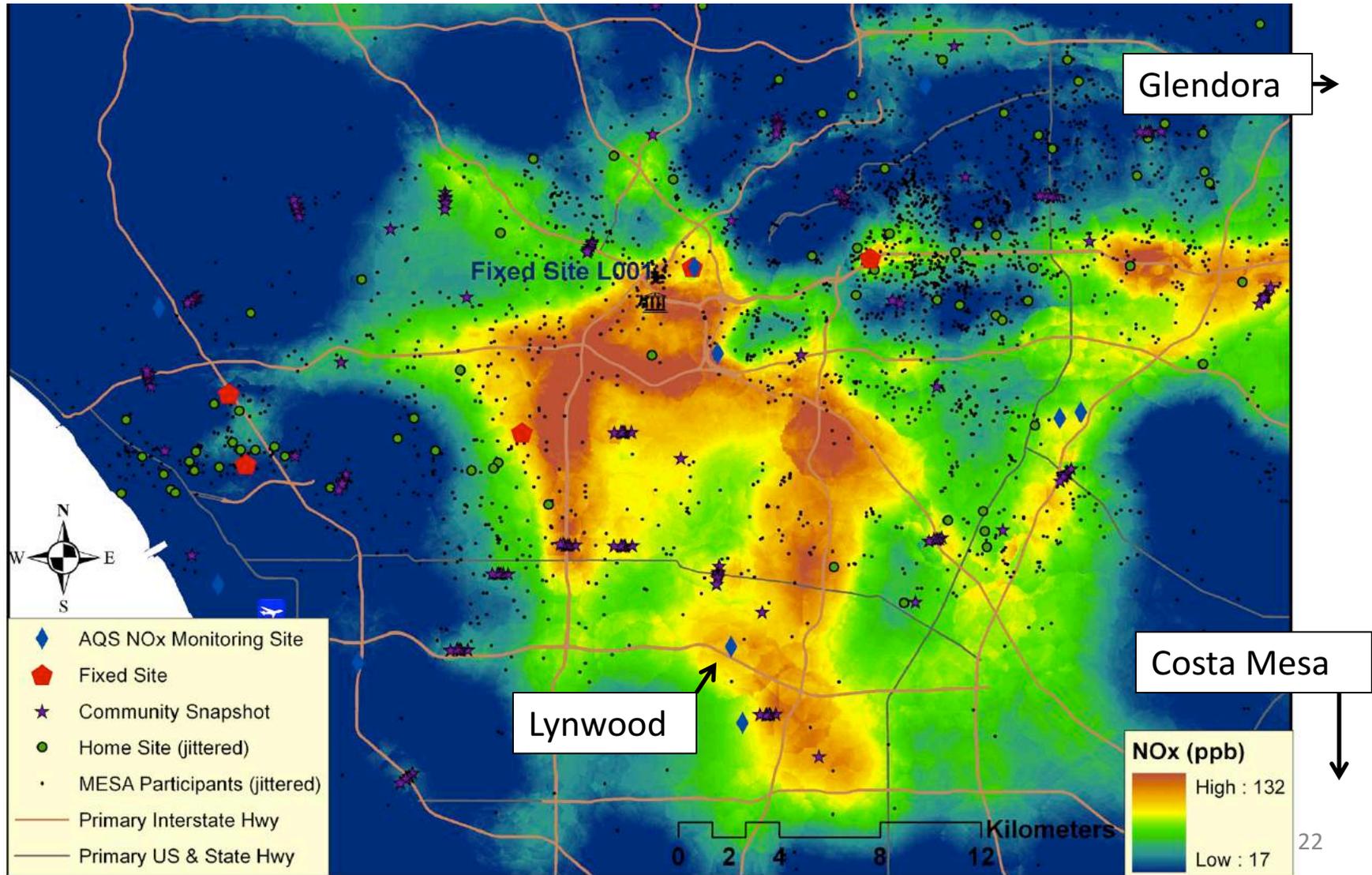
Predictions* are similar to observations:

and available at all times:

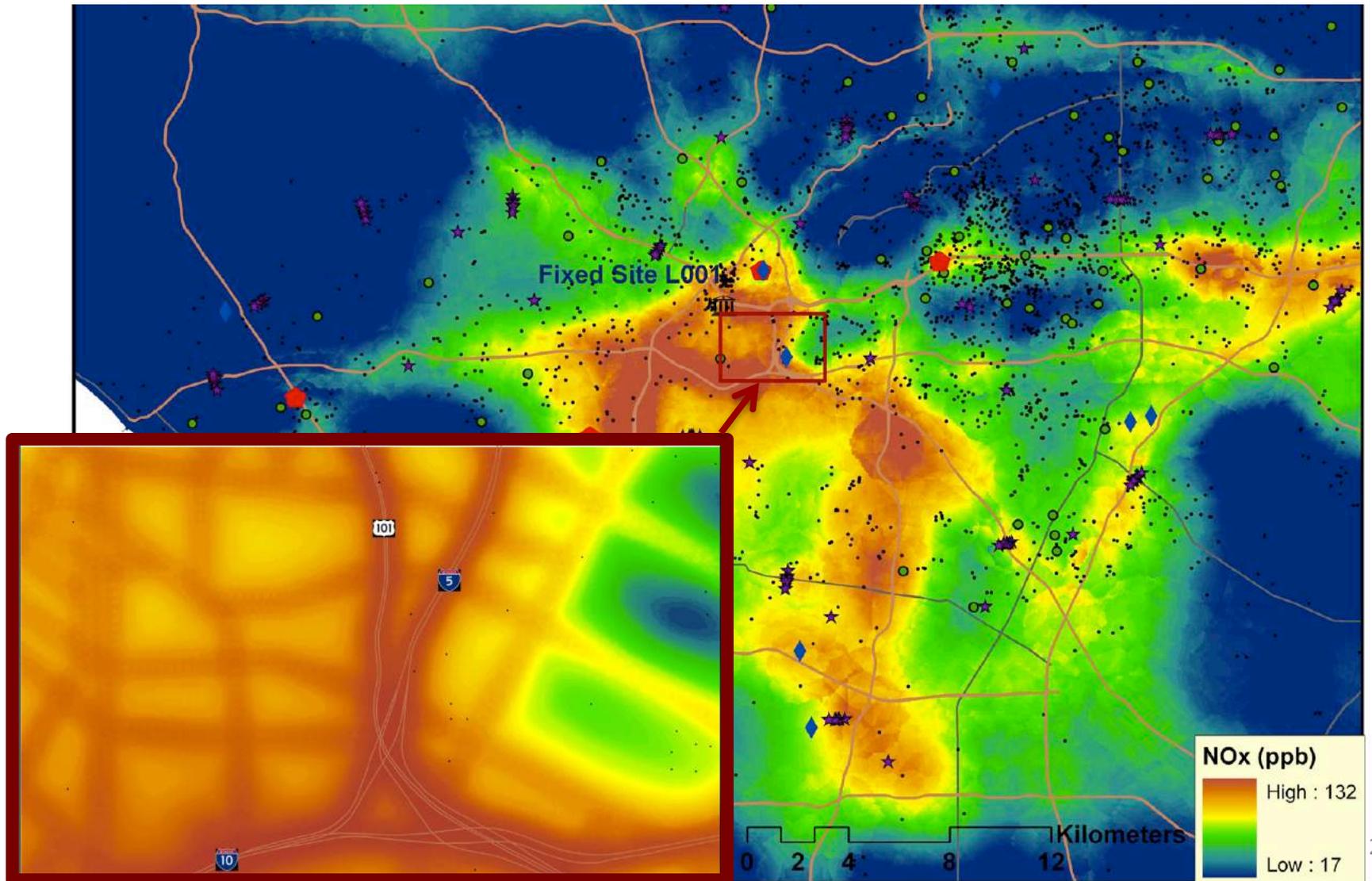


*Cross-validated

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

ACT-AP: NIEHS & NIA R01 ES026187

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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>