CENTER FOR CLEAN AIR RESEARCH

UNIVERSITY *of* WASHINGTON

# UW CCAR Year 2 Scientific Advisory Committee Meeting

September 27th & 28th 2012

SCHOOL OF PUBLIC HEALTH

UNIVERSITY *of* WASHINGTON

Lovelace

*LOVELACE RESPIRATORY RESEARCH INSTITUTE*

WASHINGTON STATE UNIVERSITY

*World Class. Face to Face.*

THE UNIVERSITY *of* NEW MEXICO

# CCAR projects & cores

**Project 1**
roadway exposure characterization

M Yost (PI), T Larson, C Simpson, T Jobson, T VanReken

**Project 2**
exposure atmosphere generation

J McDonald (PI), T Larson

**Project 3**
toxicology

M Campen (PI), M Rosenfeld, A Lund, J McDonald

**Project 4**
human clinical studies

J Kaufman (PI)

**Project 5**
epidemiology cohort study

J Kaufman (PI), S Vedal, C Curl

**Project 6**
multipollutant exposure modeling

L Sheppard (PI), A Szpiro, P Sampson

**Biostats Core**

**Admin Core**

# Since we last met:

1. responses to SAC review
2. Clean Air Research Centers (CLARC) meetings/seminars:
   - EPA center webinar – M Campen (projects 2 and 3)
   - Exposure chambers workshop webinar, May 2012
   - **Annual meeting Boston (Harvard center), June 2012 – updates + collaborative projects**
   - Biostatistics workshop preceding the annual meeting

# Since we last met:

3. Projects
   - P1 – St Paul and Baltimore x 2 seasons
   - P1 + P2 – Albuquerque
   - P2 + P3 – atmosphere development + toxicology findings
   - P4 – to be discussed
   - P5 – coord field work Winston-Salem and LA; develop/test instruments
   - Biostats Core – dealing with P1 data; interim work/plans for multivariate exposure model

# overview of SAC comments:

- aging vs. source mix
- linking mobile monitoring to experimental and observational exposures
- non-exhaust roadway exposures?
- streamline tox and human exposure studies
- other tox endpoints
- simple to more complex statistical modeling
- appropriate in-vehicle monitoring

# SAC input especially on:

1. reactions to early data and approaches:
    - mobile and chamber monitoring
    - experimental atmospheres and tox models/endpoints
2. project 4 – what now?
3. MESA cohort
    - short- and long-term approach to developing multipollutant exposure model
    - in-transit exposures
4. hypotheses
5. our CLARC collaborative projects

# **Outline of today's activities**

1. Individual project reviews, updates, discussions
   - project 1, 4
   - highlight project 4 issues

[LUNCH]

   - projects 5, 2, 3, Biostats Core

2. Cross-center collaborations
3. General discussion

[DINNER]

# Tomorrow's activities

1. SAC closed meeting
2. SAC report and discussion

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# EPA Clean Air Research Center
# Project 1: Exposure Mapping –
## Characterization of Gases and Particles for Exposure Assessment in Health Effects and Laboratory Studies

**External Science Advisory Meeting, Sept 27, 2012**

Investigators: Michael Yost, Tim Larson, Chris Simpson, UW;
Tom Jobson, Tim VanReken, WSU

# University of Washington
# Center for Clean Air Research (CCAR)

## Project 1: Aims

1. Characterize spatial and temporal gradients of selected air pollutants along roadways and within neighborhoods in MESA cities using a mobile platform
2. Measure spatial variation in concentrations of selected air pollutants at two-week average fixed sites
3. Characterize rapid aging of air pollutant components transported from roadway sources to neighborhood receptor locations
4. Provide detailed characterization of controlled laboratory atmospheres available for toxicology testing, and identify likely laboratory conditions that mimic those found in urban settings

# Project 1: Instrumentation

| Parameter | Mobile Platform | Fixed Site - Supporting Mobile Platform | Stationary Sites - Integrated Coarse Particles and Gases |
|---|---|---|---|
| Aerosol Light Scattering | Nephelometer | Nephelometer | |
| PAHs | PAS 2000CE | PAS 2000CE | |
| Ultrafine Particle Counts | PTRAK w/Diffusion Screen | PTRAK w/Diffusion Screen | |
| Black Carbon | dual channel micro-aethelometer (AE52) | single channel micro-aethelometer (AE51) | |
| Particle Counter | Particle Counter: 31 Sizes (NanoCheck 1.320) | Particle Counter: 6 Sizes (Aerotrak 9306) | Coarse Mass (LA and Winston-Salem only) |
| Ozone | Optec analyzer | Optec analyzer | O3: Ogawa passive badge |
| NO | 2B tech model 410 | 2B tech model 410 | SO2, NO*, NO2, NOx Ogawa passive badge |
| NOx, NO2 by Difference | 2B tech model 410 w/ converter | 2B tech model 410 w/ converter | |
| CO | Langan T15N | Langan T15N | 3M passive sampler: Six VOC Compounds: pentane, nonane, benzene, toluene, m-xylene, o-xylene |
| $CO_2$ | IR sensor | IR sensor | |
| VOCs | ppbPID (Photovac) | ppbPID (Photovac) | |
| VOCs – integrated | charcoal sorbent | charcoal sorbent | |
| Temperature & RH | Sensor | | |
| Position & Real-Time Tracking | GPS | | |
| Visual Recording of Route | WebCam | | * NO by difference |

# Project 1: Sampling Schedule

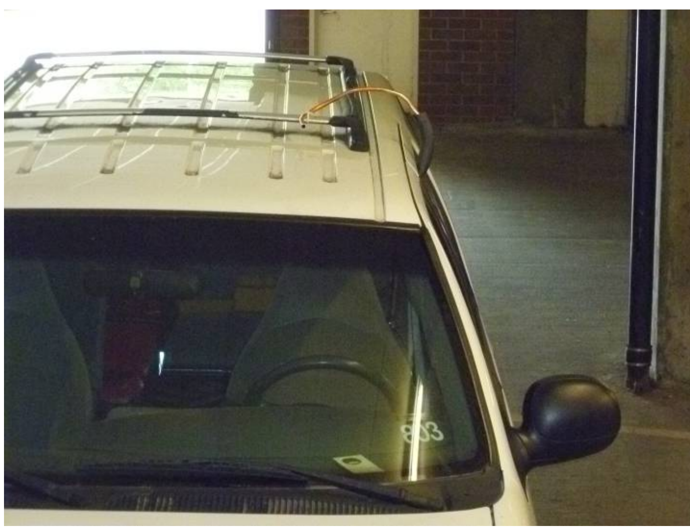
| Activity | Est. Begin Date | Est. End Date | Year of Study | Location - New |
|---|---|---|---|---|
| Pilot Testing of Mobile system | 8/15/11 | 11/15/11 | 1 | Seattle, WA |
| Field Sampling, City 1 (Heating) | 11/29/11 | 12/20/11 | 1 | St. Paul, MN |
| Field Sampling, City 2 (Heating) | 2/5/12 | 2/25/12 | 2 | Baltimore, MD |
| Characterization of LRRI Exposure Atmospheres | 4/16/12 | 5/17/12 | 2 | Albuquerque, NM |
| Field Sampling, City 2 (Non-Heating) | 6/8/12 | 6/30/12 | 2 | Baltimore, MD |
| Field Sampling, City 1 (Non-Heating) | 7/25/12 | 8/15/12 | 2 | St. Paul, MN |
| Field Sampling, City 3 (Heating) | 1/3/13 | 1/23/13 | 3 | Winston-Salem, NC |
| Field Sampling, City 4 (Heating) | 2/5/13 | 2/25/13 | 3 | Los Angeles, CA |
| Characterization of UW Exposure Atmospheres | 4/1/13 | 5/1/13 | 3 | Seattle, WA |
| Field Sampling, City 4 (Non-Heating) | 6/1/13 | 6/20/13 | 3 | Los Angeles, CA |
| Field Sampling, City 3 (Non-Heating) | 8/1/13 | 8/20/13 | 3 | Winston-Salem, NC |
| *Expanded Sampling with GT CLARC Instrumentation* | *9/1/13* | *9/20/13* | *3* | *Atlanta* |

# Preliminary Data

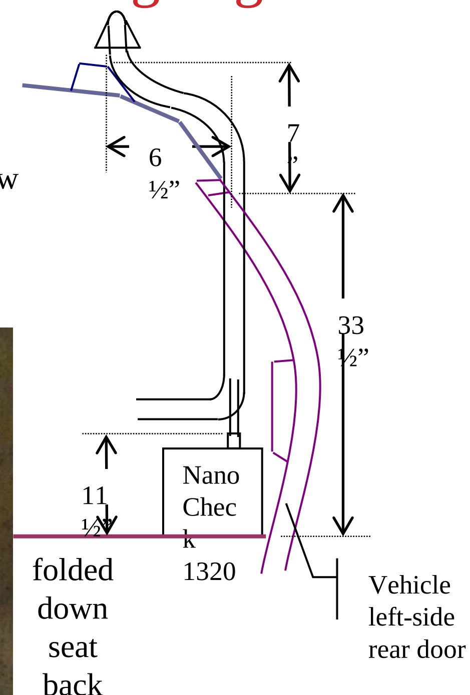
- Two Data sources:
  - PASSIVE – Passive samplers (2-week averages)
  - MOBILE – Mobile data (30s & ~15 min.; time-corrected)
- 3 Mobile Routes
  - One fixed route, 2-7 pm (**evening commute**)
  - All routes time adjusted to central fixed site
  - 15 Fuzzy points per route (43 total)
  - Fuzzy points coincident with passive samplers

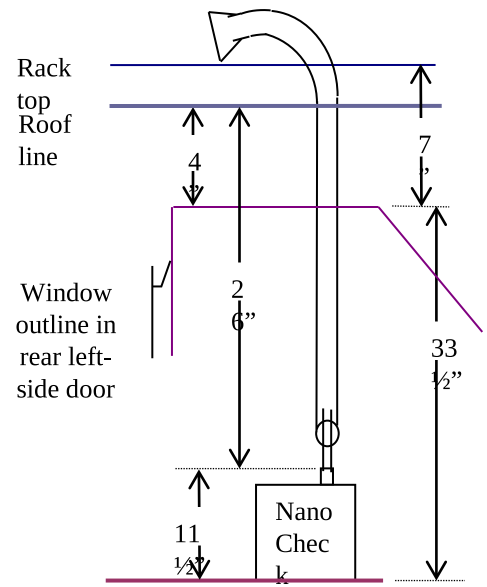
# Mobile Platform

- Use same vehicle in all cities
  - Sample inlet attached to roof rack; matched to ~22 mph speed
  - Instrument package; samples drawn from common manifold
  - Data vector: 10-sec moving avg for all components, + position



Front of vehicle view (probe out left-side window)



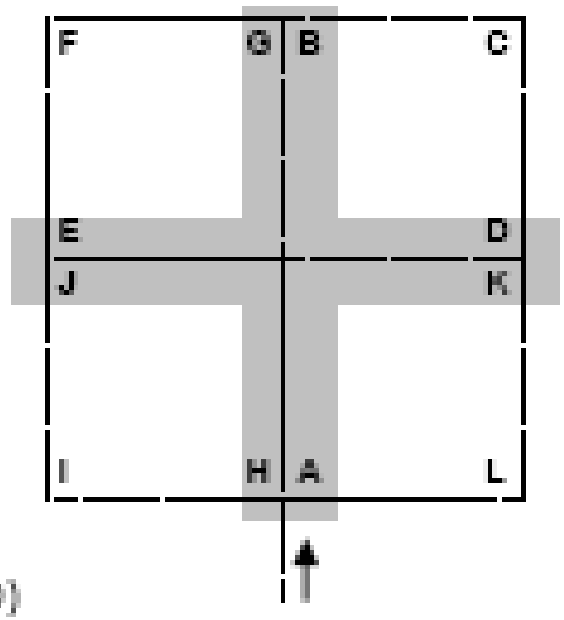




Side of vehicle view (probe extends out left-side window)

# Mobile Platform Analysis

## Traffic Intersections as "Fuzzy Points"

- Measure pollutant marker (e.g. $\sigma_{ap}$) at selected traffic intersections during peak afternoon traffic period
- Trace a cloverleaf / figure 8 at each intersection (~5-8 minutes); repeat
- Adjust the observed readings using fixed site data
- Calculate the median of the adjusted readings for each pass through a fuzzy point

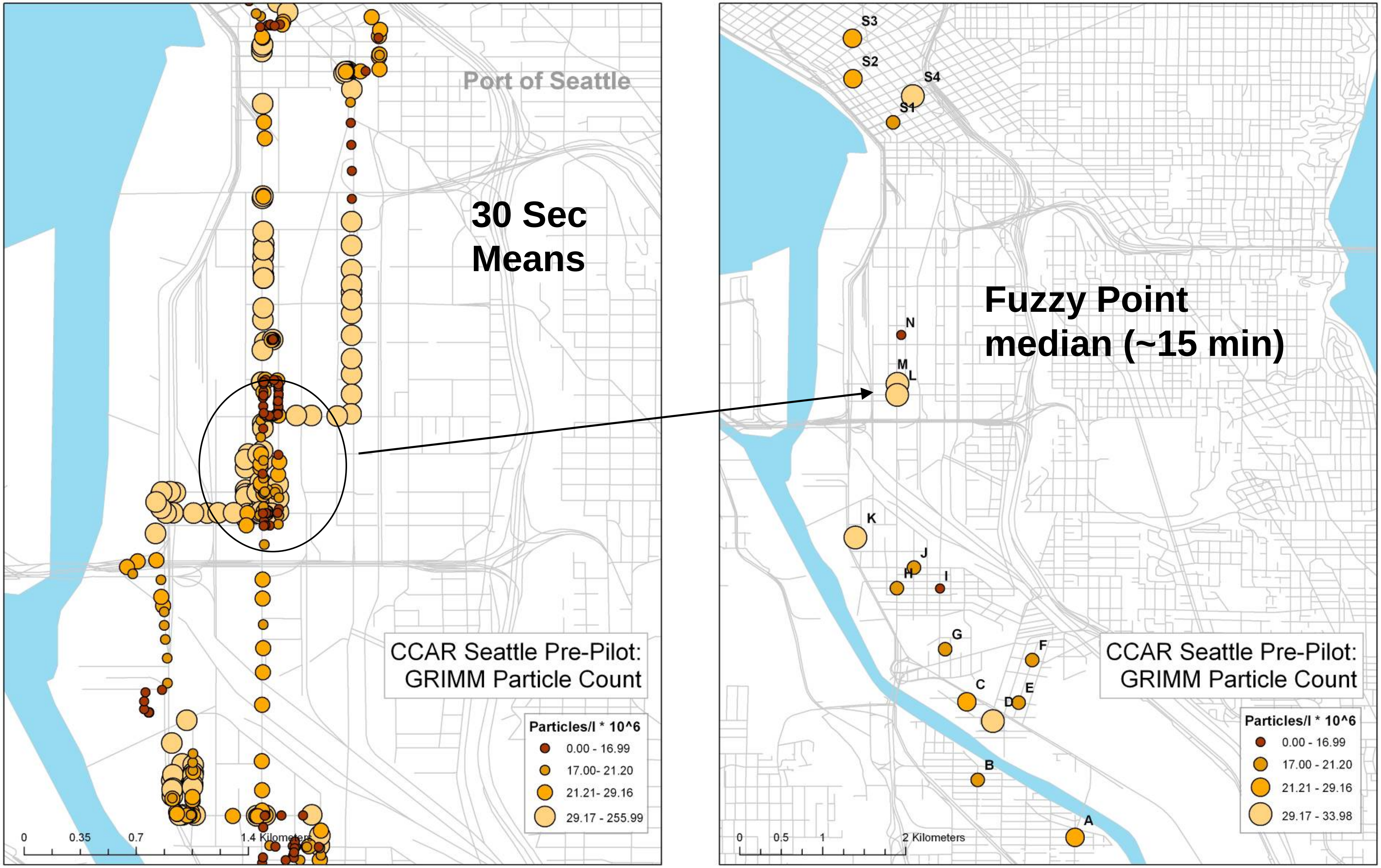



(b)

$$\text{Adjusted Reading} = \frac{\text{Observed 10-sec reading from mobile} \times \text{Campaign median from fixed}}{\text{30-min moving median from fixed}}$$

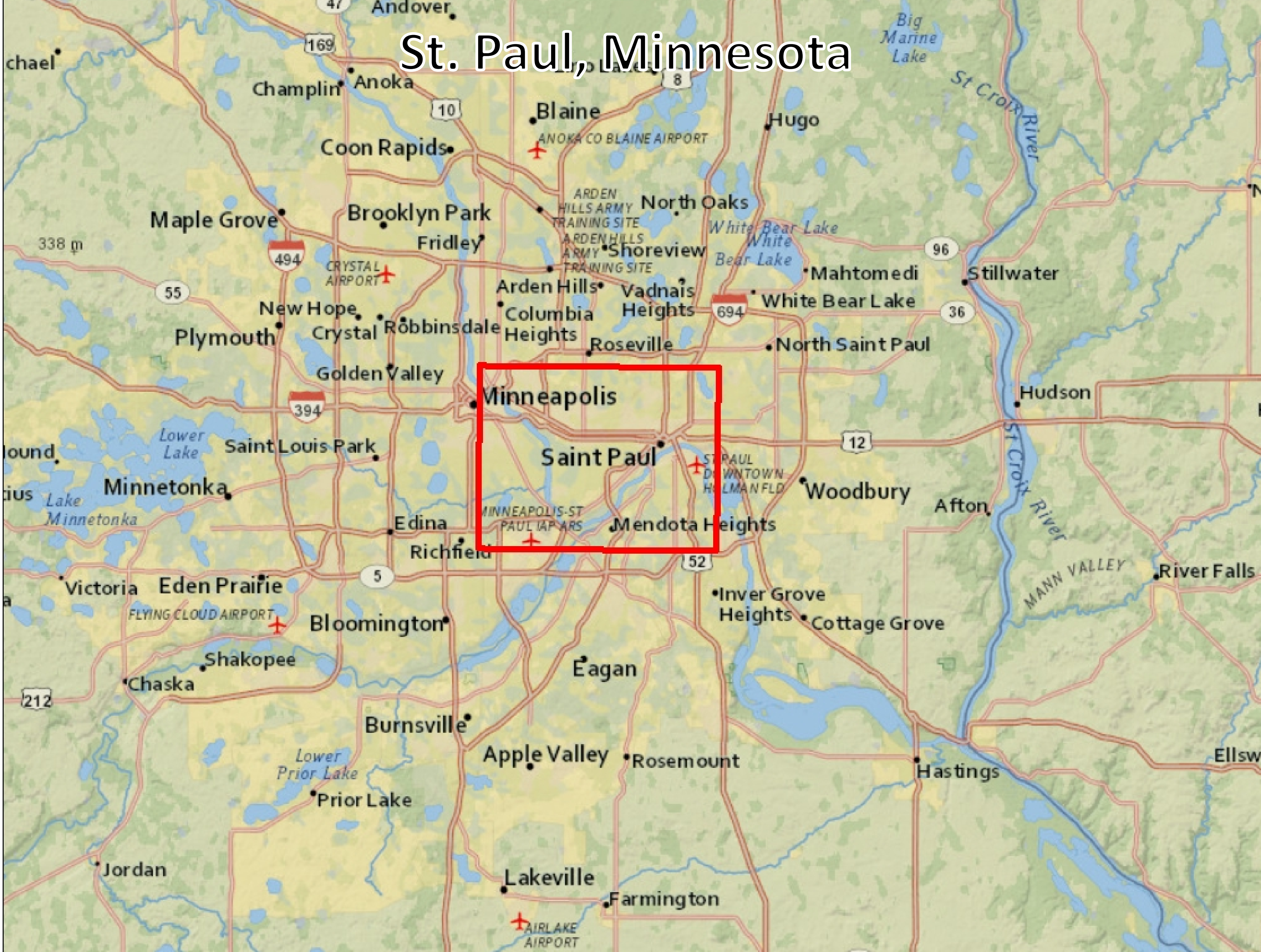
# Streaming data and video

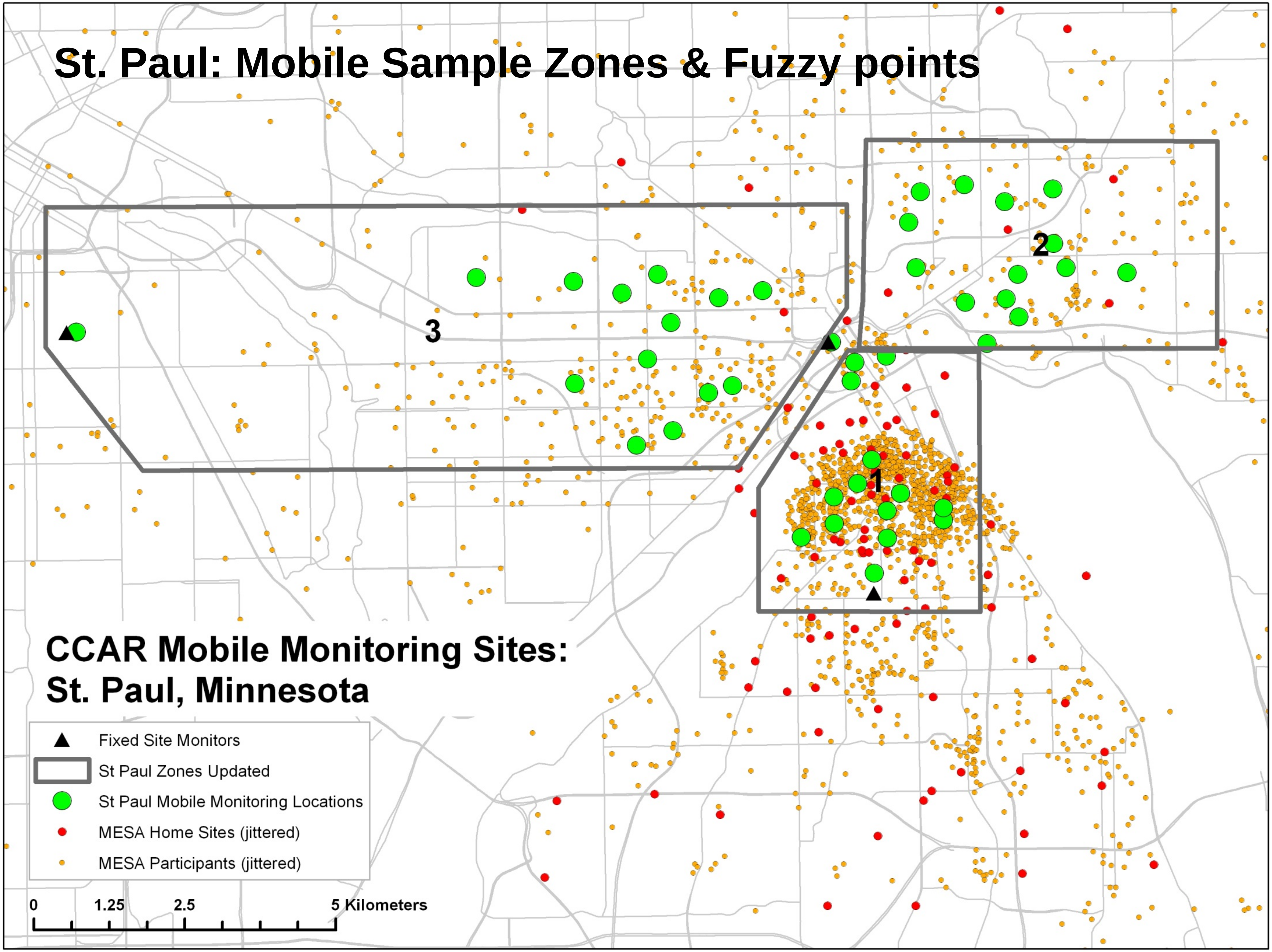
# Fuzzy Points - Detail Maps

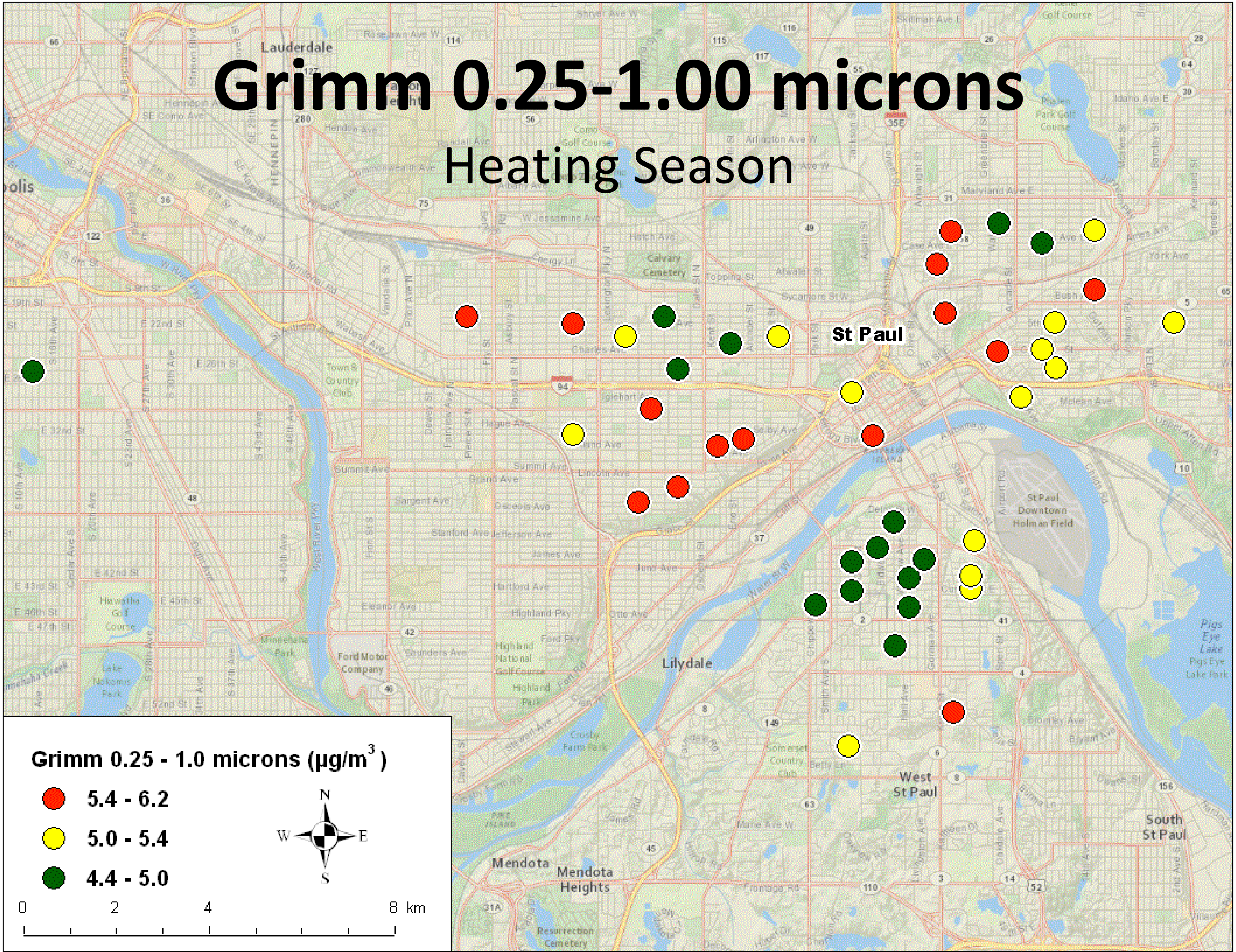


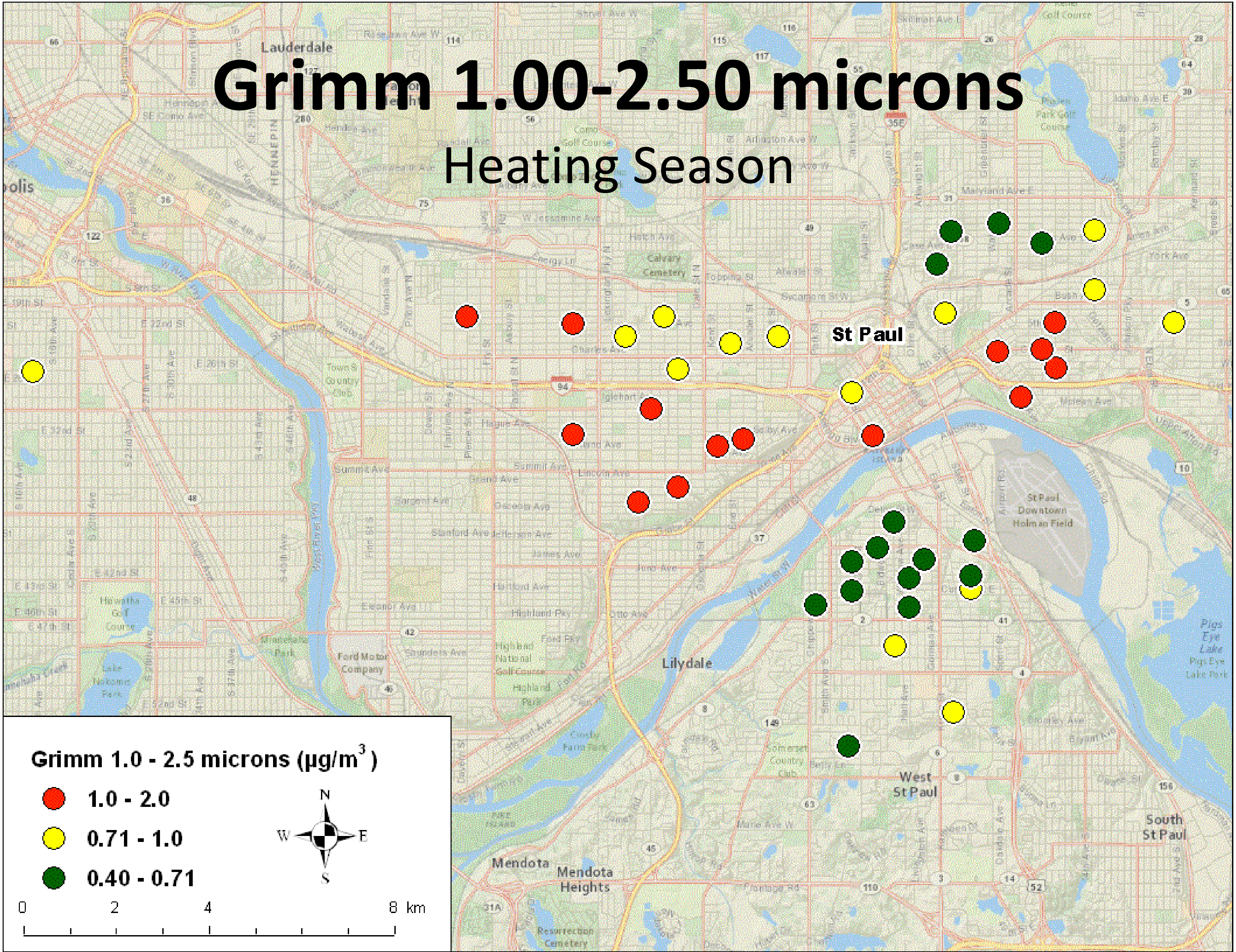
# St. Paul Heating Season

# St. Paul, Minnesota



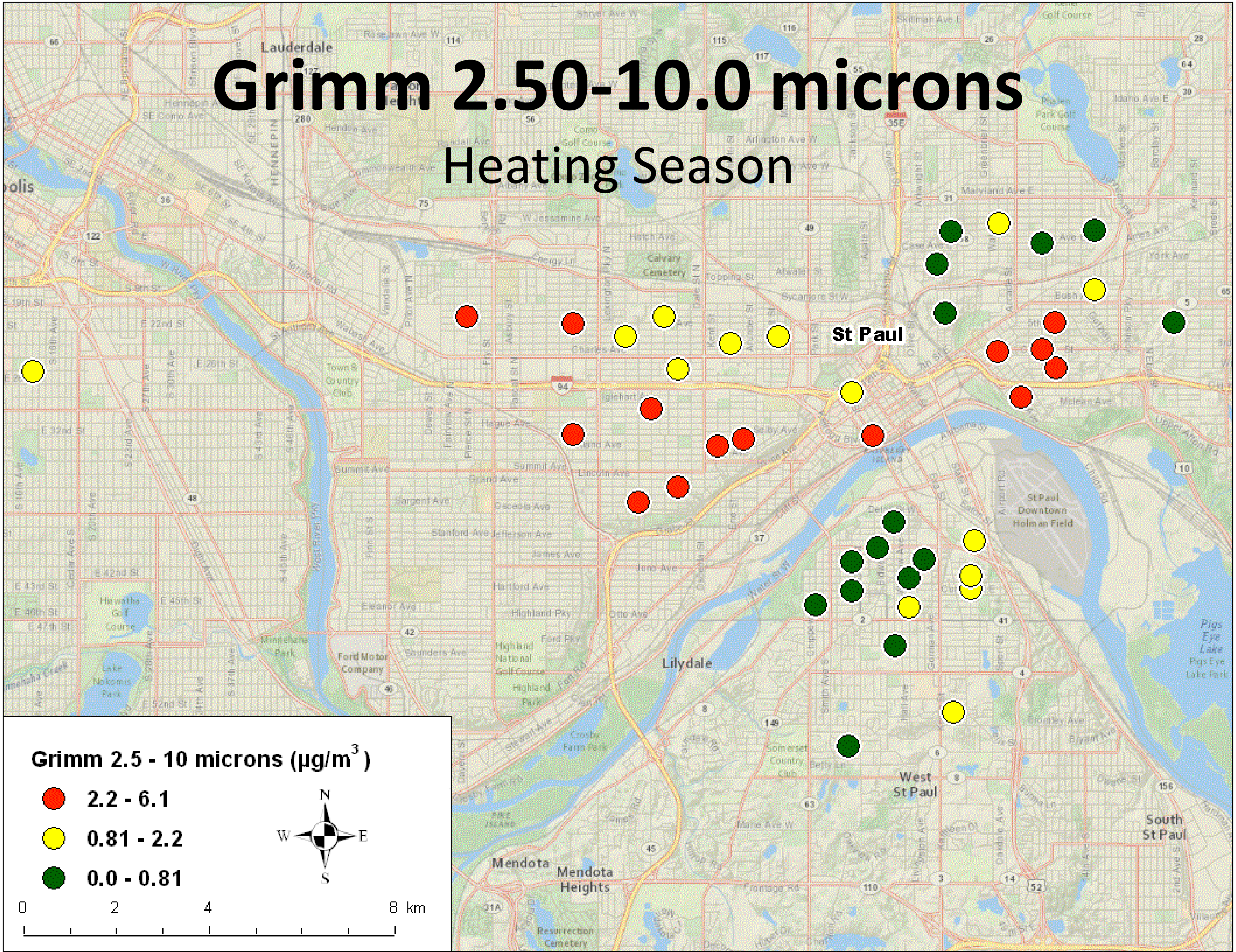

St. Paul: Mobile Sample Zones & Fuzzy points
1
2
3
CCAR Mobile Monitoring Sites:
St. Paul, Minnesota
Fixed Site Monitors
St Paul Zones Updated
St Paul Mobile Monitoring Locations
MESA Home Sites (jittered)
MESA Participants (jittered)
0
1.25
2.5
5 Kilometers

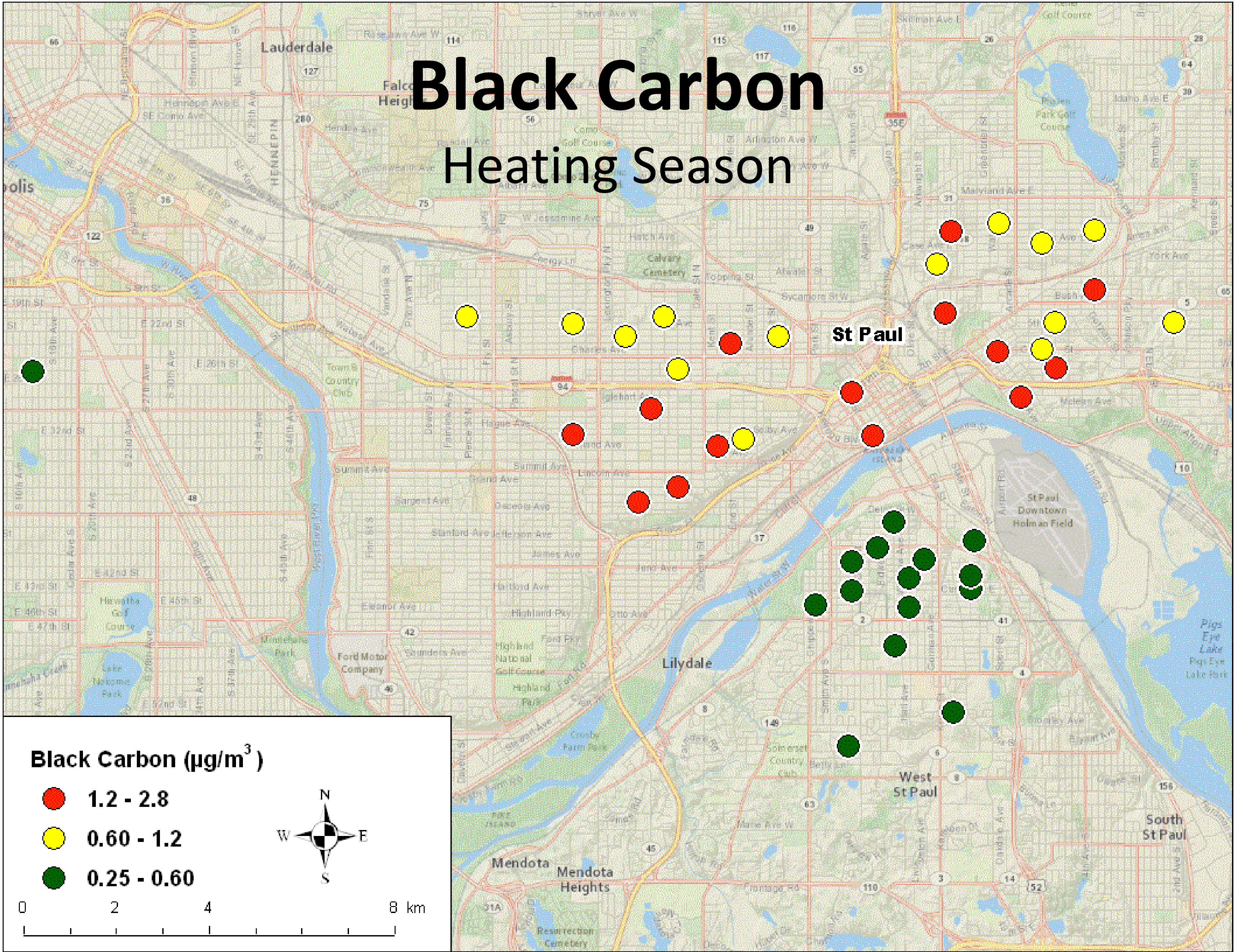

Grimm 0.25-1.00 microns
Heating Season
St Paul
Lauderdale
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights
St Paul Downtown Holman Field
Pigs Eye Lake
Grimm 0.25 - 1.0 microns (µg/m³ )
5.4 - 6.2
5.0 - 5.4
4.4 - 5.0
N
W
E
S
0
2
4
8 km

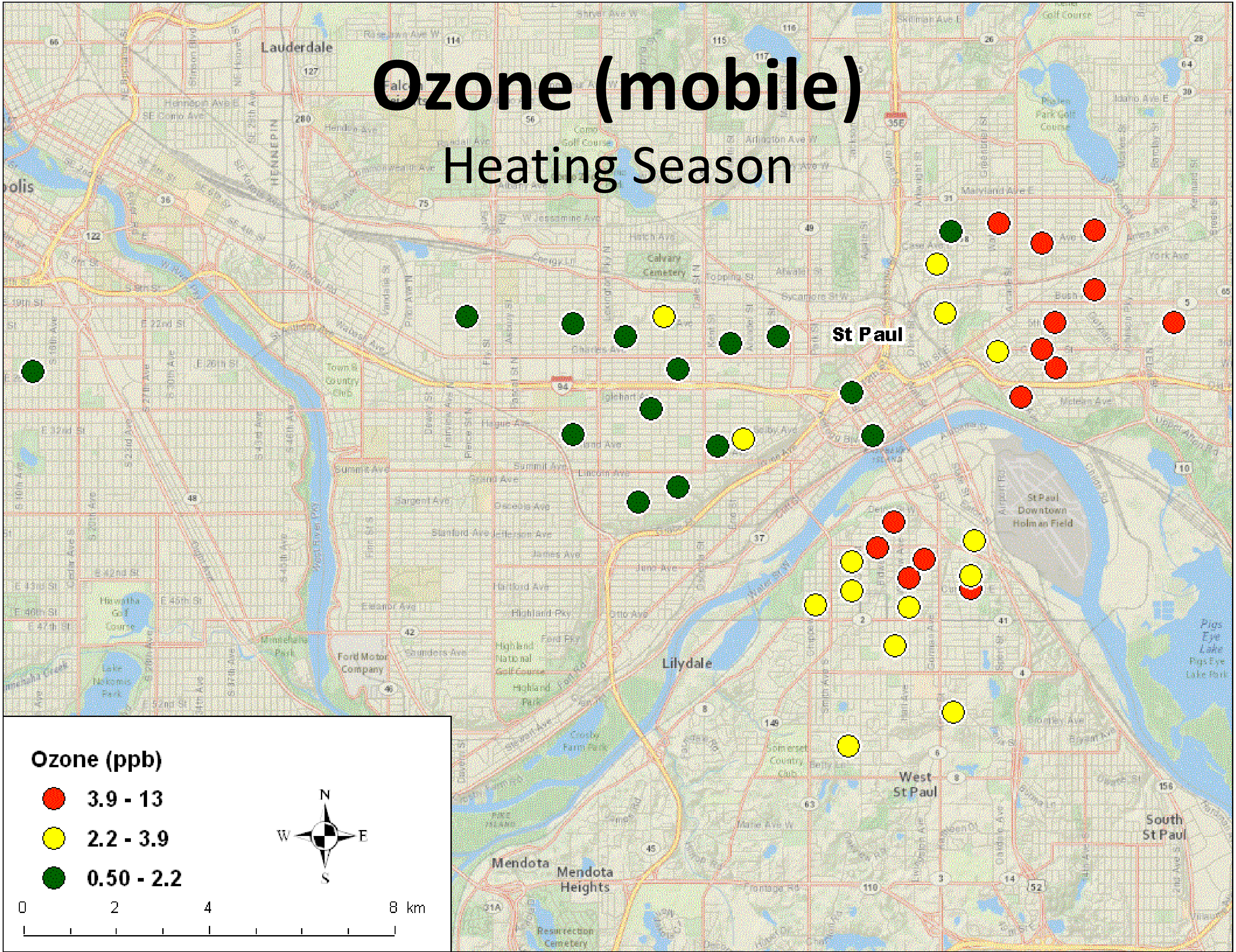

Grimm 1.00-2.50 microns
Heating Season
Grimm 1.0 - 2.5 microns (µg/m³)
1.0 - 2.0
0.71 - 1.0
0.40 - 0.71
N
W
E
S
0
2
4
8 km
St Paul
Lauderdale
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights
St Paul Downtown Holman Field
Ford Motor Company
Pigs Eye Lake

# Grimm 2.50-10.0 microns

## Heating Season

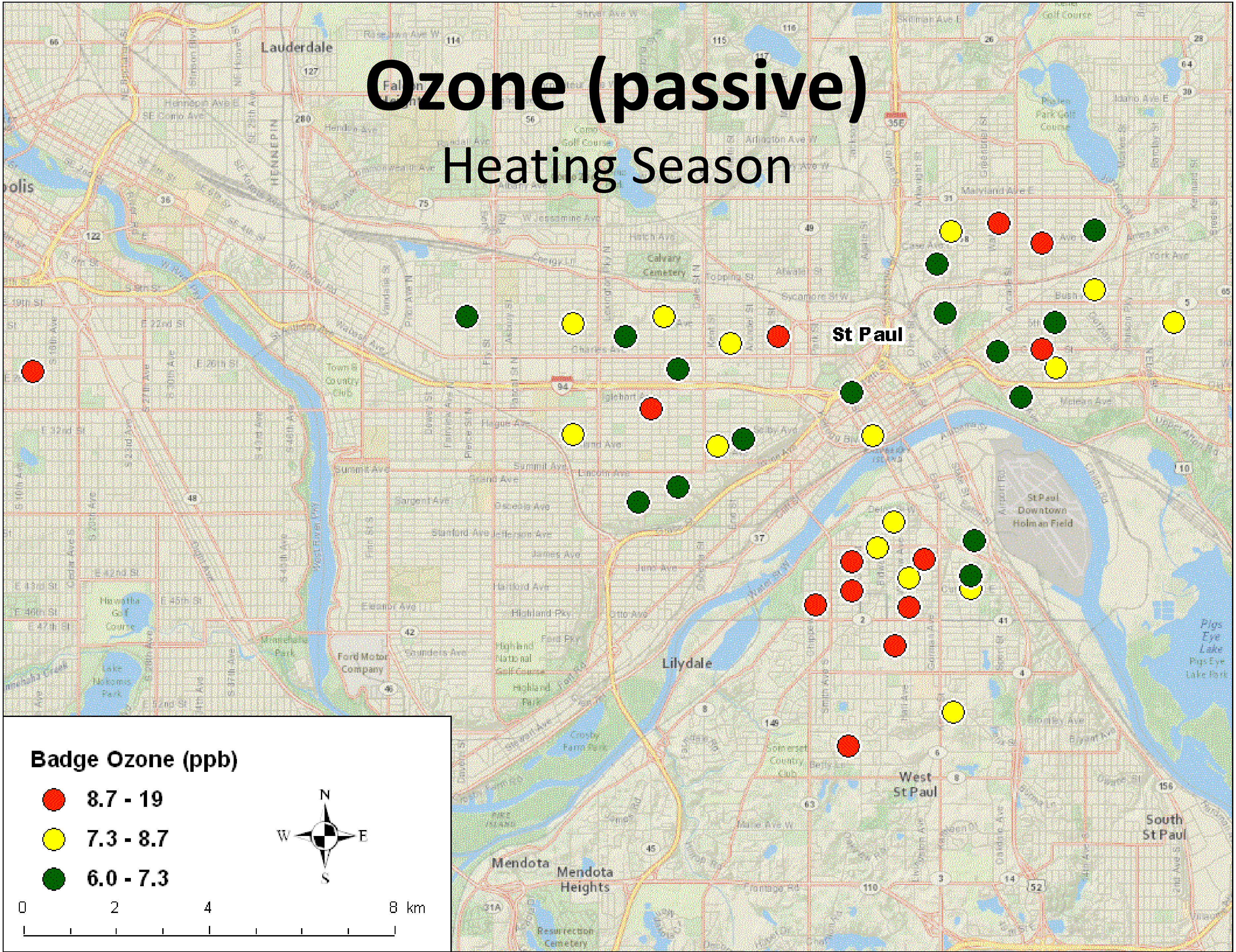


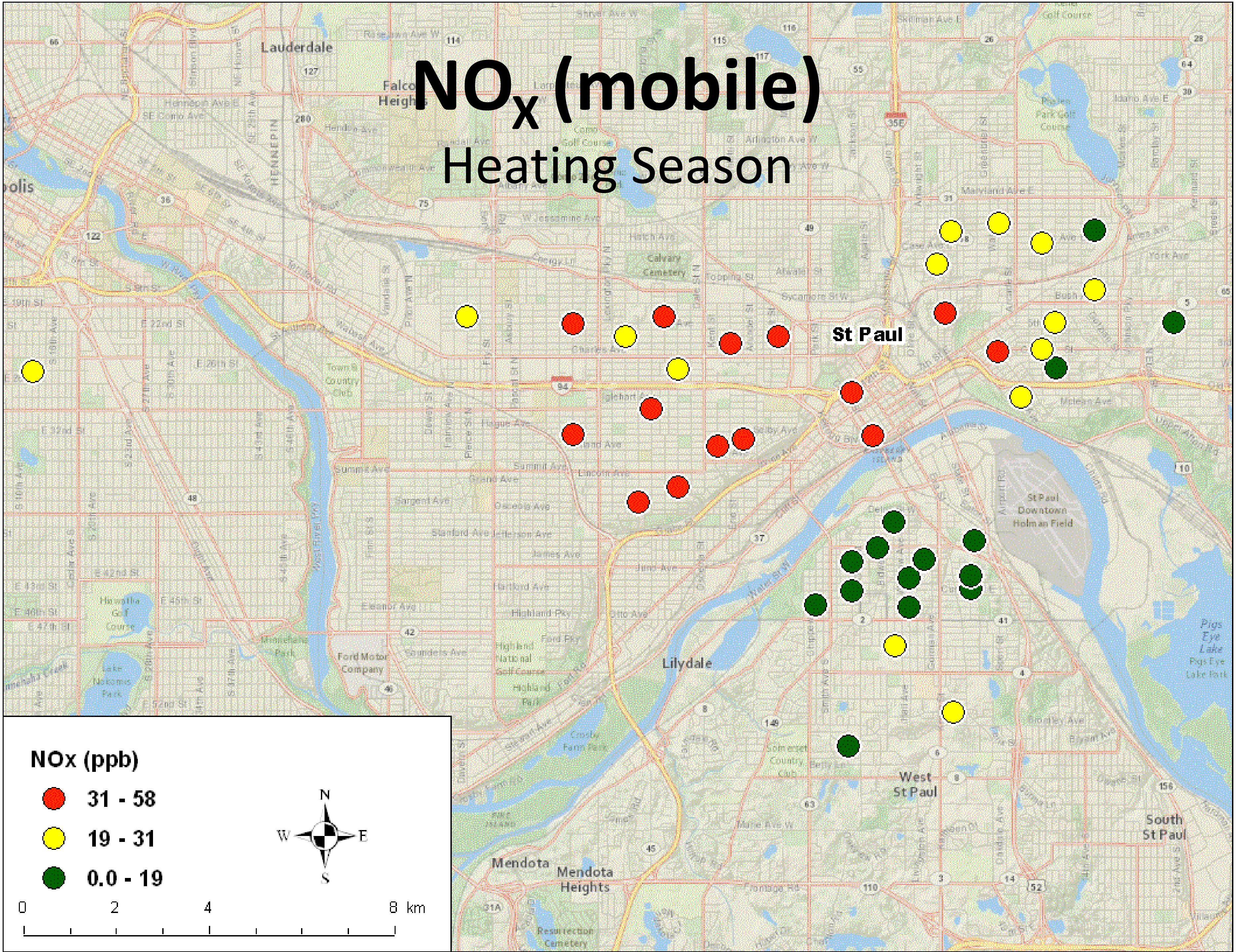

Black Carbon
Heating Season
St Paul
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights
Lauderdale
Black Carbon (µg/m3)
1.2 - 2.8
0.60 - 1.2
0.25 - 0.60
N
S
W
E
0
2
4
8 km


Ozone (mobile)
Heating Season
Ozone (ppb)
3.9 - 13
2.2 - 3.9
0.50 - 2.2
N
W
E
S
0
2
4
8 km
St Paul
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights
Lauderdale

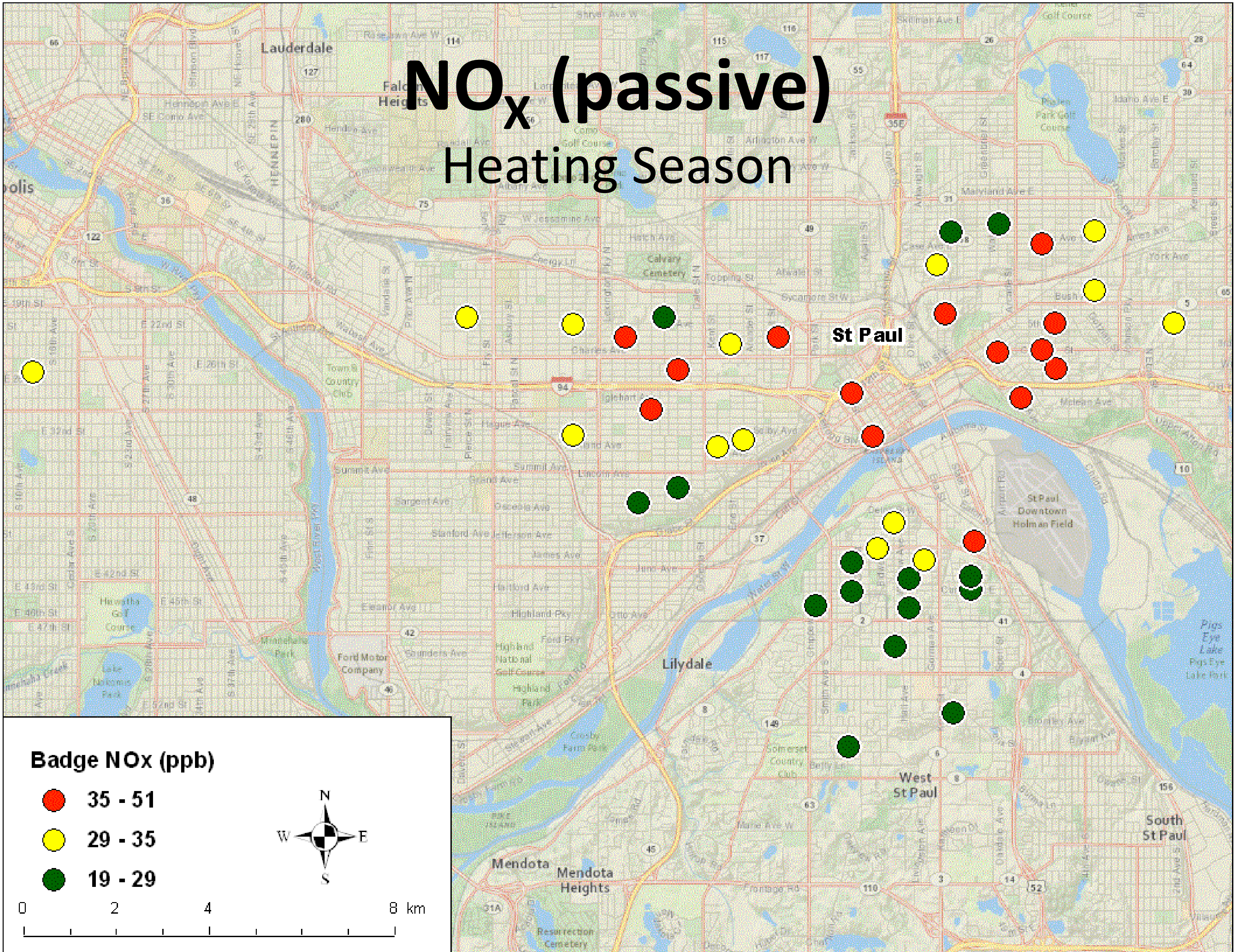
# Ozone (passive)

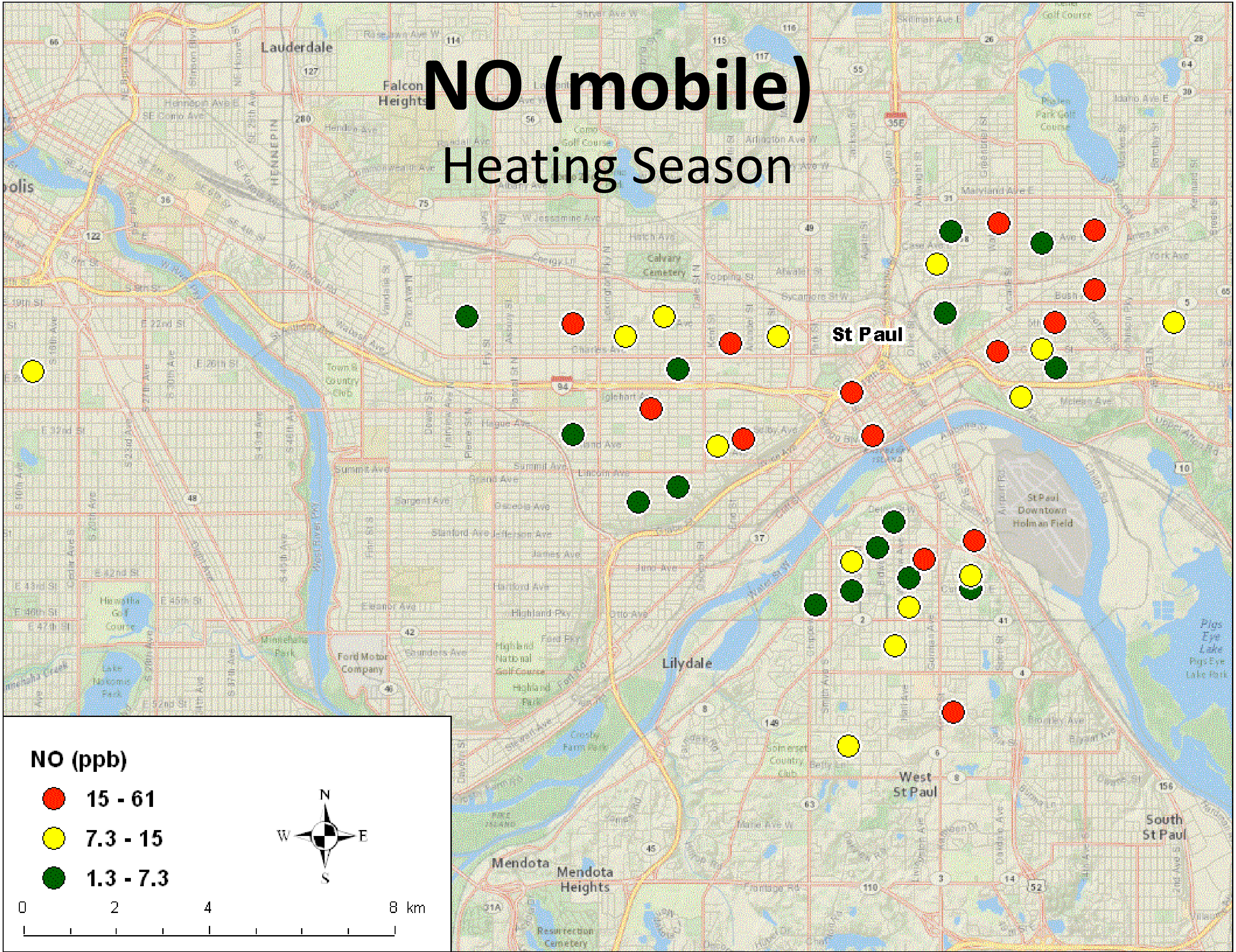
## Heating Season

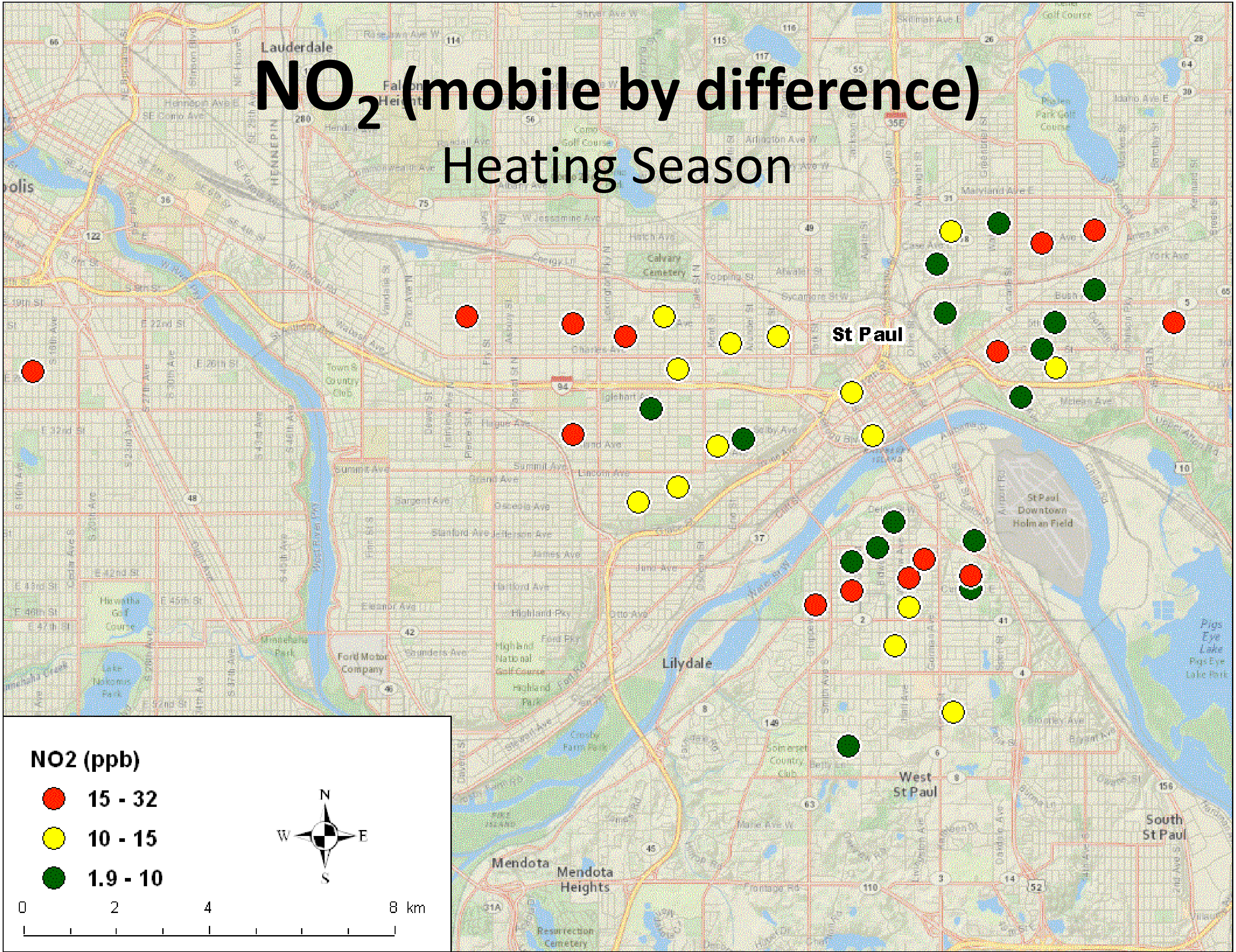




NO$_X$ (mobile)
Heating Season
NOx (ppb)
31 - 58
19 - 31
0.0 - 19
N
W
E
S
0
2
4
8 km
St Paul
Lauderdale
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights
St Paul Downtown Holman Field


NOx (passive)
Heating Season
Badge NOx (ppb)
35 - 51
29 - 35
19 - 29
N
W
E
S
0
2
4
8 km
St Paul
Lauderdale
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights
St Paul Downtown Holman Field
Pigs Eye Lake

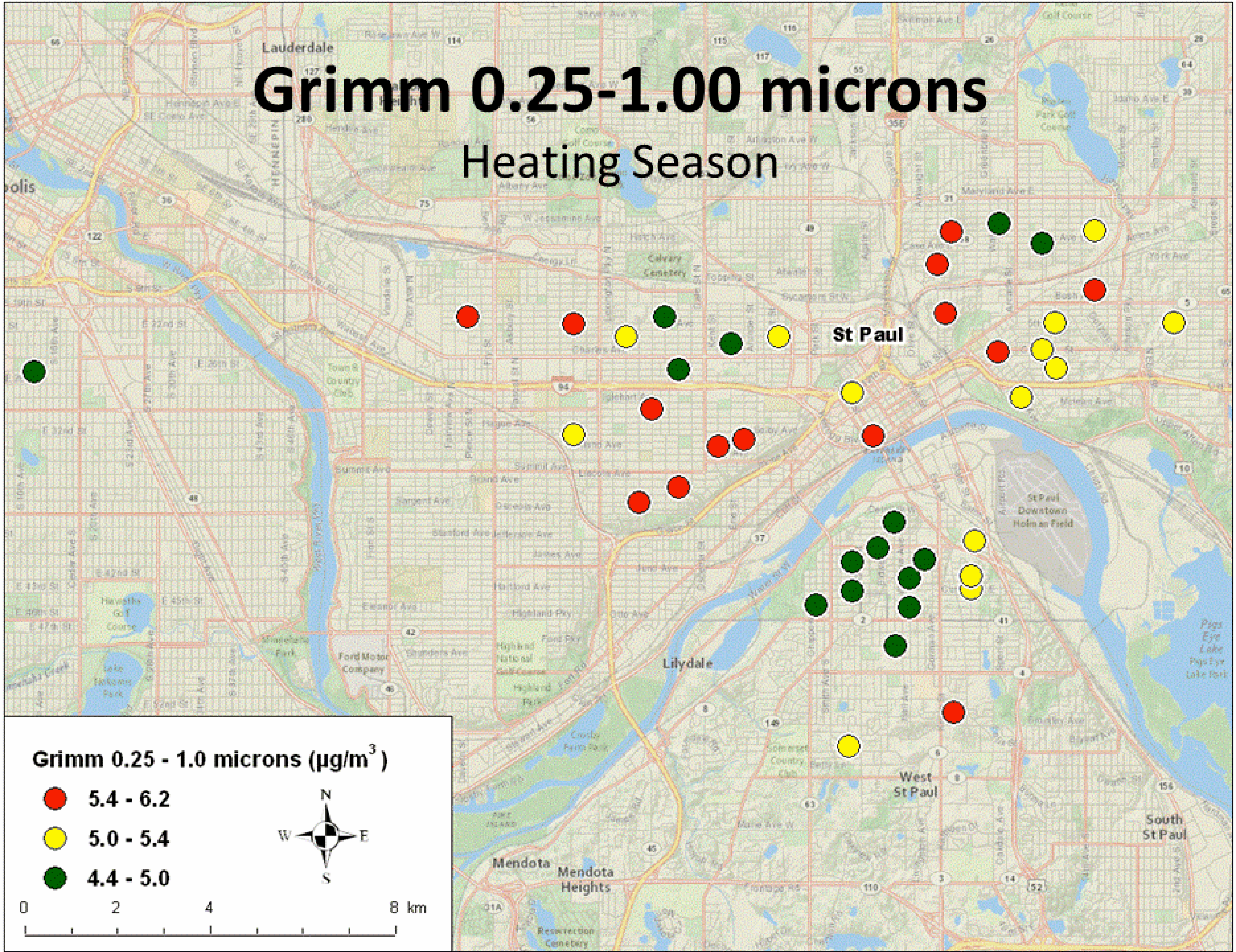

NO (mobile)
Heating Season
NO (ppb)
15 - 61
7.3 - 15
1.3 - 7.3
N
W
E
S
0
2
4
8 km
St Paul
Lauderdale
Falcon Heights
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights



NO$_2$ (mobile by difference)
Heating Season
NO2 (ppb)
15 - 32
10 - 15
1.9 - 10
N
S
E
W
0
2
4
8 km
St Paul
Lauderdale
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights

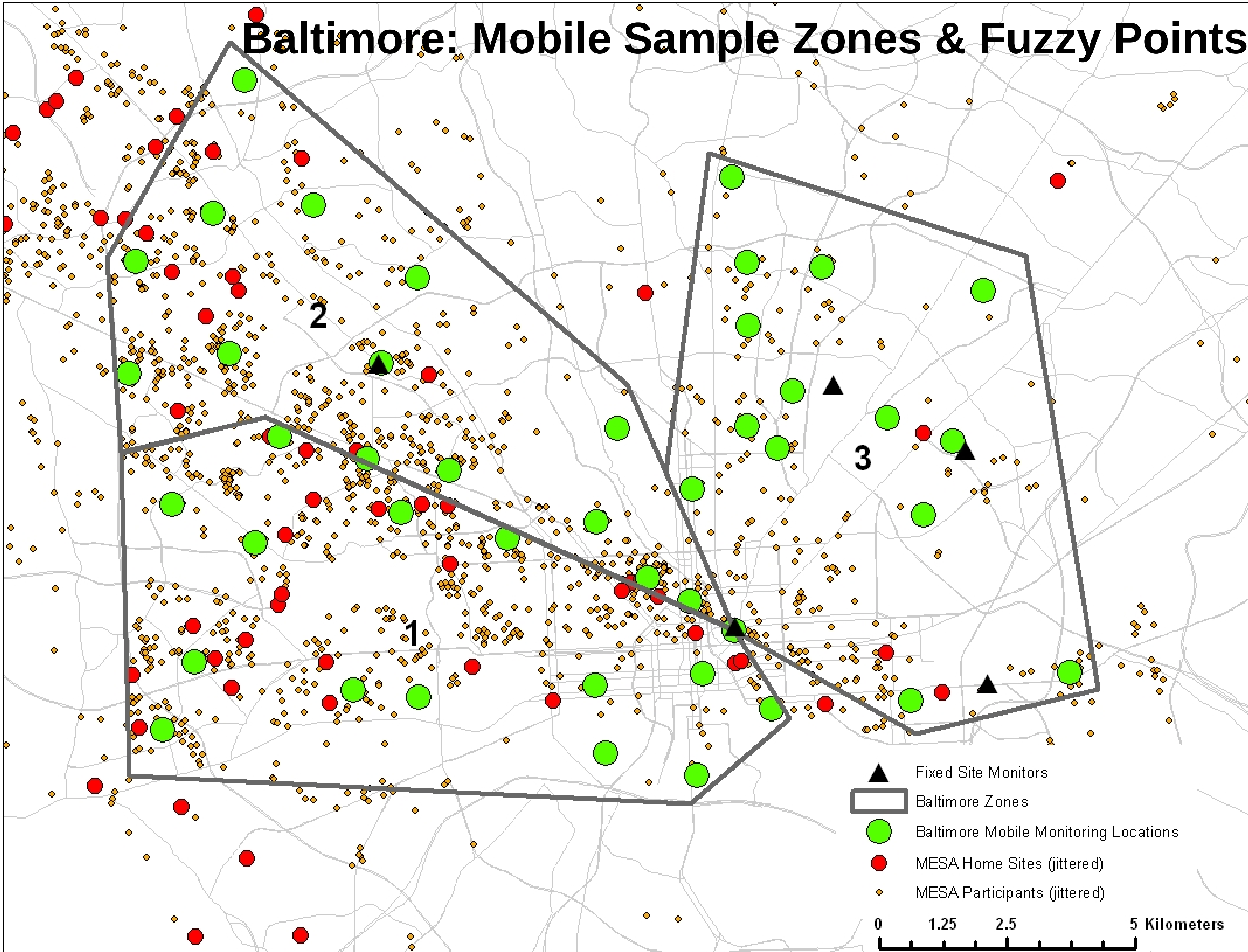
# St. Paul: Set in motion….

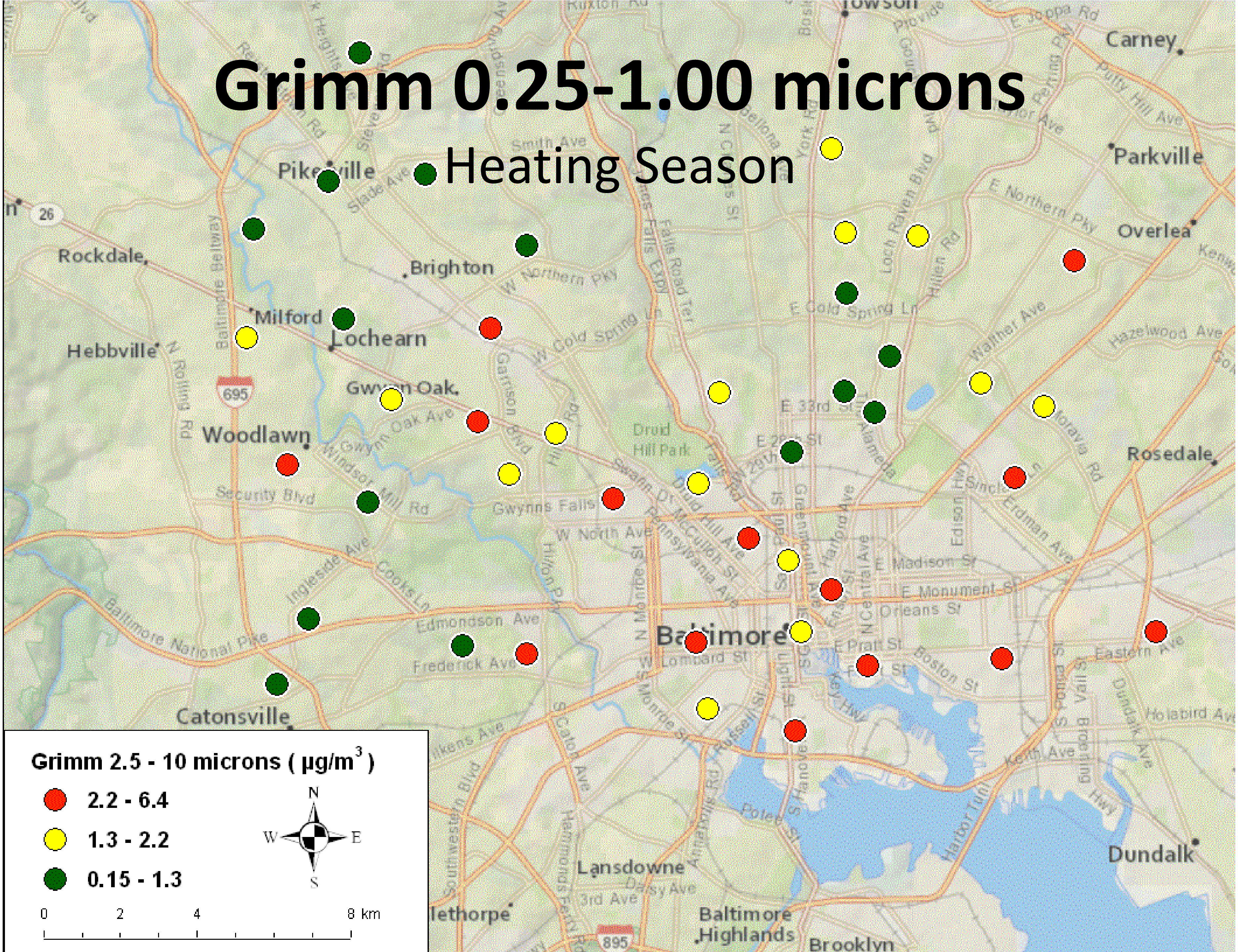
- Loop animation of fuzzy point results
- Time-Averaged over sample period
- Each pollutant plotted as Tertiles (High →Low)

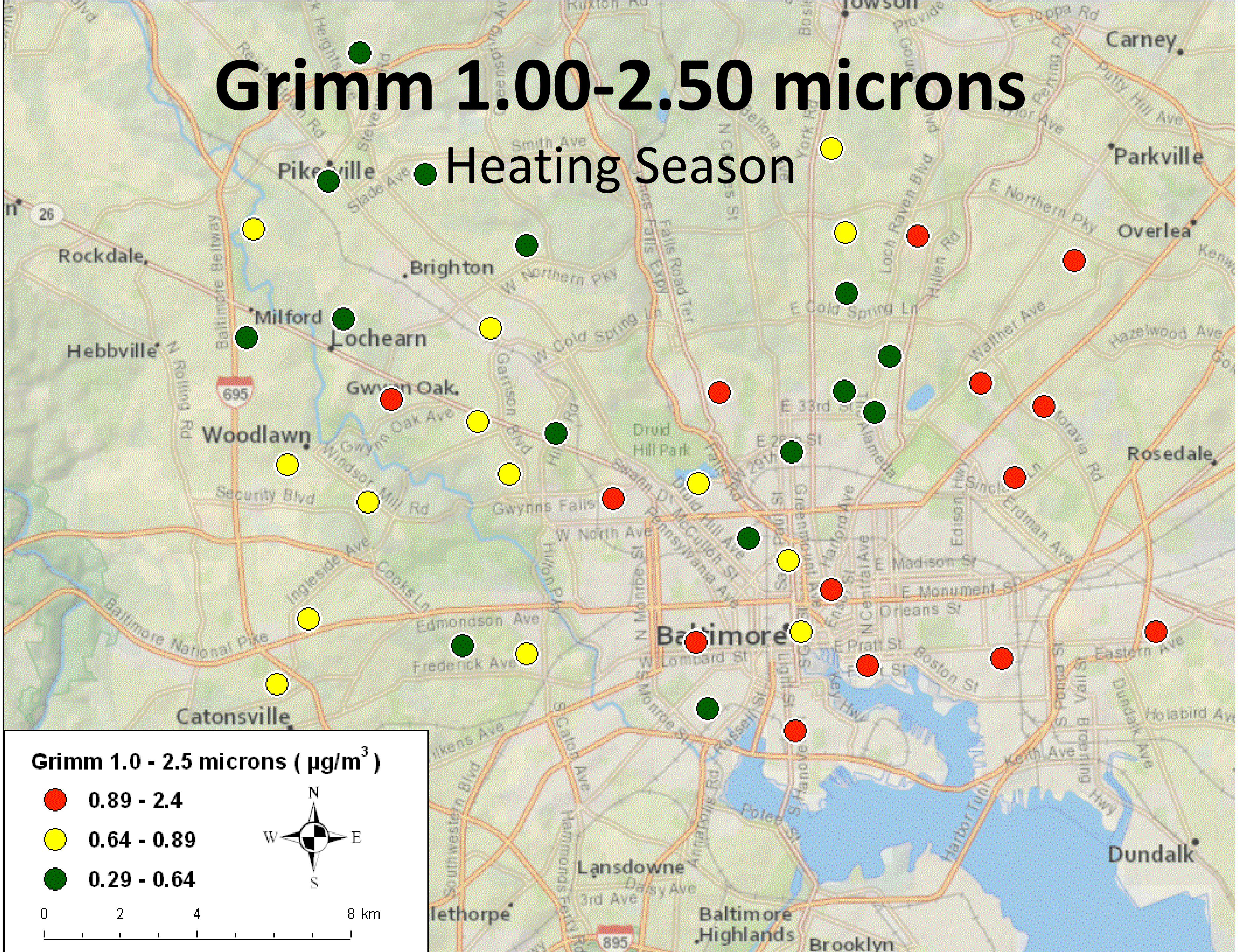


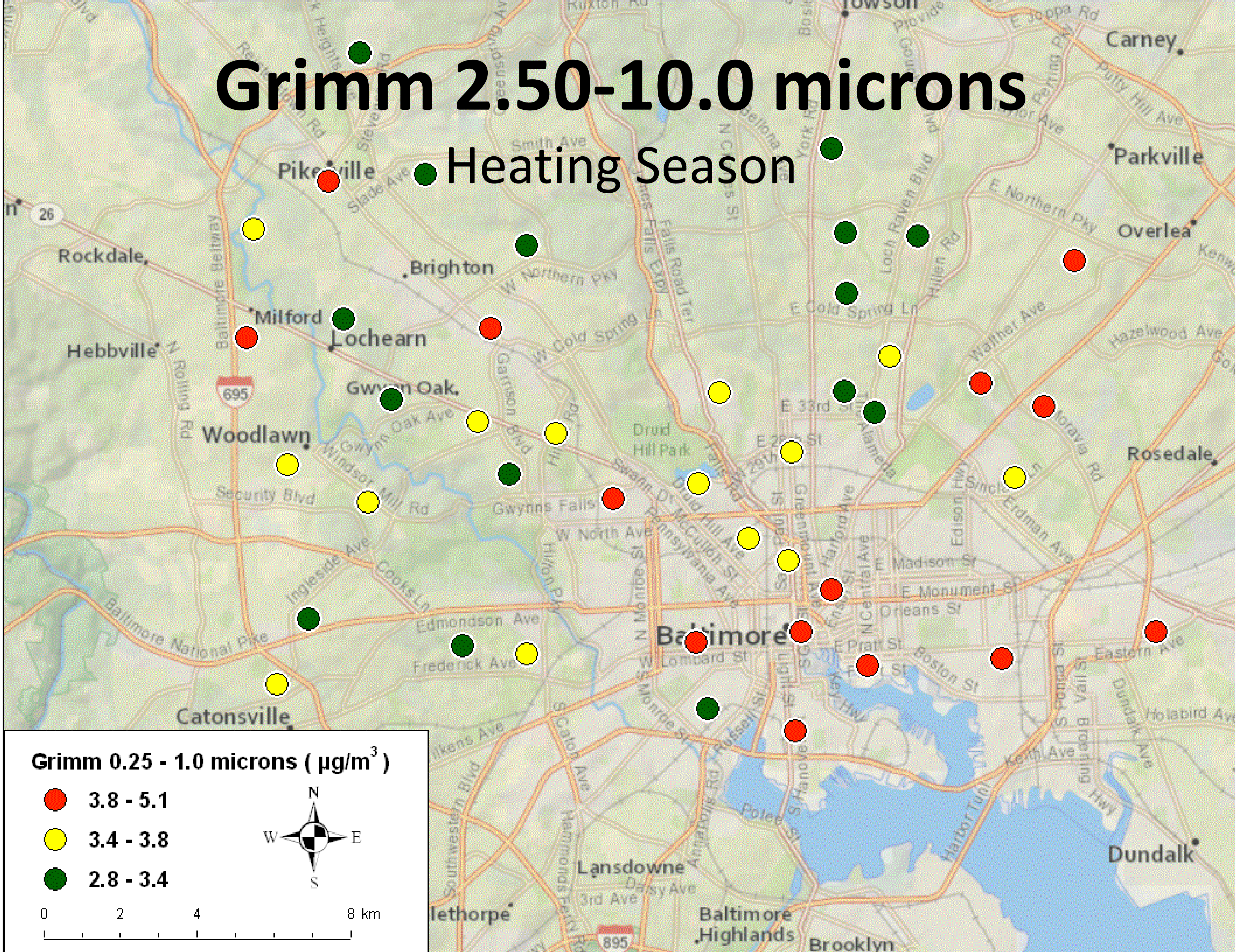
Grimm 0.25-1.00 microns
Heating Season
Grimm 0.25 - 1.0 microns (µg/m³)
5.4 - 6.2
5.0 - 5.4
4.4 - 5.0
N
W
E
S
0
2
4
8 km
St Paul
Lauderdale
Lilydale
West St Paul
South St Paul
Mendota
Mendota Heights

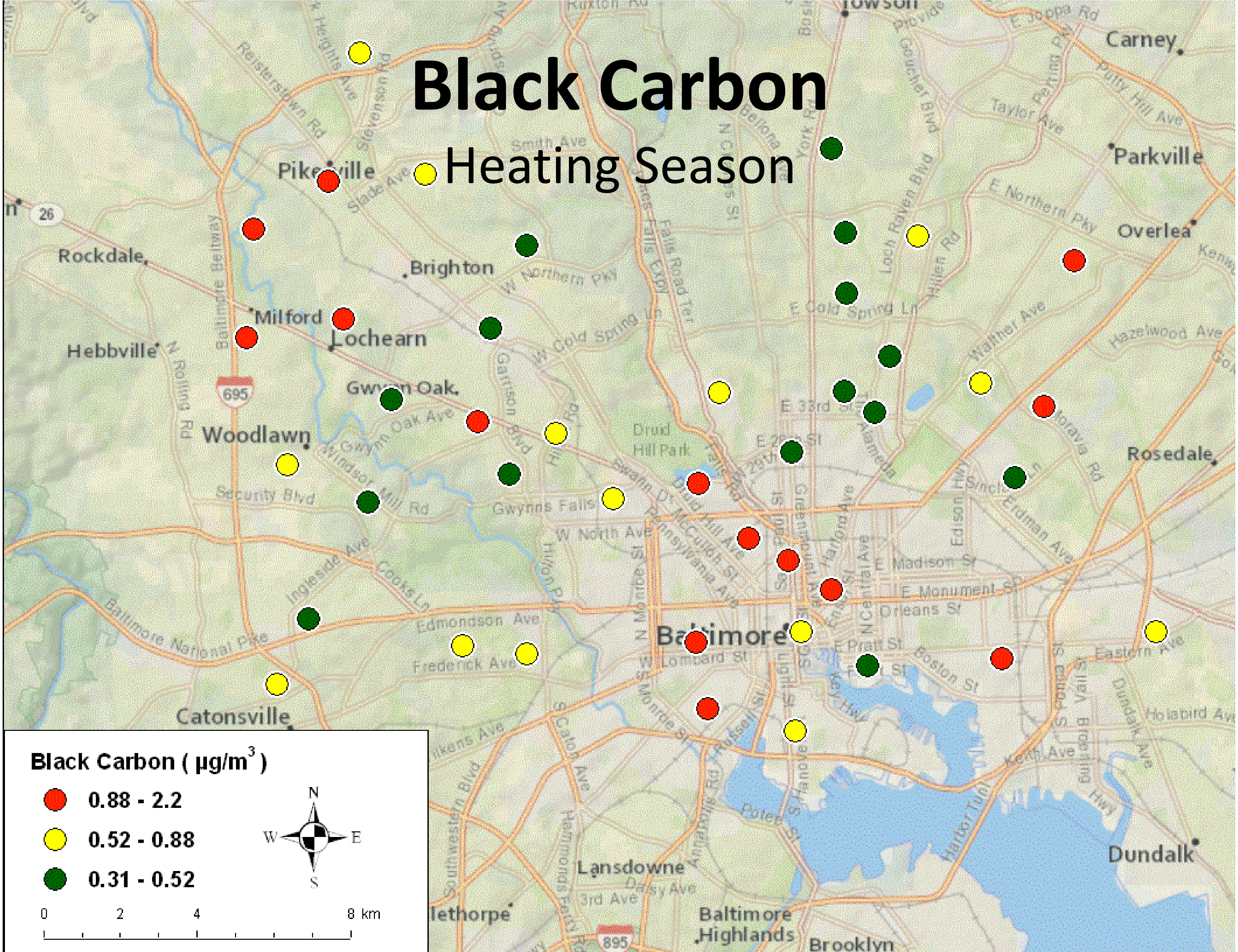
# Baltimore Heating Season

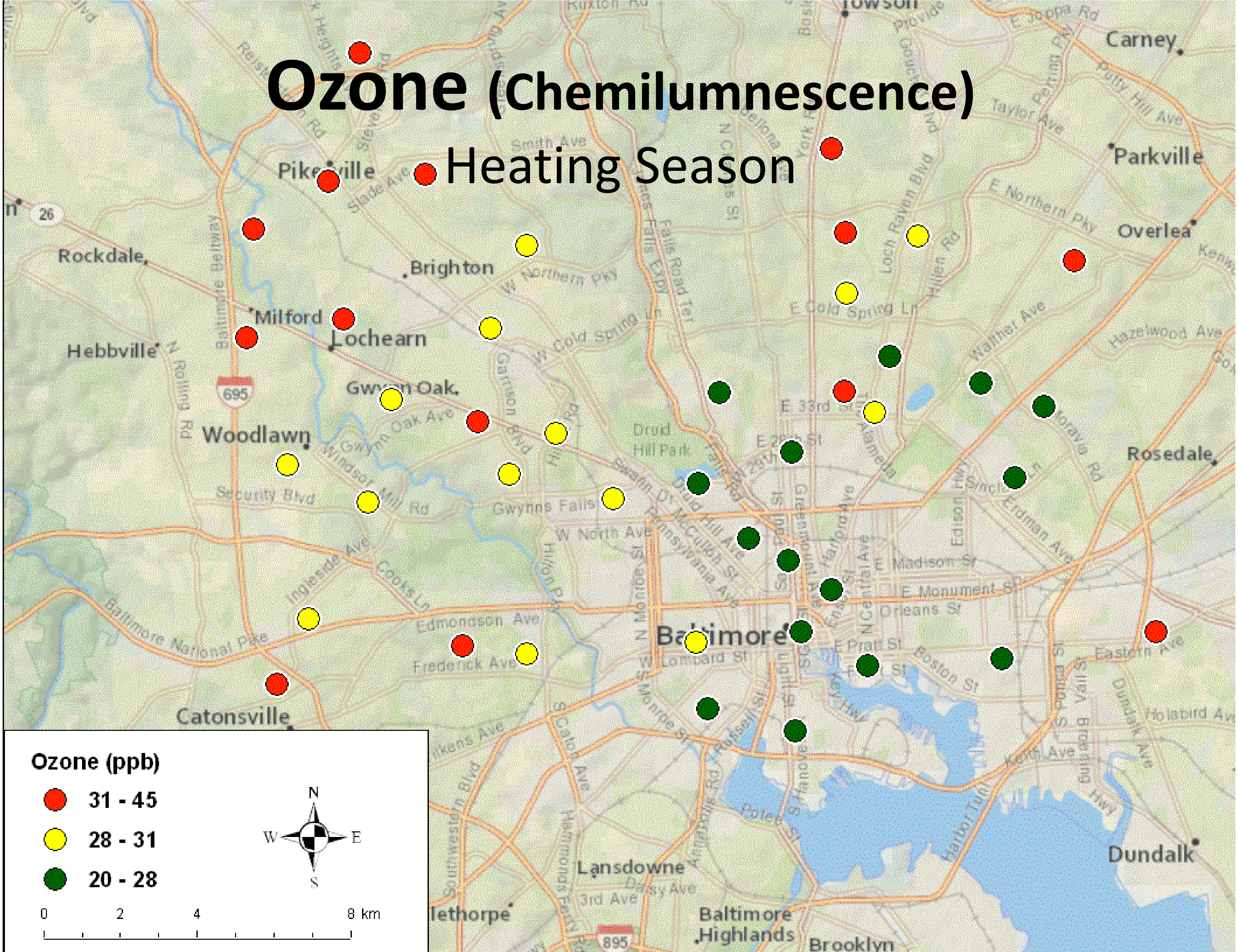

Baltimore: Mobile Sample Zones & Fuzzy Points
1
2
3
Fixed Site Monitors
Baltimore Zones
Baltimore Mobile Monitoring Locations
MESA Home Sites (jittered)
MESA Participants (jittered)
0 1.25 2.5 5 Kilometers

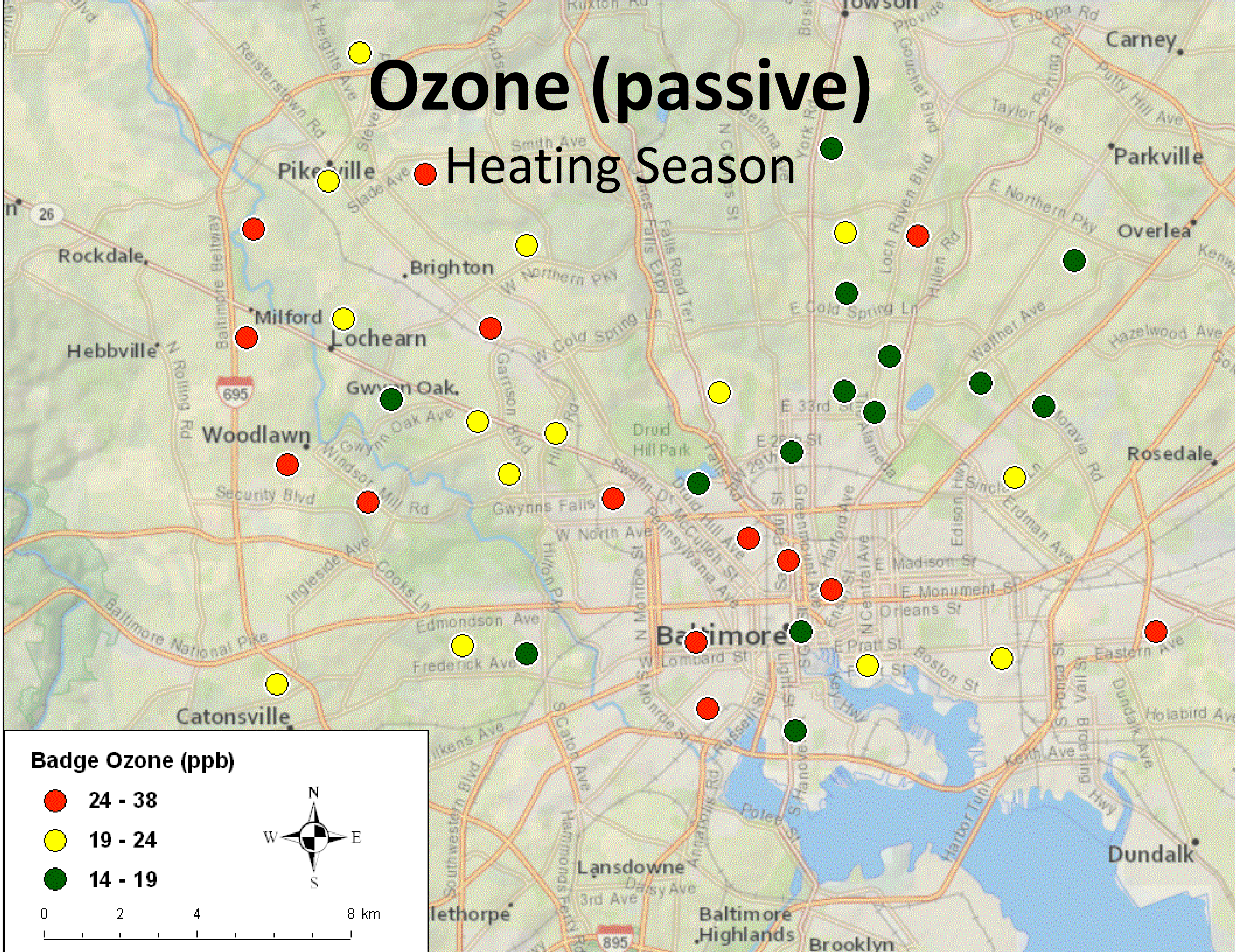

Grimm 0.25-1.00 microns
Heating Season
Grimm 2.5 - 10 microns ( µg/m³ )
2.2 - 6.4
1.3 - 2.2
0.15 - 1.3
N
W
E
S
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Rosedale
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Catonsville
Baltimore
Lansdowne
Baltimore Highlands
Brooklyn
Dundalk
Druid Hill Park

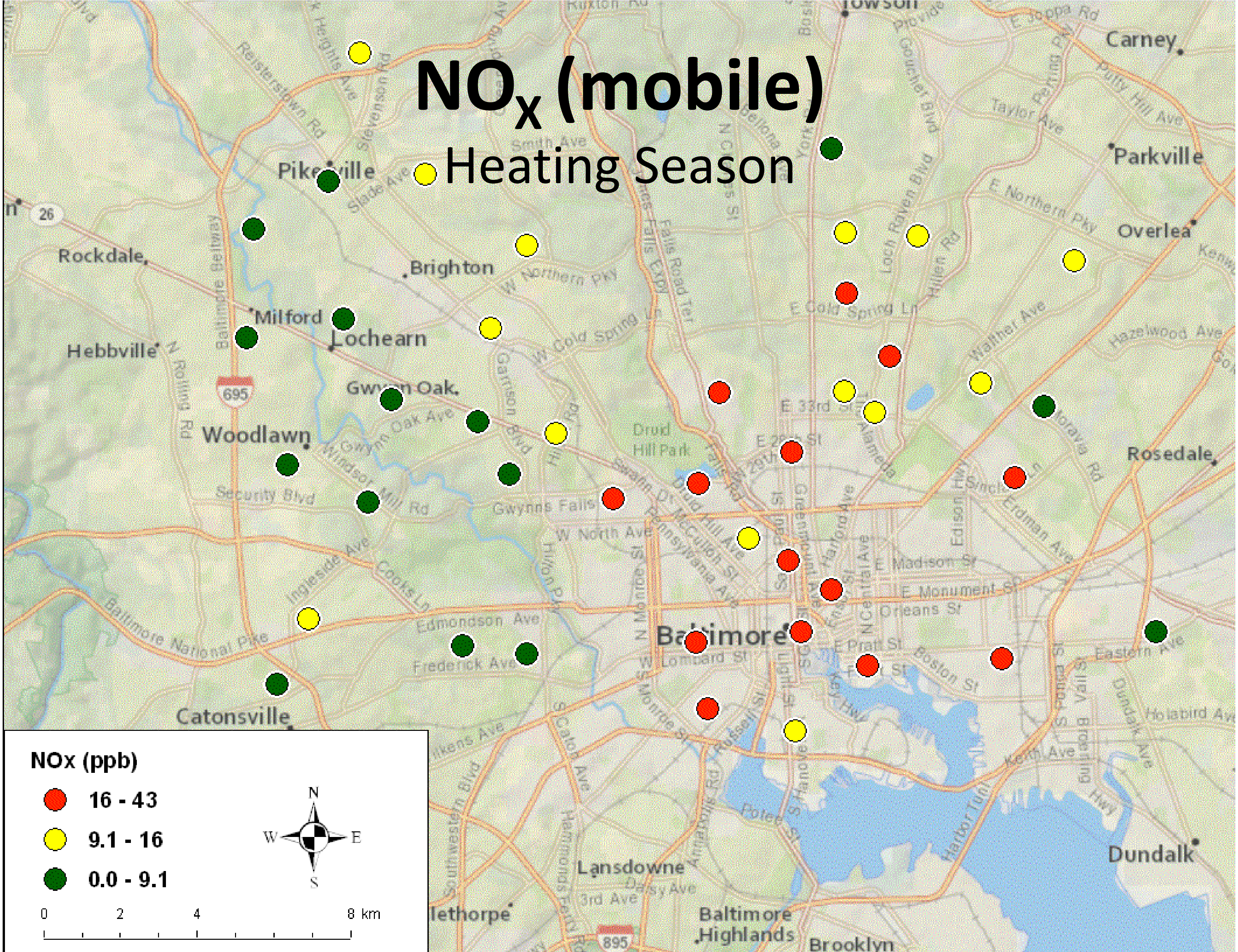

Grimm 1.00-2.50 microns
Heating Season
Grimm 1.0 - 2.5 microns ( µg/m³ )
0.89 - 2.4
0.64 - 0.89
0.29 - 0.64
N
W
E
S
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Rosedale
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Catonsville
Baltimore
Dundalk
Lansdowne
Baltimore Highlands
Brooklyn
Druid Hill Park


Grimm 2.50-10.0 microns
Heating Season
Grimm 0.25 - 1.0 microns ( µg/m³ )
3.8 - 5.1
3.4 - 3.8
2.8 - 3.4
N
W
E
S
0
2
4
8 km
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Catonsville
Baltimore
Carney
Parkville
Overlea
Rosedale
Dundalk
Lansdowne
Baltimore Highlands
Brooklyn
Towson
Druid Hill Park

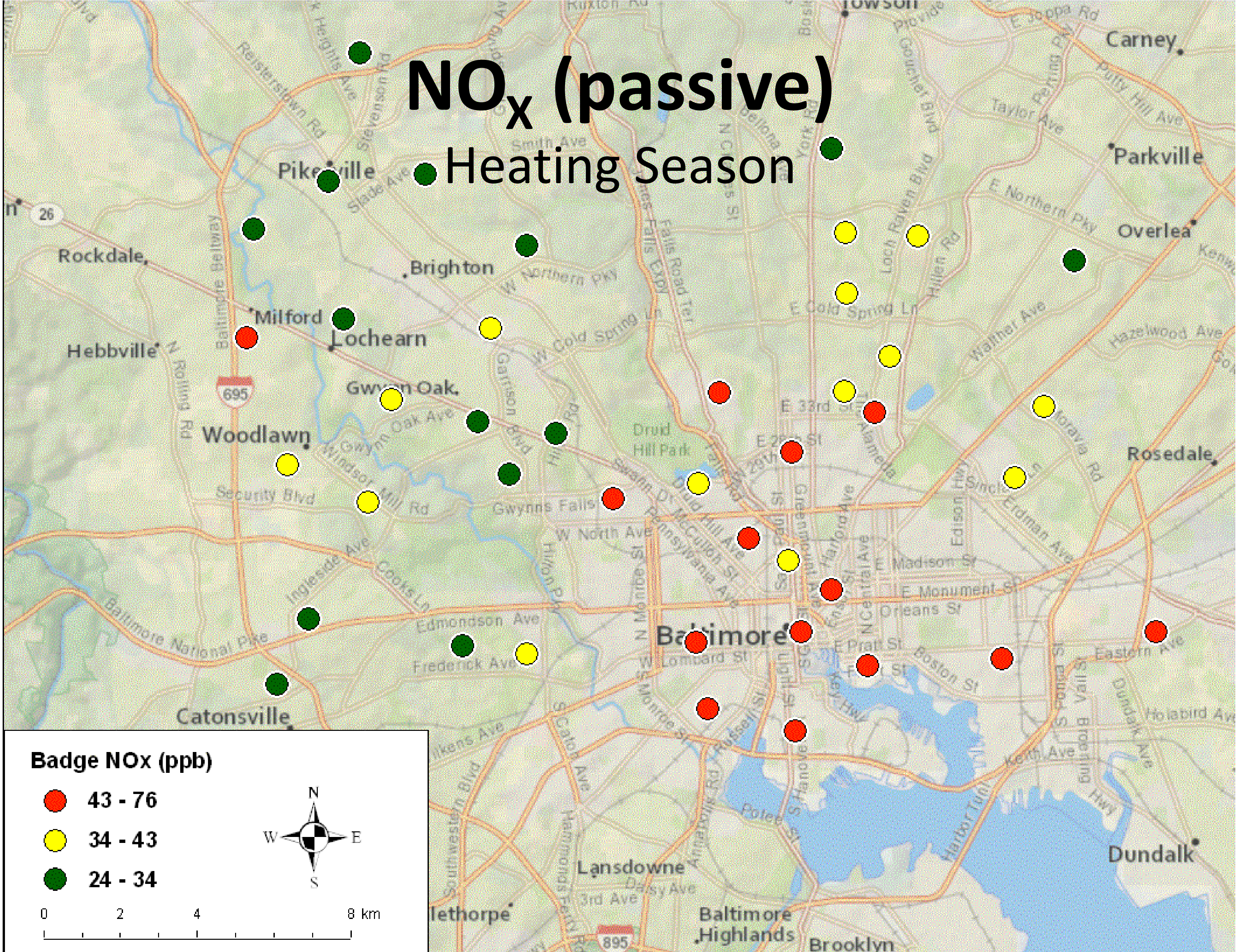

Black Carbon
Heating Season
Black Carbon ( μg/m³ )
0.88 - 2.2
0.52 - 0.88
0.31 - 0.52
N
W
E
S
0
2
4
8 km
Baltimore
Pikesville
Rockdale
Milford
Lochearn
Hebbville
Woodlawn
Gwynn Oak
Brighton
Catonsville
Carney
Parkville
Overlea
Rosedale
Dundalk
Lansdowne
Baltimore Highlands
Brooklyn


Ozone (Chemilumnescence)
Heating Season
Ozone (ppb)
31 - 45
28 - 31
20 - 28
N
S
W
E
0
2
4
8 km
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Catonsville
Baltimore
Carney
Parkville
Overlea
Rosedale
Dundalk
Lansdowne
Baltimore Highlands
Brooklyn
Towson

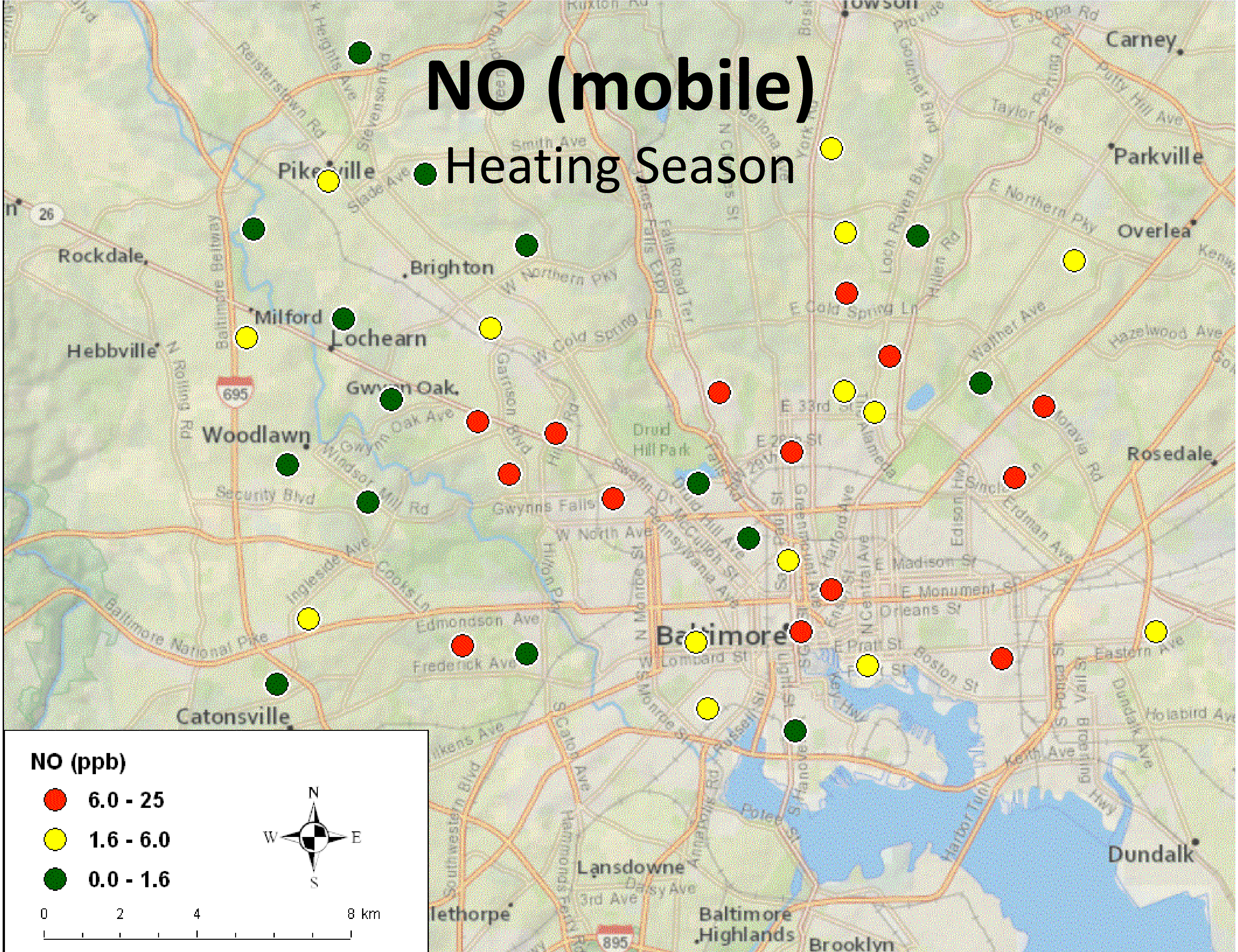

Ozone (passive)
Heating Season
Badge Ozone (ppb)
24 - 38
19 - 24
14 - 19
N
W
E
S
0
2
4
8 km
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Catonsville
Baltimore
Towson
Carney
Parkville
Overlea
Rosedale
Dundalk
Lansdowne
Baltimore Highlands
Brooklyn



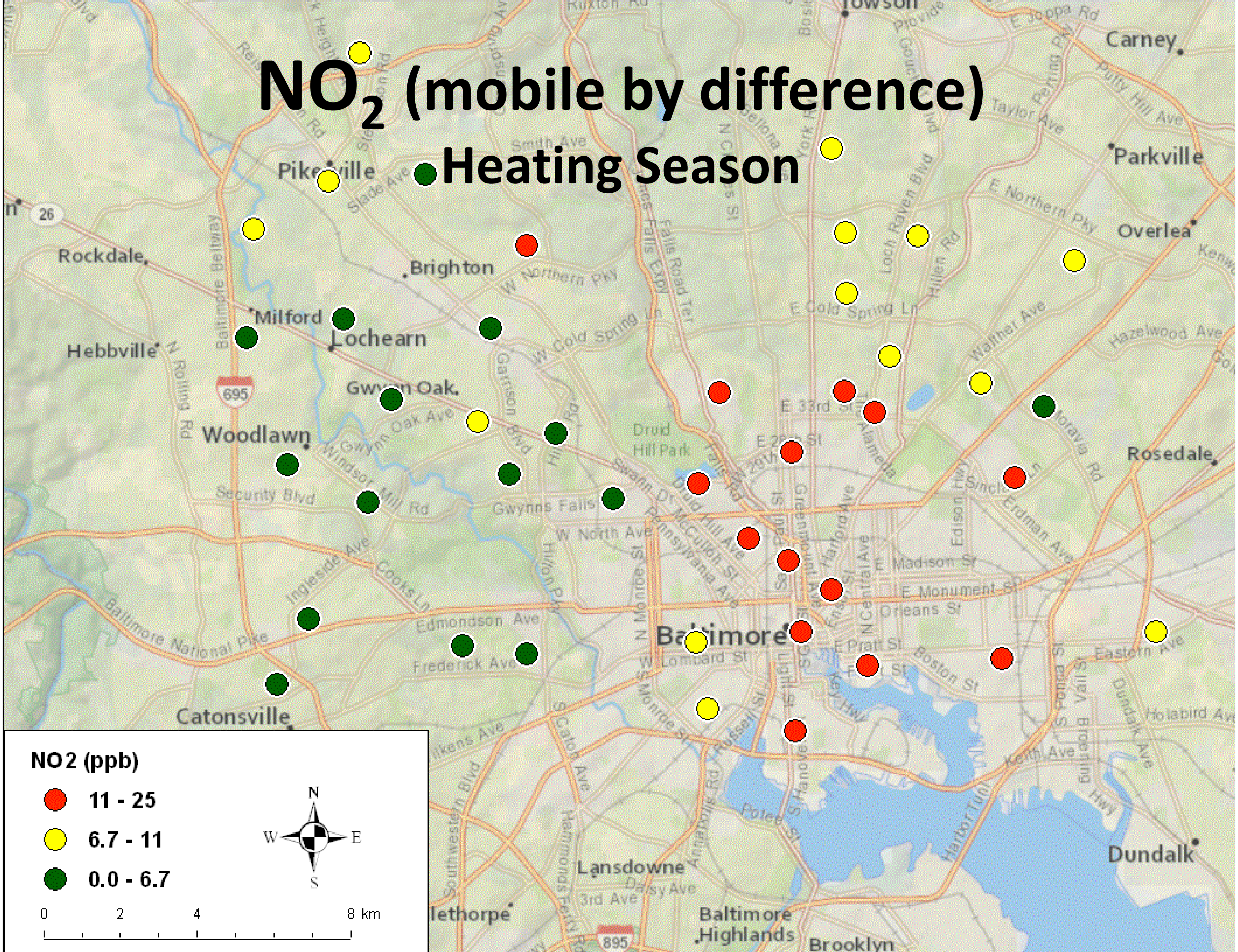
NOx (mobile)
Heating Season
NOx (ppb)
16 - 43
9.1 - 16
0.0 - 9.1
N
W
E
S
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Druid Hill Park
Rosedale
Baltimore
Catonsville
Lansdowne
Baltimore Highlands
Brooklyn
Dundalk
695
895
26



NOx (passive)
Heating Season
Badge NOx (ppb)
43 - 76
34 - 43
24 - 34
N
W
E
S
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Rosedale
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Druid Hill Park
Baltimore
Catonsville
Lansdowne
Baltimore Highlands
Brooklyn
Dundalk



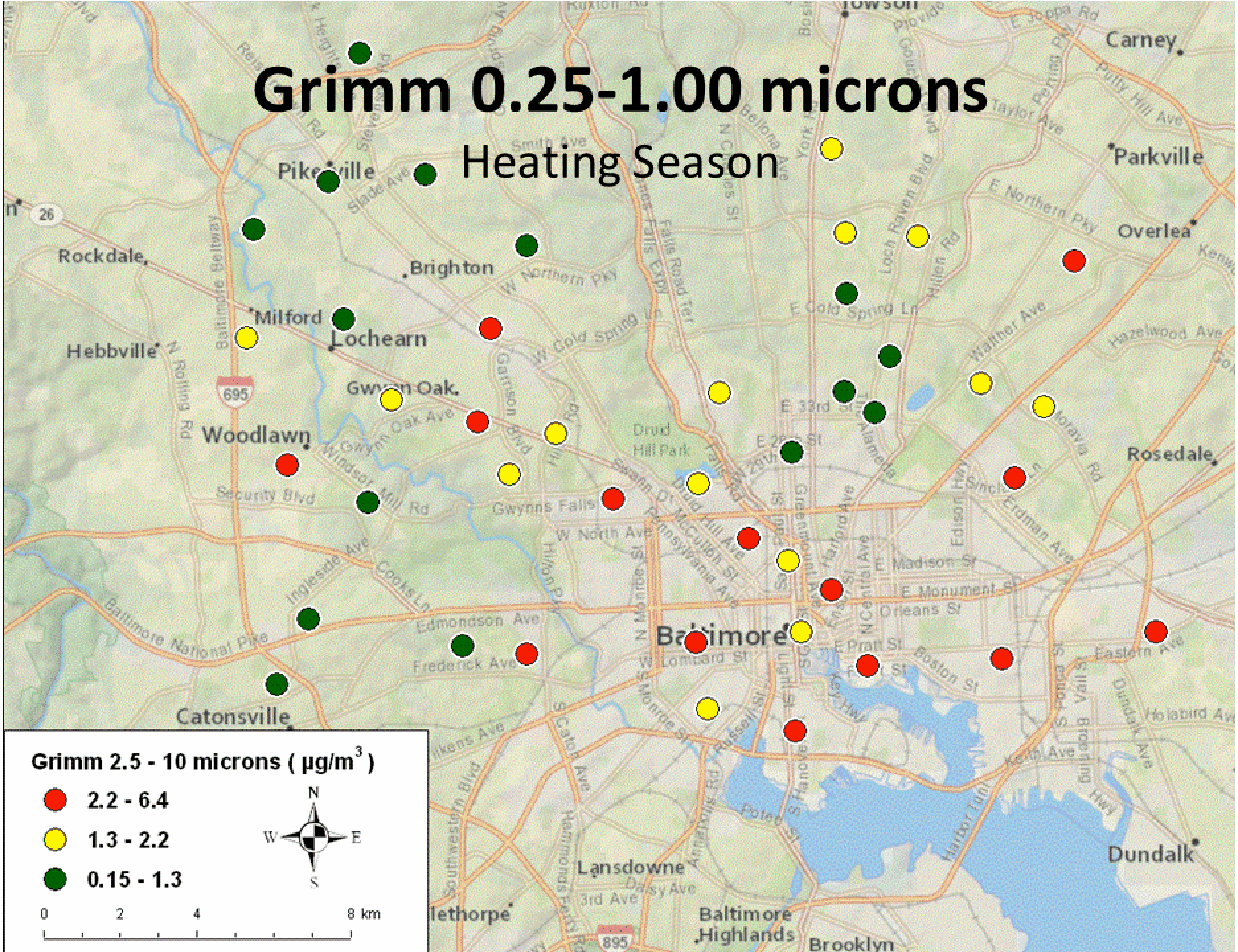
NO (mobile)
Heating Season
NO (ppb)
6.0 - 25
1.6 - 6.0
0.0 - 1.6
N
S
E
W
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Druid Hill Park
Rosedale
Baltimore
Catonsville
Lansdowne
Baltimore Highlands
Brooklyn
Dundalk



$NO_2$ (mobile by difference)
Heating Season
NO2 (ppb)
11 - 25
6.7 - 11
0.0 - 6.7
N
W
E
S
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Rosedale
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Druid Hill Park
Baltimore
Catonsville
Dundalk
Lansdowne
Baltimore Highlands
Brooklyn

# Baltimore: Set in motion….

- Loop animation of fuzzy point results
- Time-Averaged over sample period
- Each pollutant plotted as Tertiles (High →Low)


Grimm 0.25-1.00 microns
Heating Season
Grimm 2.5 - 10 microns ( µg/m³ )
2.2 - 6.4
1.3 - 2.2
0.15 - 1.3
N
W
E
S
0
2
4
8 km
Towson
Carney
Parkville
Overlea
Rosedale
Pikesville
Rockdale
Brighton
Milford
Lochearn
Hebbville
Gwynn Oak
Woodlawn
Catonsville
Baltimore
Lansdowne
Baltimore Highlands
Brooklyn
Dundalk
Druid Hill Park

# VOC - Fuzzy Point Correlations: St Paul

Passive Data

| | Pentane | n-Nonane | Benzene | Toluene | m-Xylene | o-Xylene | NO2 | NOx |
|---|---|---|---|---|---|---|---|---|
| Pentanes | | | | | | | | |
| n-Nonane | **0.77**$^{**}$ | | | | | | | |
| Benzene | **0.85**$^{**}$ | **0.76**$^{**}$ | | | | | | |
| Toluene | **0.88**$^{**}$ | **0.87**$^{**}$ | **0.92**$^{**}$ | | | | | |
| m-Xylene | **0.86**$^{**}$ | **0.86**$^{**}$ | **0.84**$^{**}$ | **0.97**$^{**}$ | | | | |
| o-Xylene | **0.85**$^{**}$ | **0.85**$^{**}$ | **0.82**$^{**}$ | **0.96**$^{**}$ | **0.99**$^{**}$ | | | |
| NO2 | **0.34**$^{*}$ | **0.34**$^{*}$ | **0.48**$^{**}$ | **0.35**$^{*}$ | **0.34**$^{*}$ | 0.31 | | |
| NOx | 0.28 | 0.28 | 0.26 | 0.25 | 0.29 | 0.27 | **0.62**$^{**}$ | |
| Ozone | -0.18 | -0.11 | -0.07 | -0.13 | -0.11 | -0.09 | 0.01 | **-0.33**$^{*}$ |

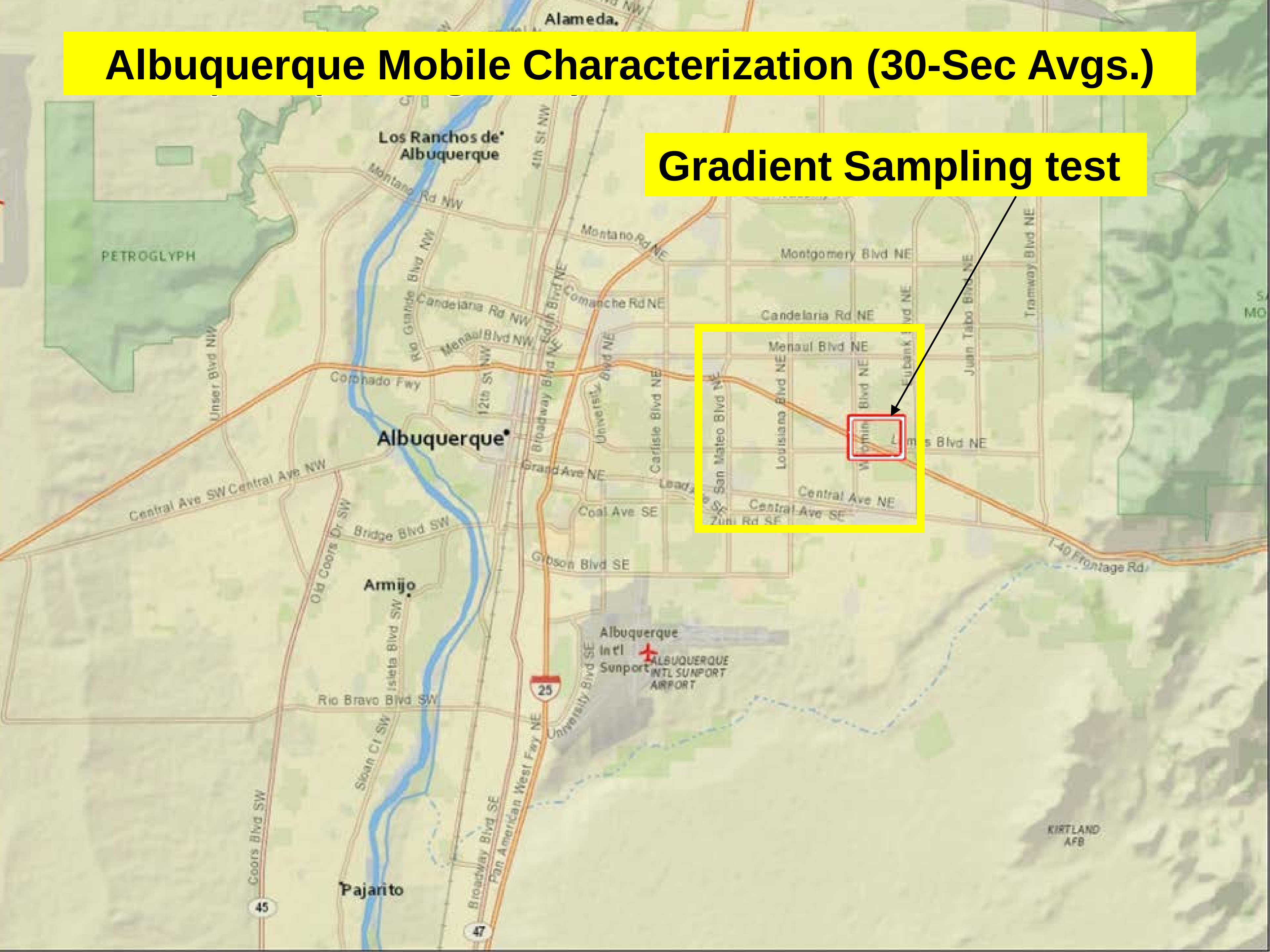
****. Correlation is significant at the 0.01 level (2-tailed).**

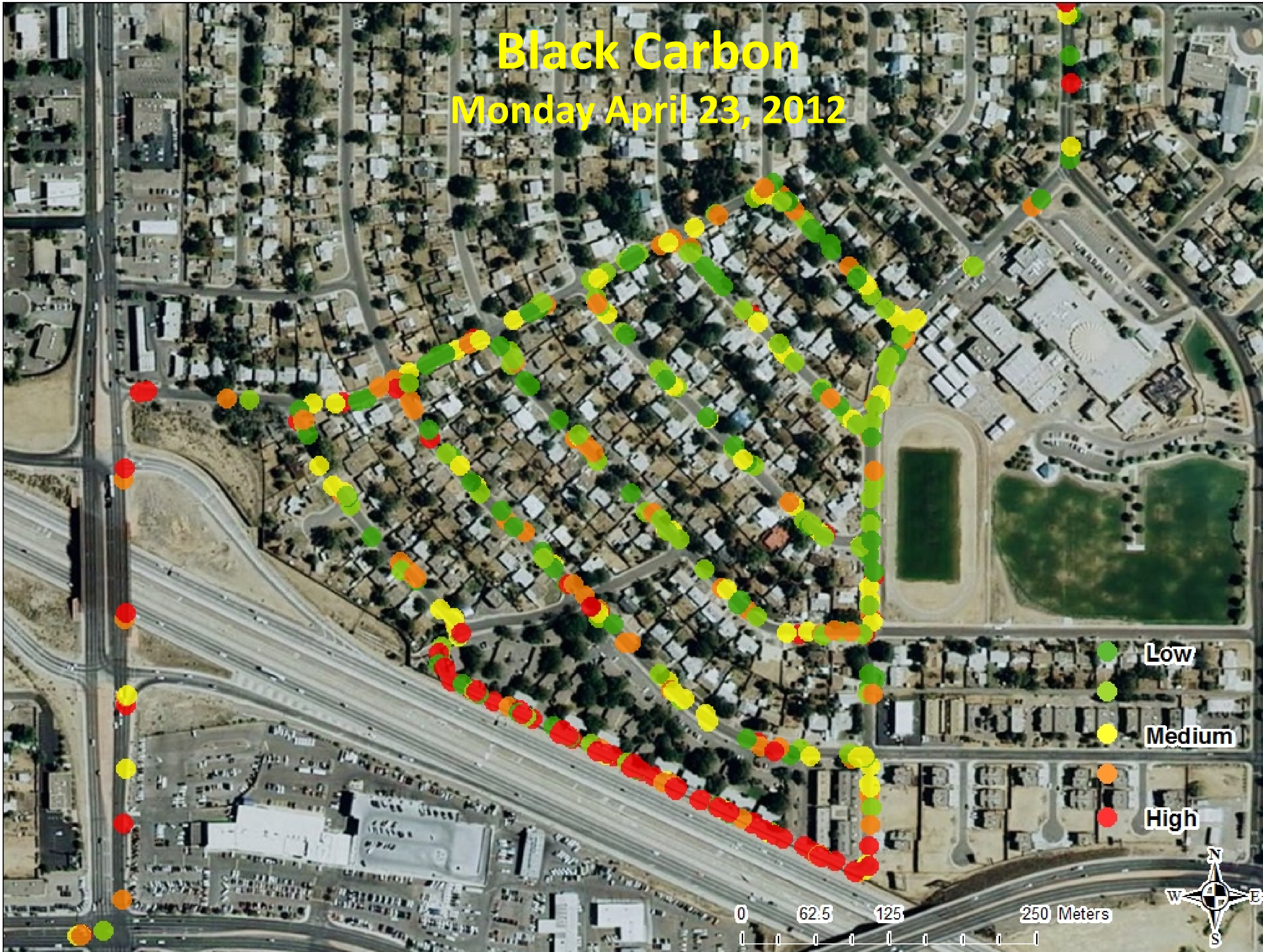
***. Correlation is significant at the 0.05 level (2-tailed).**

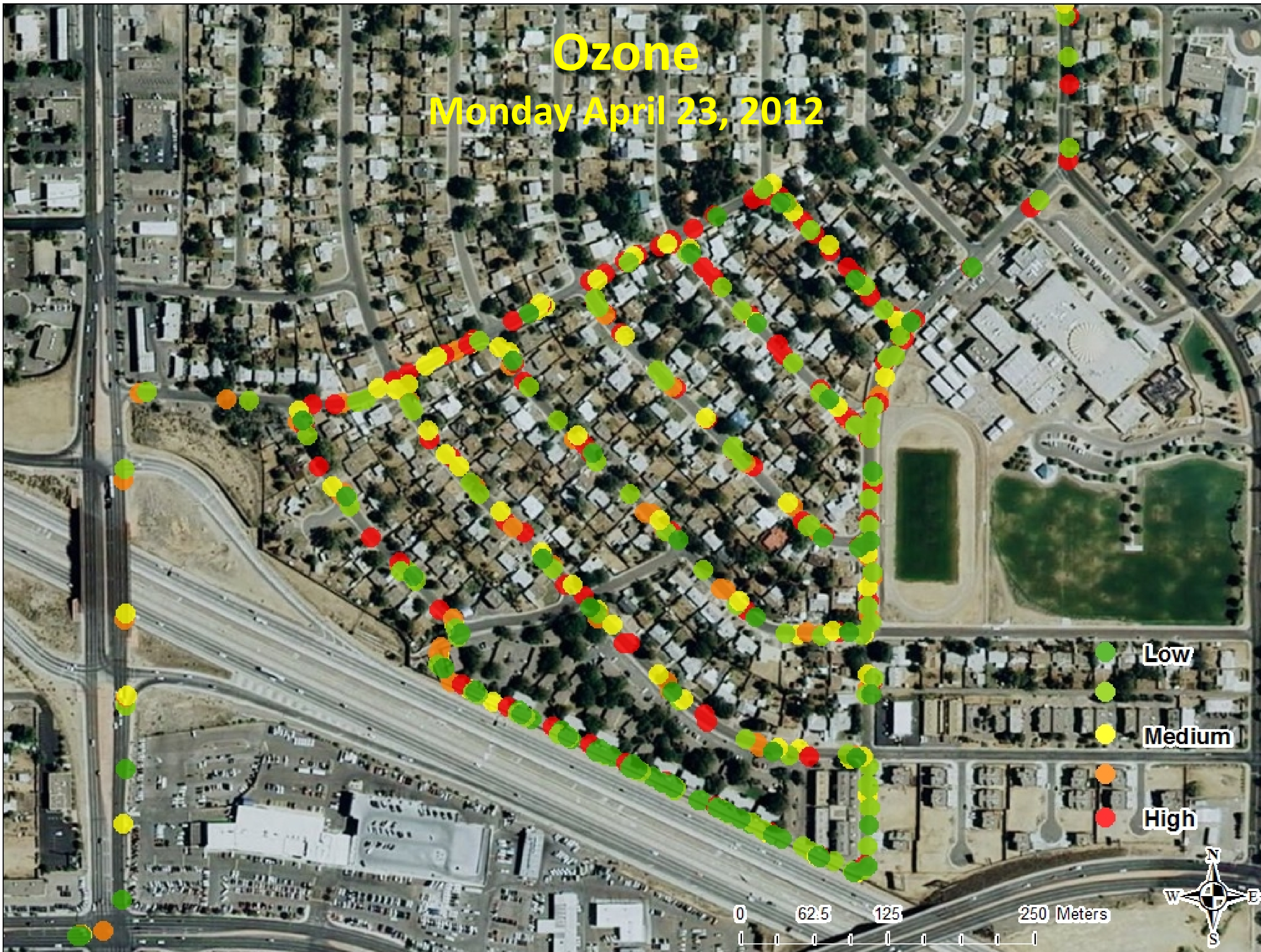
# Roadway Gradient Sampling

- SAC recommendation to attempt "detailed spatial/road and traffic source characteristics information"
- Developed alternative mobile sampling scheme to assess near-roadway pollutants
- Tested this approach in Albuquerque

# Albuquerque Mobile Characterization (30-Sec Avgs.)

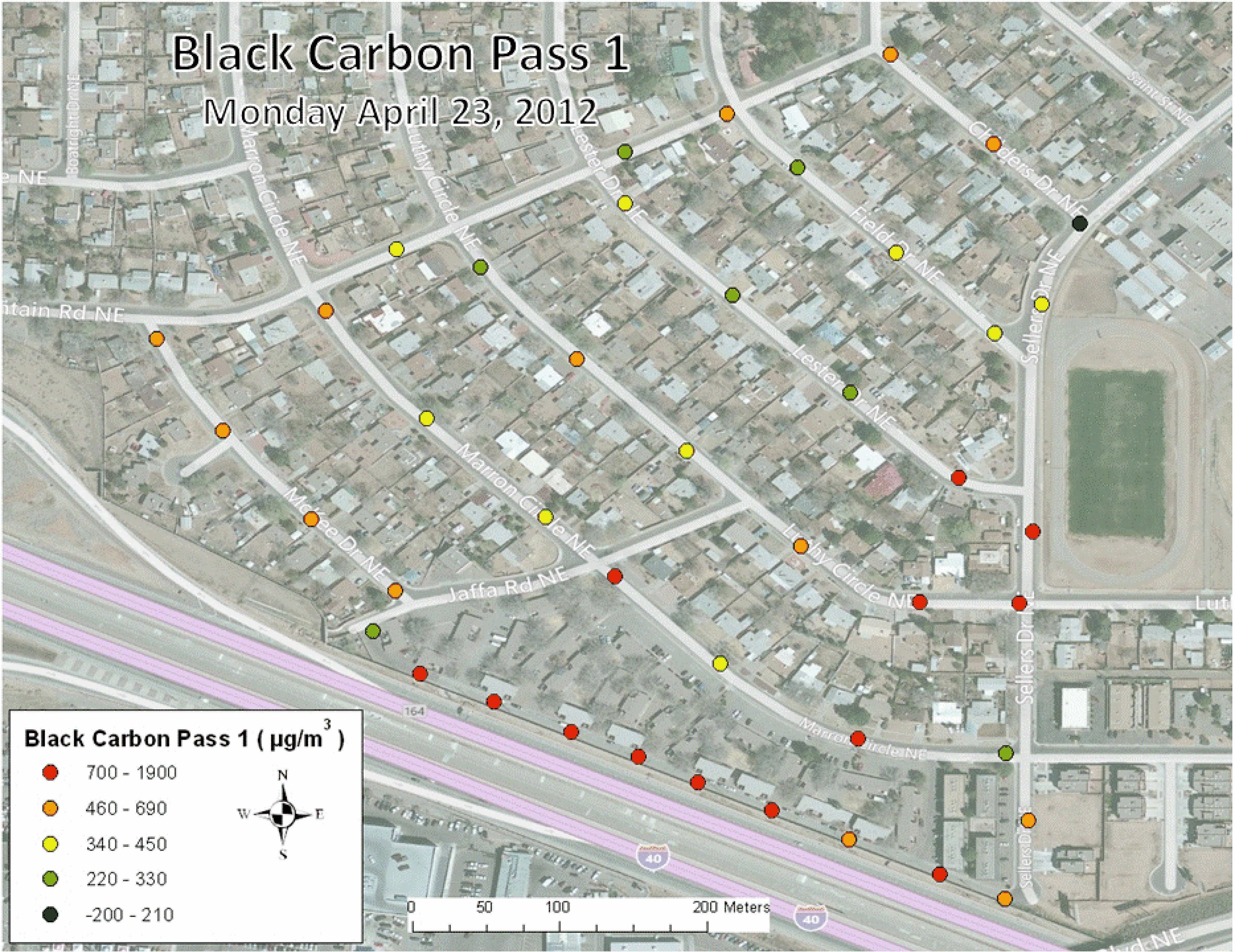



Black Carbon
Monday April 23, 2012
Low
Medium
High
0
62.5
125
250 Meters
N
W
E
S


Ozone
Monday April 23, 2012
Low
Medium
High
0
62.5
125
250 Meters
N
W
E
S

# Set it in motion….

- Sequence of raw data
- pass 1, 2, 3 etc. for BC; then
- pass 1, 2, 3 etc. for O3

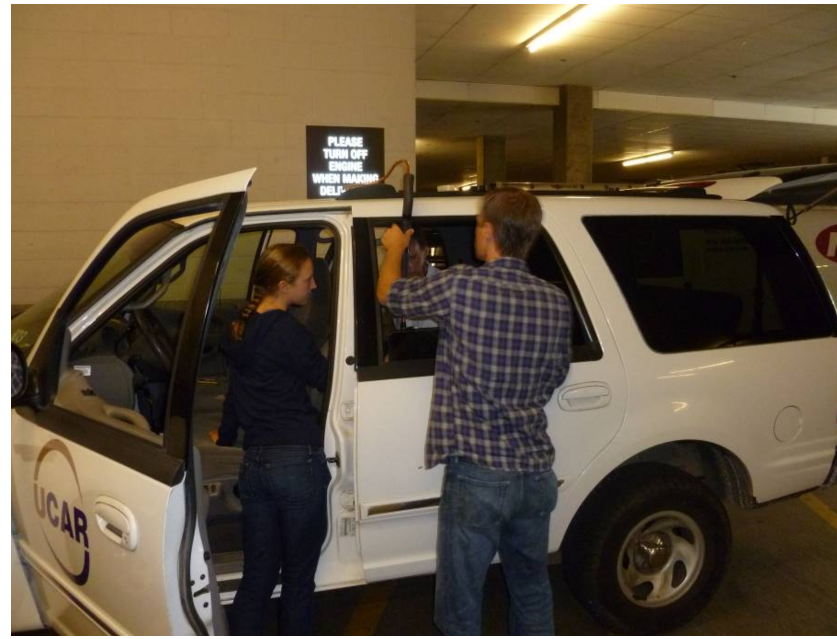


Black Carbon Pass 1
Monday April 23, 2012
Black Carbon Pass 1 ( μg/m3 )
700 - 1900
460 - 690
340 - 450
220 - 330
-200 - 210
N
W
E
S
0
50
100
200 Meters
Marron Circle NE
Luthy Circle NE
Lester Dr NE
Field Dr NE
Sellers Dr NE
Jaffa Rd NE
Mcgee Dr NE
Boatright Dr NE
Saint St NE
164
40

# Next Steps…

- Continue data collection schedule…
  - Added roadway gradient sampling to all cities
- QC & Preliminary analysis of Summer data
- Analysis of Seasonal Differences
  - Integration with Biostatistics Core
- Mobile data in Atlanta - 2013

# Thank You!




CCAR
Center for Clean Air Research

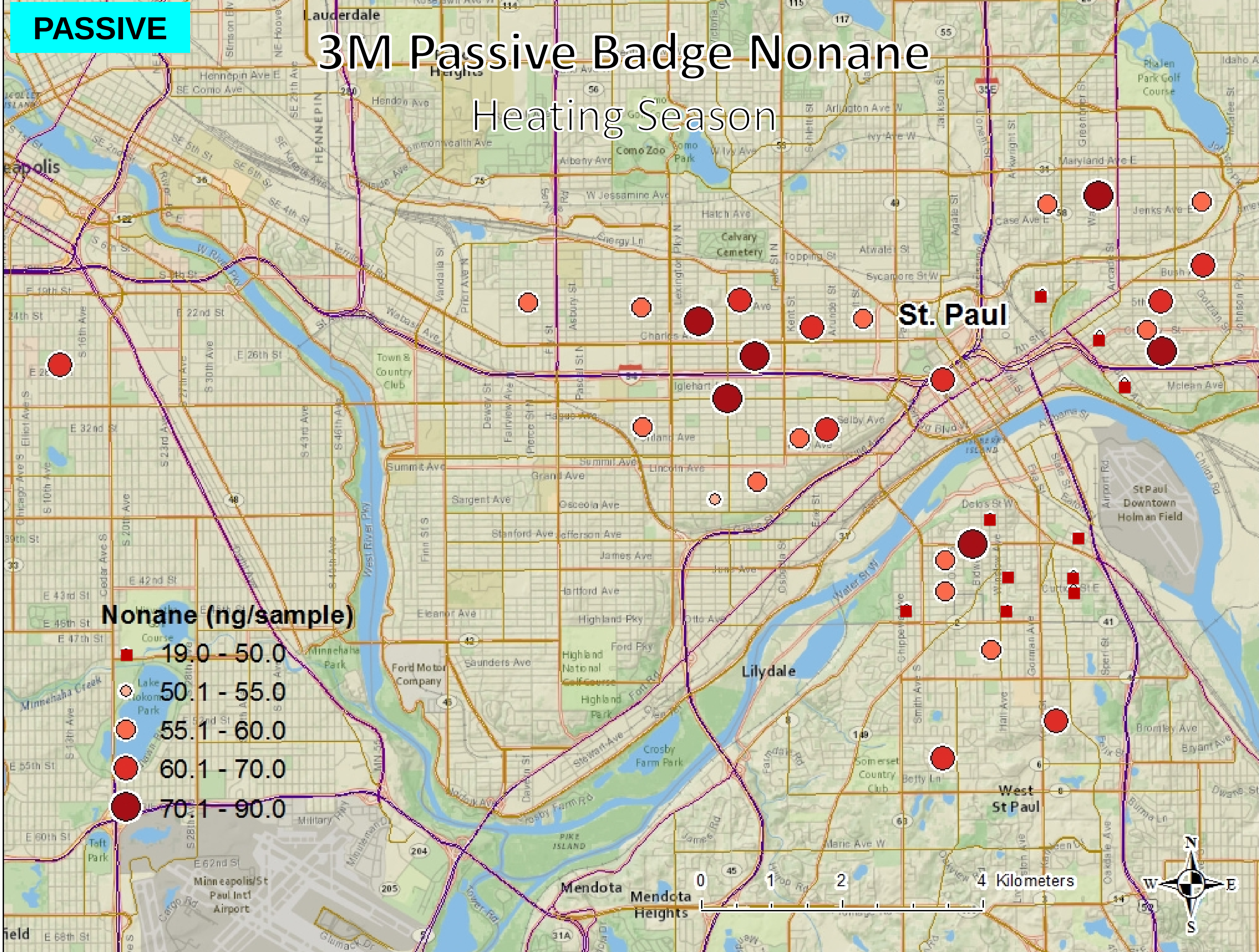
CENTER FOR CLEAN AIR RESEARCH

UNIVERSITY *of* WASHINGTON

PASSIVE

# 3M Passive Badge Nonane

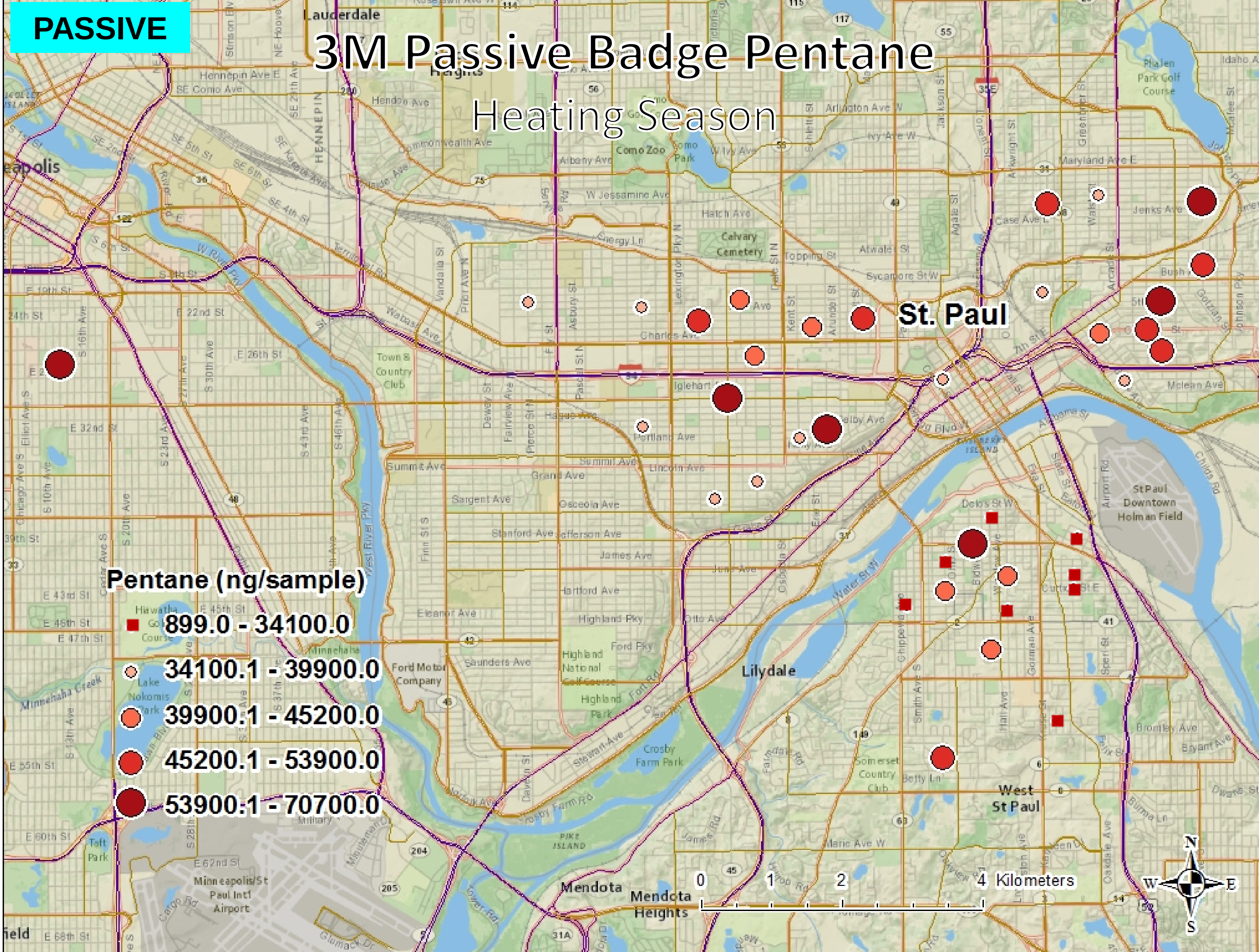
## Heating Season



PASSIVE

# 3M Passive Badge Pentane

## Heating Season



# EPA Clean Air Research Center

## Project 1:
## Aerosol Characterization of LRRI Exposure Chamber

**External Science Advisory Meeting September 2012**

Investigators:
Tom Jobson, Tim VanReken, WSU
Michael Yost, Tim Larson, Chris Simpson, UW
Jake MacDonald, LRRI

# Lovelace Respiratory Research Institute Exposure Chamber Study

April – May,  2012

**Task 1**.  Characterize gas and particle composition in the 1-$m^3$ engine exhaust exposure chambers.  Sample mixtures of diesel and gasoline engine exhaust.

**Task 2**.  Characterize 11.5-$m^3$ Teflon chamber for engine exhaust irradiation → SOA

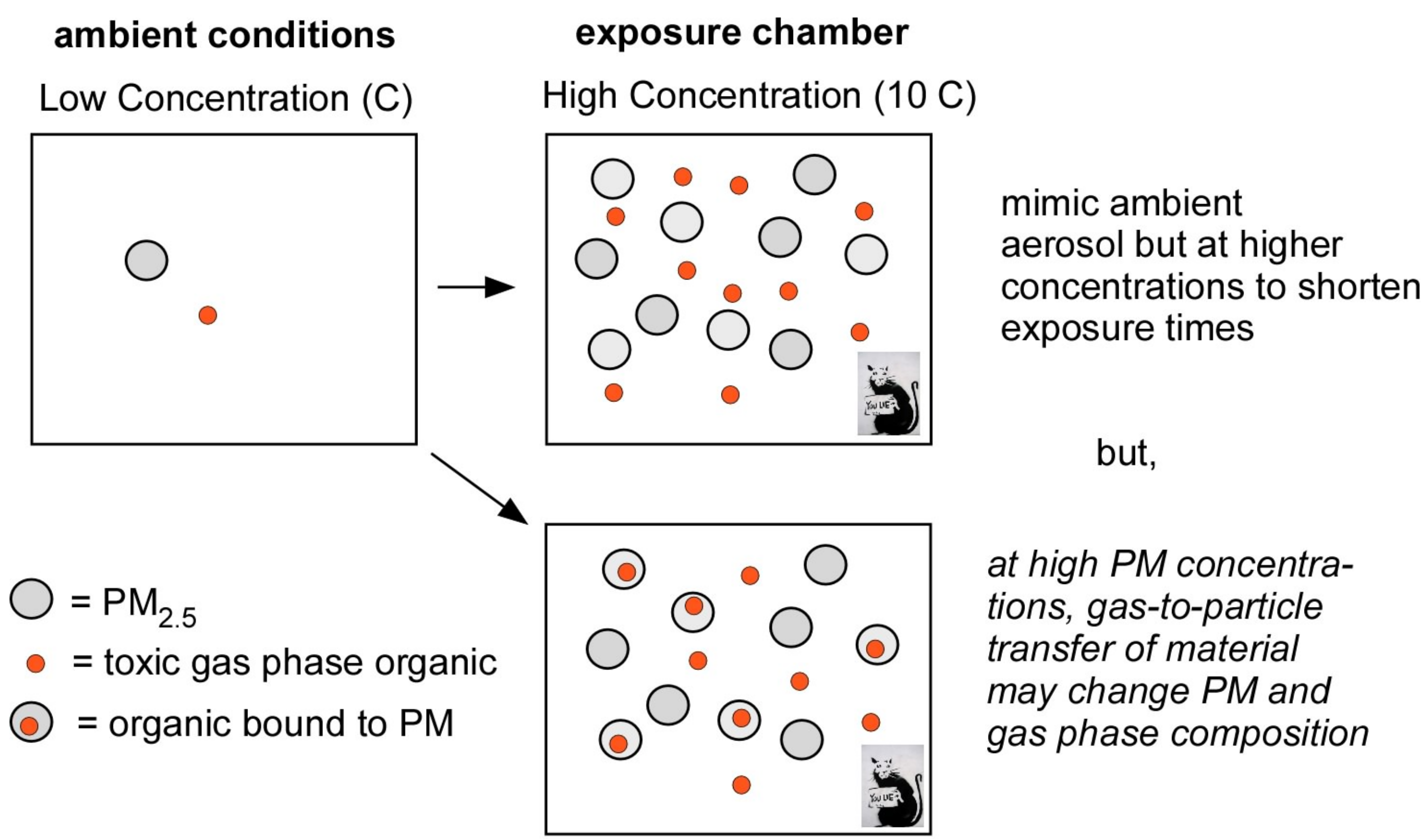
**Task 1**

**Task 2**

# Purpose

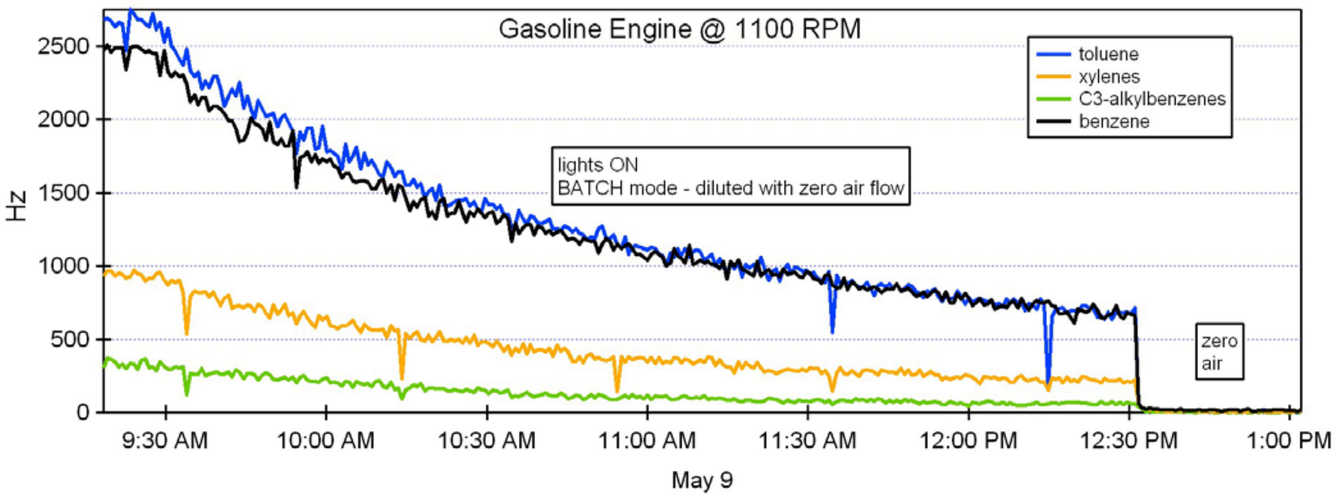
Examine engine exhaust aerosol composition measured in chambers to real-world scenarios to provide guidance on generating the most realistic exposures for toxicologic and human clinical trials.

***Do high concentration exposures reflect real world aerosol composition?***

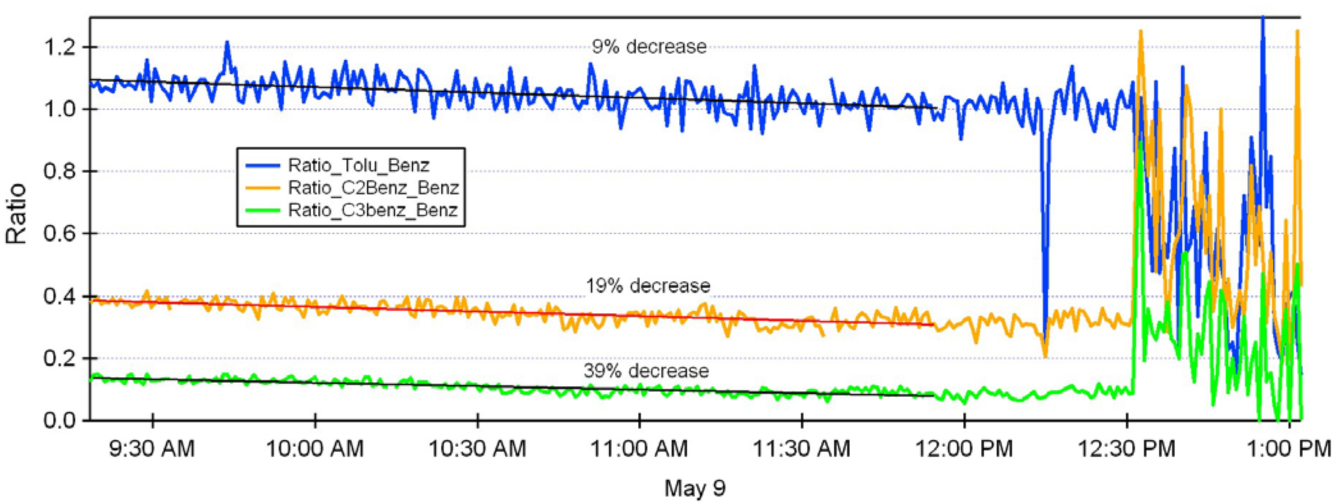


# TASK 2. Hard sledding.

**6 experiments performed: gasoline exhaust, diesel exhaust, and mixtures**




**Example:**
**May 9 Test**
**Gasoline engine exhaust**
**Initial conditions:**
**400 ppbv NOx +**
**400 ppbv Toluene**




**Changes in relative abundance of aromatic compounds indicate photochemical oxidation by HO radical**

# Task1. Exposure Chamber

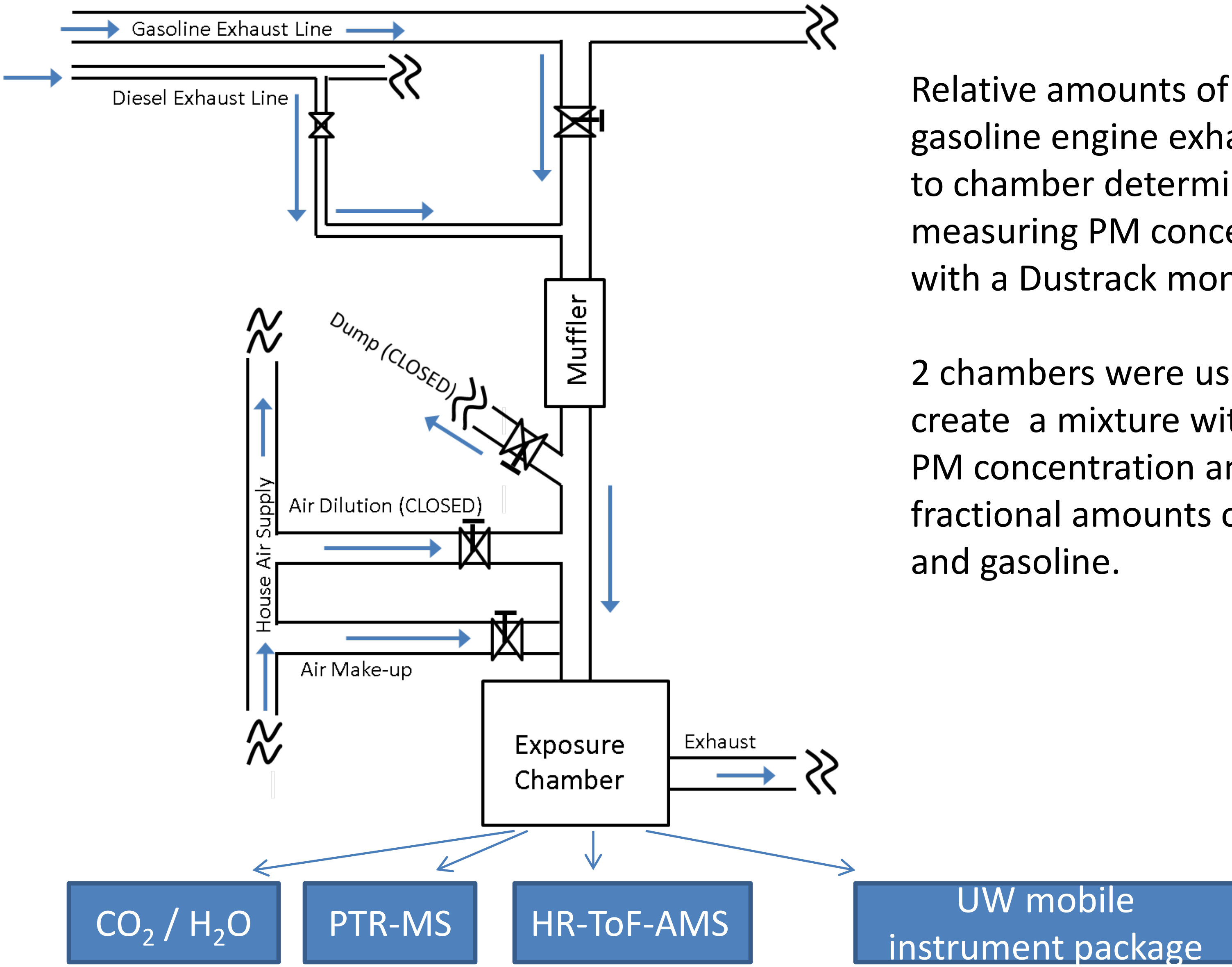
**Experimental Matrix** – many combinations of diesel / gasoline engine exhaust mixtures at different engine loads and total PM concentrations

| Engine Loading Condition | Gas | Diesel |
|---|---|---|
| Typical (average) | Throttle (11%)<br>1123 RPM | 4.5 kW |
| Low | Throttle (1%)<br>600 RPM | 1.5 kW |
| Medium | Throttle (6 %)<br>857 RPM | 3.5 kW |
| High | Throttle (27 %)<br>1922 RPM | 5.5 kW |

| Particle Loading Condition | Gas (ug/m$^3$) | Diesel (ug/m$^3$) |
|---|---|---|
| Low | < 10 | < 190 |
| Medium | 10 - 35 | 190- 310 |
| High | > 35 | > 310 |

** currently ranges are arbitrarily set

# Flow schematic of exposure chamber plumbing.




Relative amounts of diesel / gasoline engine exhaust added to chamber determined by measuring PM concentrations with a Dustrack monitor.

2 chambers were used to create a mixture with varying PM concentration and fractional amounts of diesel and gasoline.

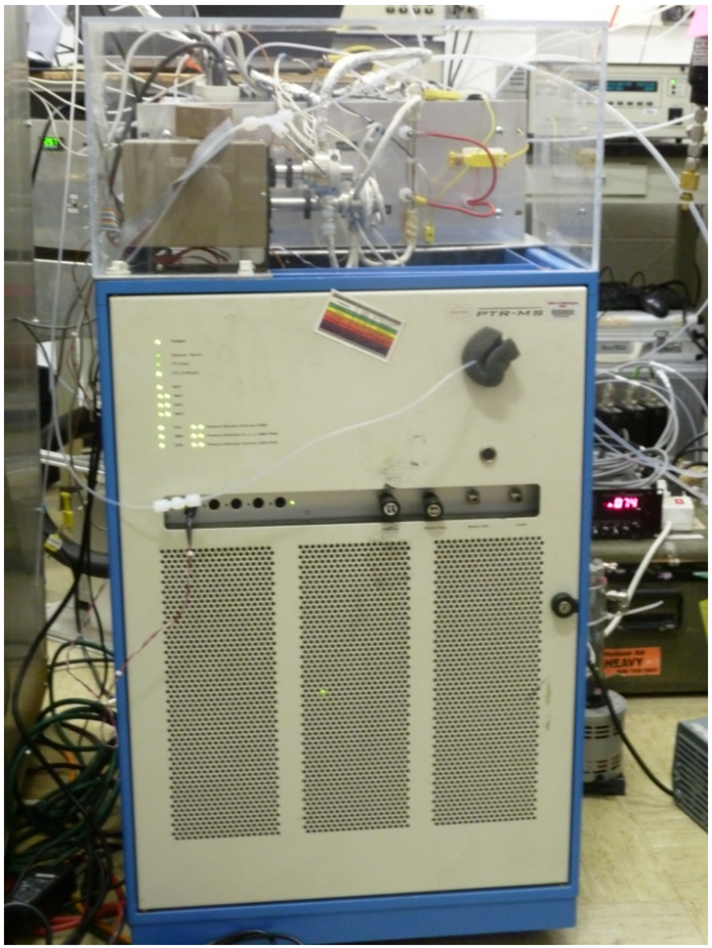
| Test Name | Gas (ug/m$^3$) | Diesel (ug/m$^3$) | Particle Gas : Diesel Loading Type | Engine Load Type Gasoline : Diesel |
|---|---|---|---|---|
| Test04 | 0 | 292 | None : Medium 04, 16 | Ø : TYP |
| Test05 | 12 | 370 | Medium : High 05, 15, 24 | TYP : TYP |
| Test06 | 30 | 0 | High : None ** | TYP : Ø |
| Test07 | 50 | 73 | High : Low 07, 17 | TYP : TYP |
| Test08 | 3 | 4 | Low: Low 08, 18 | TYP : TYP |
| Test09 | 0 | 8 | None: Low 09, 13, 19 | Ø : TYP |
| Test10 | 20 | 0 | Medium : None 10, 26 | TYP : Ø |
| Test11 | 22 | 10 | Medium : Low 11, 22 | TYP : TYP |
| Test12 | 22 | 202 | Medium : Medium 12, 20 | TYP : TYP |
| Test13 | 0 | 34 | None : Low | Ø : TYP |
| Test15 | 30 | 504 | Medium : High | HIGH : LOW |
| Test16 | 0 | 288 | None : Medium | HIGH : LOW |
| Test17 | 45 | 16 | High : Low | HIGH : LOW |
| Test18 | 4 | 114 | Low : Low | LOW : HIGH |
| Test19 | 0 | 72 | None : Low | Ø : HIGH |
| Test20 | 33 | 304 | Medium : Medium | LOW : HIGH |
| Test21 | 42 | 236 | High : Medium ** | HIGH : HIGH |
| Test22 | 34 | 52 | Medium : Low | HIGH : HIGH |
| Test23 | 11 | 0 | Low : None ** | HIGH : Ø |
| Test24 | 35 | 409 | Median : High | HIGH : HIGH |
| Test25 | 10 | 269 | Low: Medium ** | HIGH : HIGH |
| Test26 | 24 | 0 | Medium : None | HIGH : Ø |

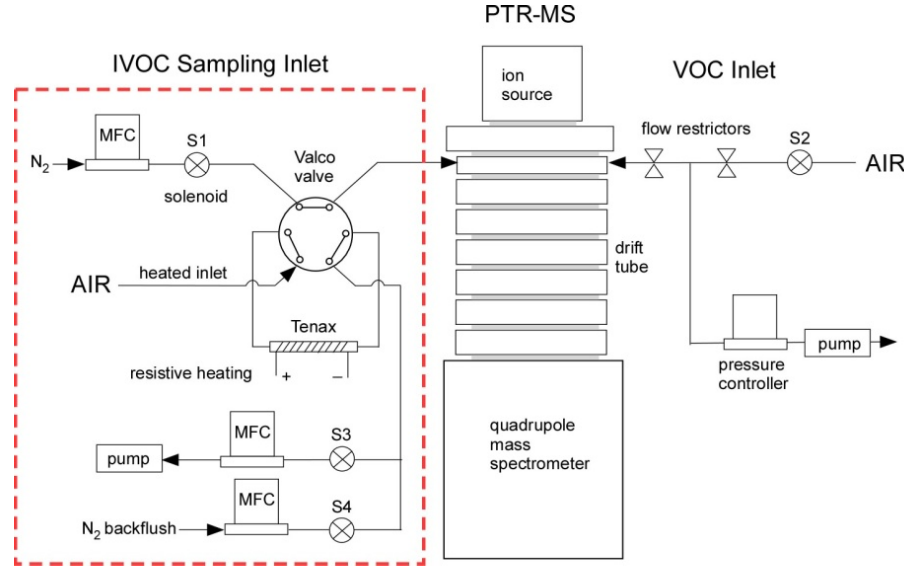
# Exposure Chamber Test Matrix

- 12 Gasoline : Diesel *particle load combinations*
- 4 Gasoline : Diesel *engine load combinations*
- 22 tests with AMS data

| Gasoline Particle Load | Diesel Particle Load | Test Run Engine Load |
|---|---|---|
| High | None | 06 T : Ø |
| | Low | 07 T : T 17 H : L |
| | Medium | 21 H : H |
| Median | None | 10 T : Ø 26 H : Ø |
| | Low | 11 T : T 22 H : H |
| | Medium | 12 T : T 20 L : H |
| | High | 05 T : T 15 H : L 24 H : H |
| Low | None | 23 H : Ø |
| | Low | 08 T : T 18 L : H |
| | Medium | 25 H : H |
| None | Low | 09 Ø : T 13 Ø : T 19 Ø : H |
| | Medium | 04 Ø : T 16 Ø : L |

# VOC Measurements
by Proton Transfer Reaction Mass Spectrometer




**Measurement principle**

$$\mathbf{H_3O^+ + R \rightarrow RH^+ + H_2O}$$

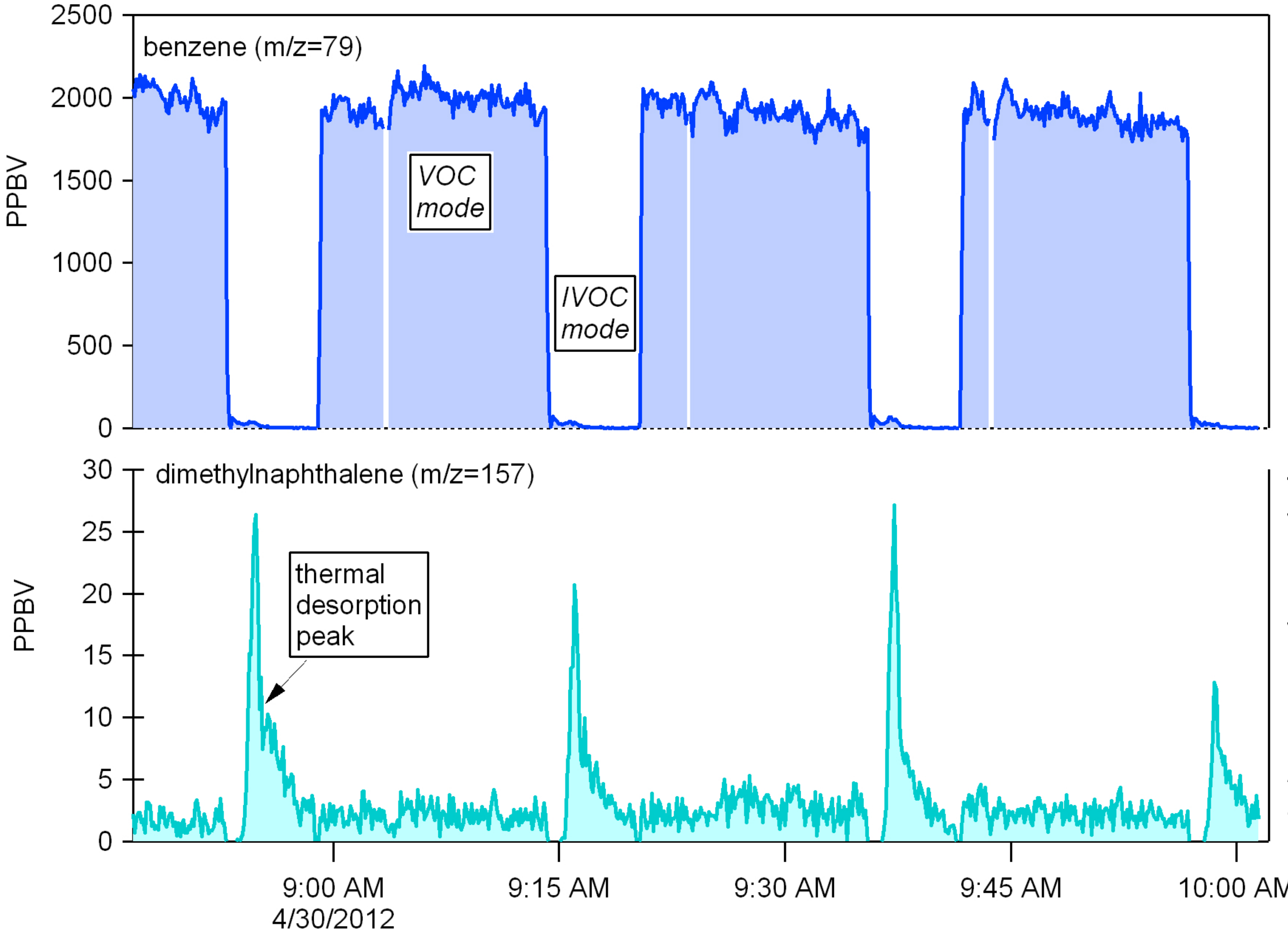
multiple ion monitoring: measured **59** organic ions over mass range **m/z=31** to **m/z=191**.

Two sampling modes, alternate between

1. VOC Mode:
   Formaldehyde, Acetaldehyde
   BTEX compounds, others …
2. IVOC mode:
   *thermal desorption based sampling for heavier organics emitted in diesel engine exhaust.*
   *long chain alkanes , polycyclic aromatics*

**Gasoline Engine Exhaust – April 30, Test 14**
**Chamber #4**

**LRRI: 42 ug/m³**
**Low engine load**



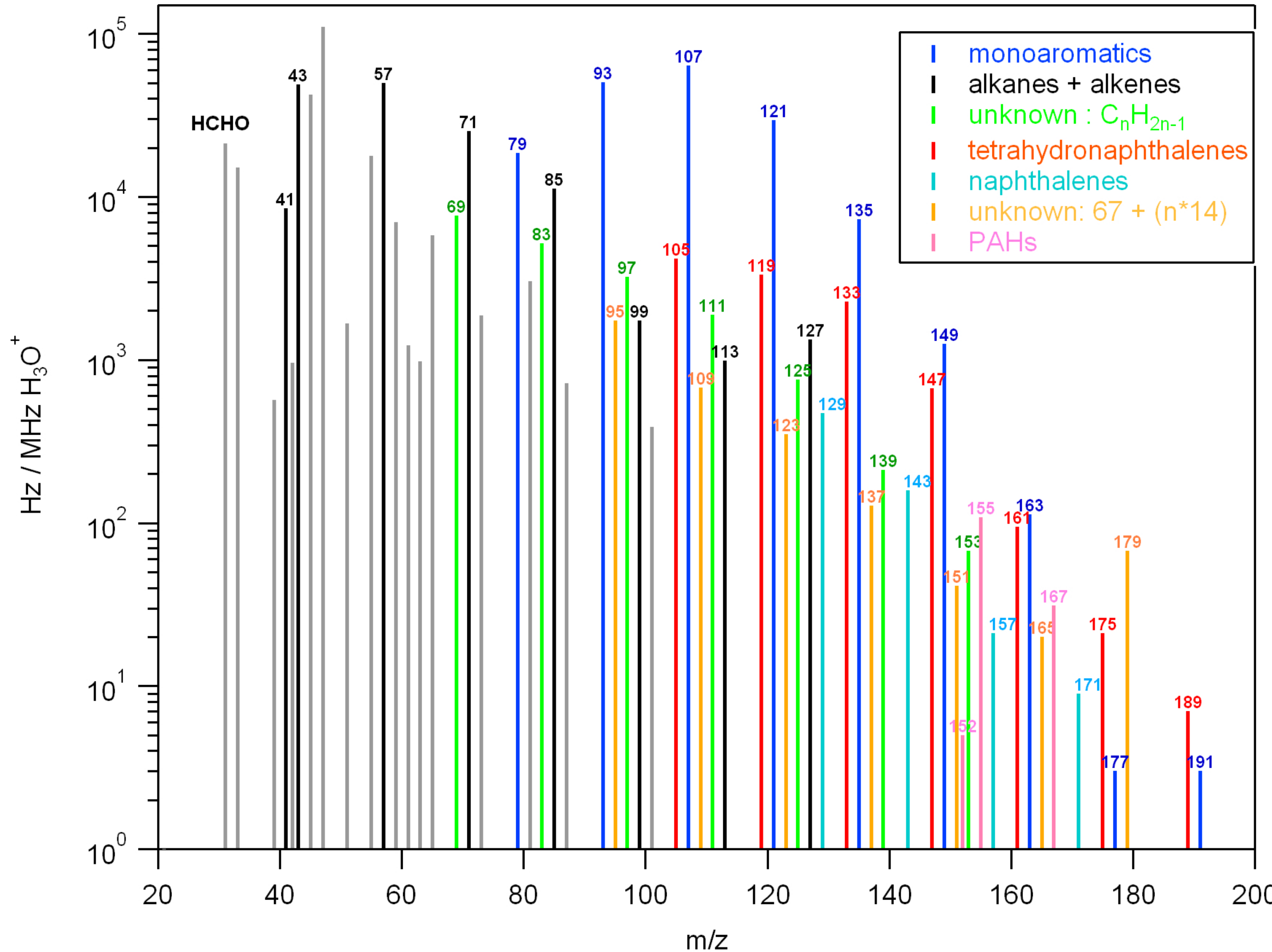

**Pre-purge trap temperature varied to discriminate against more volatile components**

***This mode measures diesel alkanes***

## Average Ion Signal Abundance in Gasoline Engine Exhaust – April 30, Test 14

*VOC mode sampling*

**LRRI: 42 ug/m$^3$**
**Low engine load**




**m107 :**
**C2-alkylbenzenes**
**8 ppmv**

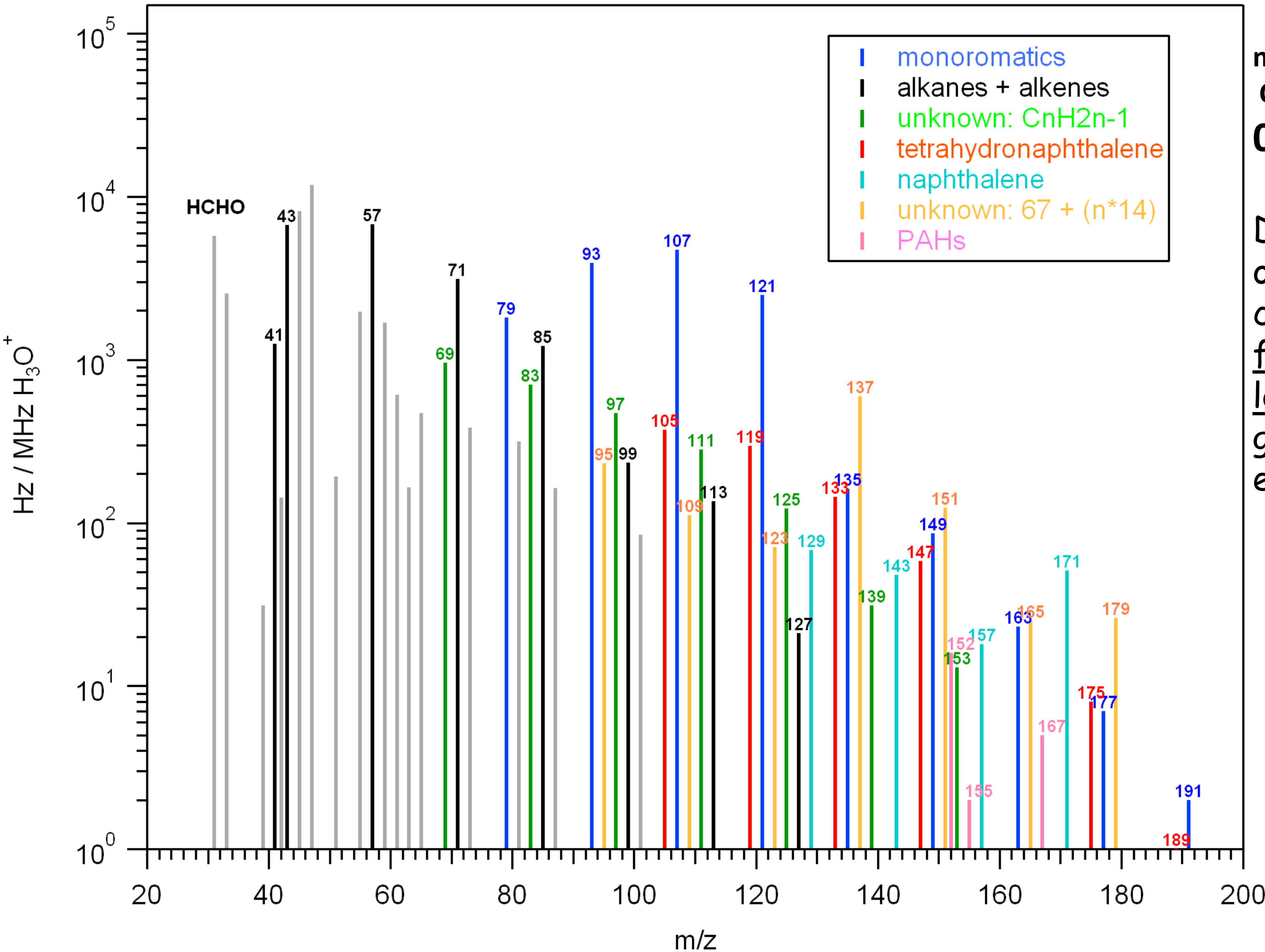
PTR-MS Insensitive to low MW alkanes < $C_7$ found in gasoline exhaust.

monoaromatic ions dominate mass spectrum

## Average Ion Signal Abundance in Diesel Engine Exhaust – April 30 test

**LRRI: 288 ug/m³**
**Low engine load**

*VOC mode sampling*

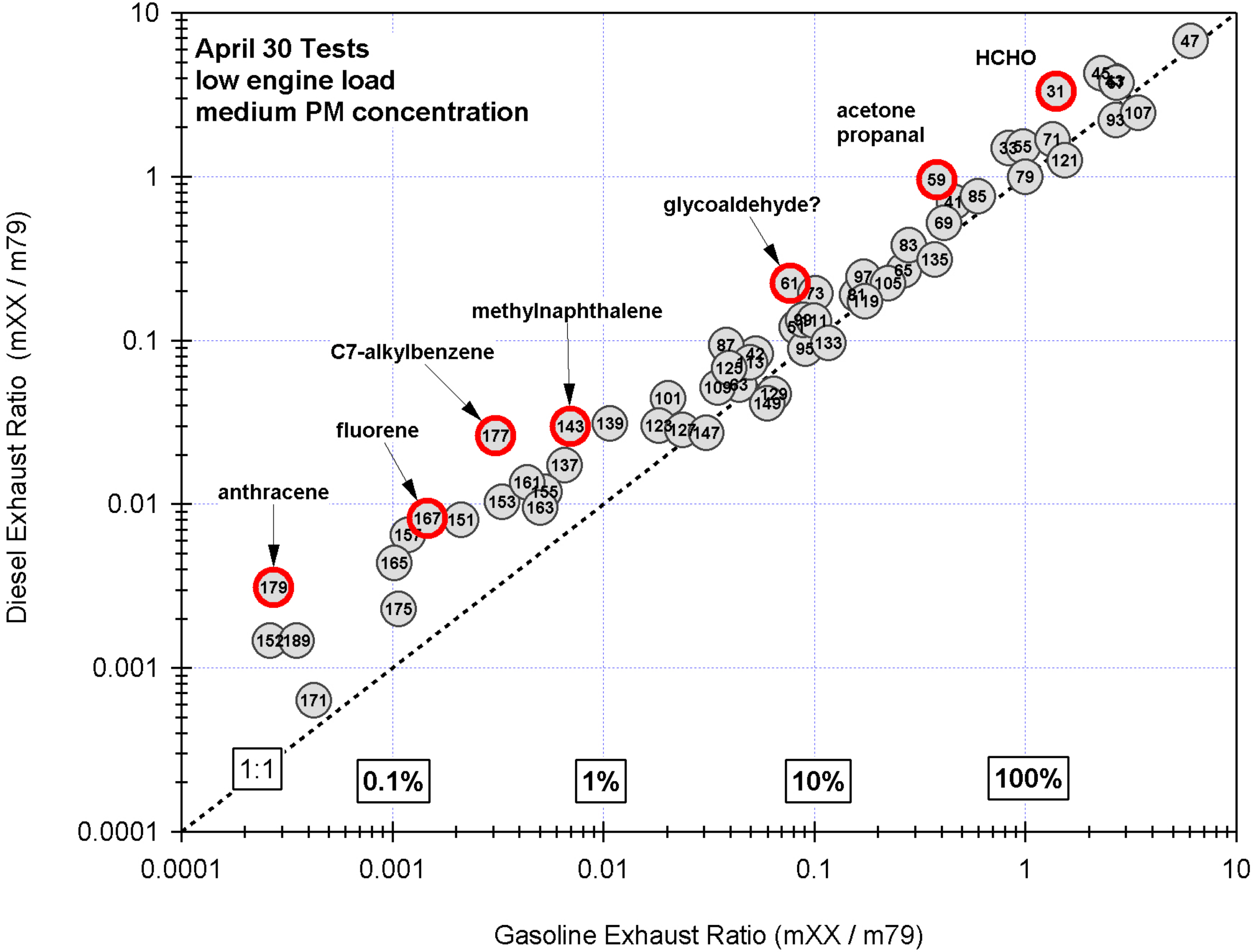



**m107 :**
**C2-alkylbenzenes**
**0.7 ppmv**

Diesel exhaust organic gas concentration factor of 10 lower than in gasoline exhaust

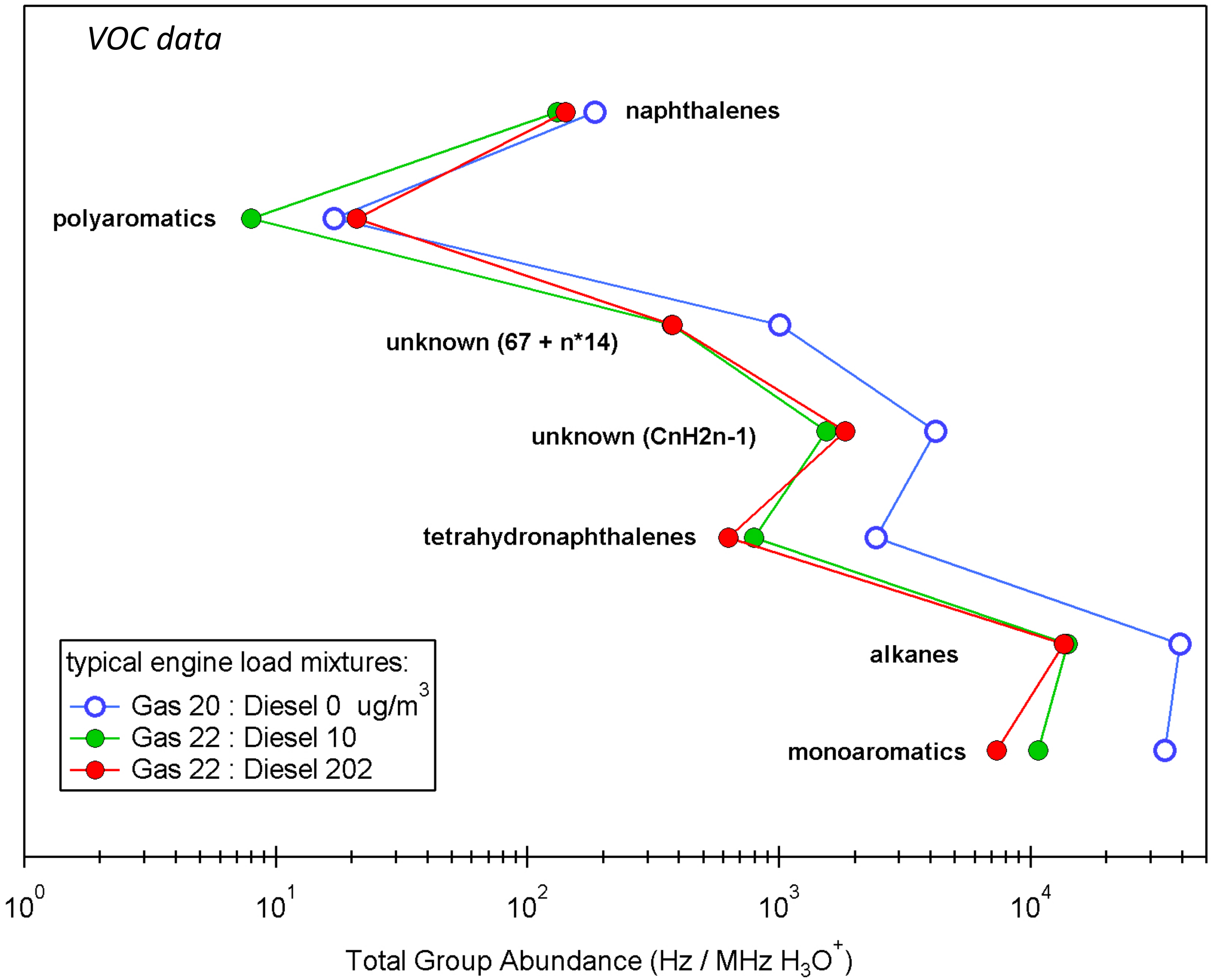
## Compound Abundance Relative to Benzene: Diesel vs. Gasoline

*Hard to distinguish between exhaust composition except at higher MW compounds*



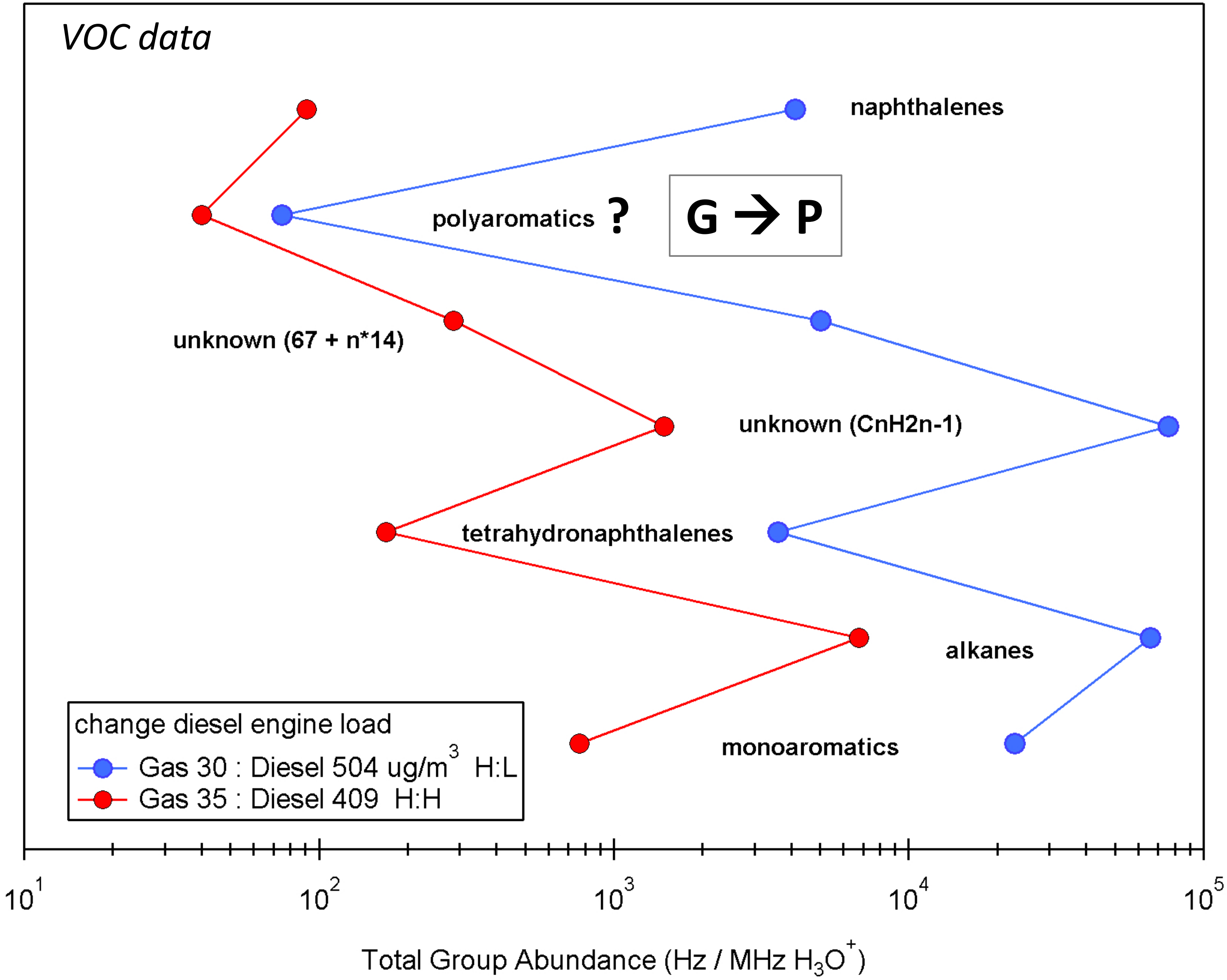
# Impact of increasing the fraction of diesel exhaust in the mixture

*PM comes from diesel engine, organic gases from the gasoline engine*

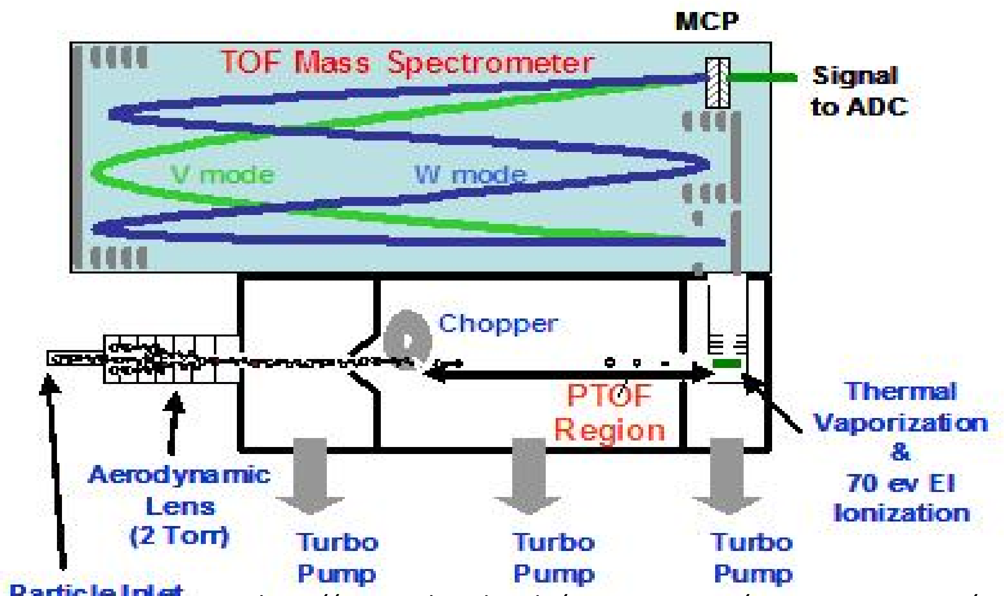


# Impact of increasing diesel engine load keeping mixture PM concentration constant

*Factor of 10-50 increase except for PAH*



# WSU High Resolution Aerosol Mass Spectrometer

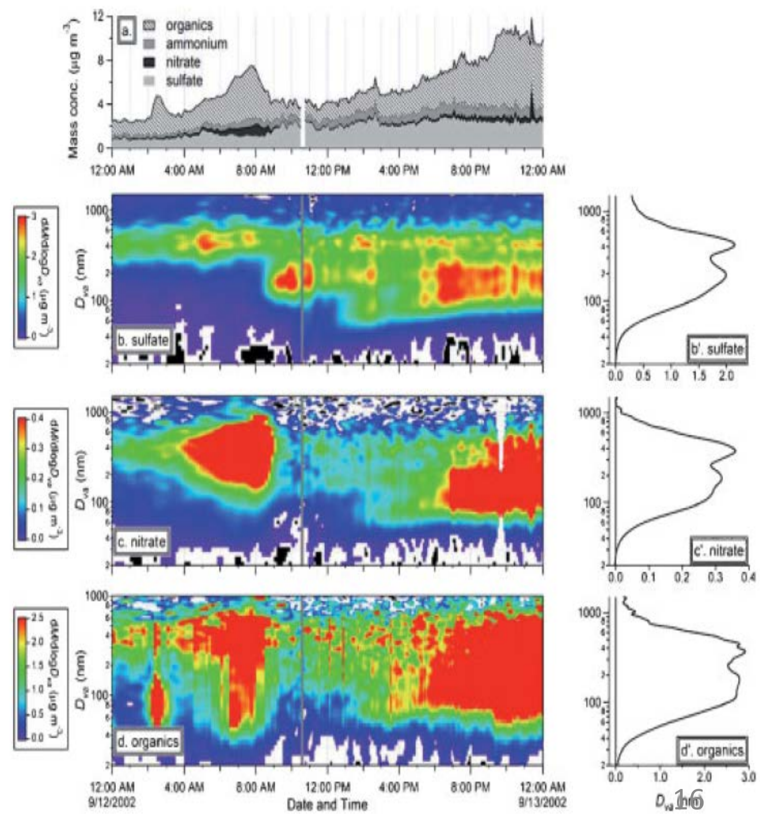



*http://cires.colorado.edu/jimenez-group/ToFAMSResources/*

Measurement principle:

- Particles 50 < *Dp* < 1000 nm are efficiently concentrated by an aerodynamic lens. **$PM_{1.0}$**
- ‘Non-refractive’: Only material that volatizes below ~600 C is measured. (***doesn’t measure soot***)
- Complex fragmentation patterns- chemical patterns can be identified, limited organic speciation is possible(i.e PAH compounds).

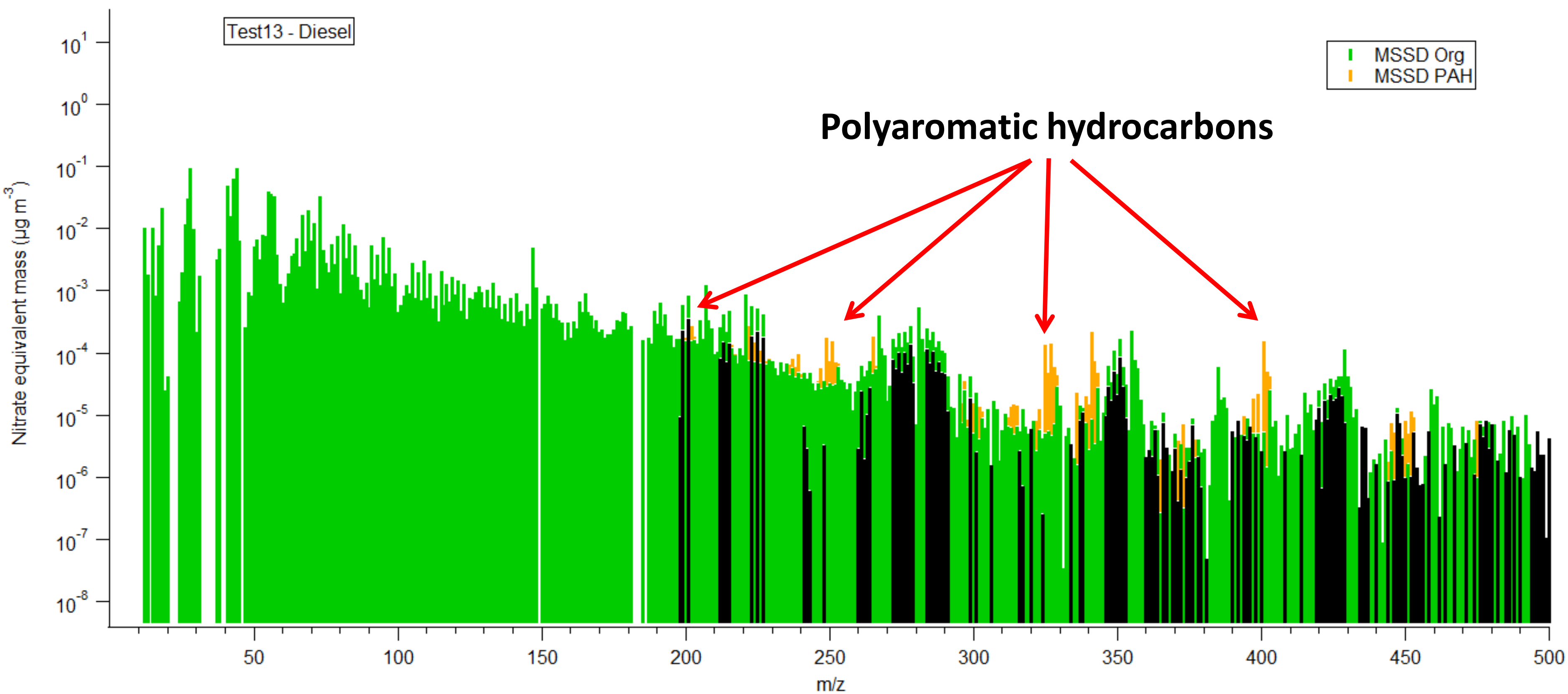
- Analysis of ambient data typically involves lumping fragments into major compositional categories:
  - o Organics, sulfate, nitrate, etc.
- Mass classification can be binned by size or integrated.
- With PMF analysis, the organics category can be further divided.



**AMS Data**

Diesel exhaust mass spectrum of particle composition

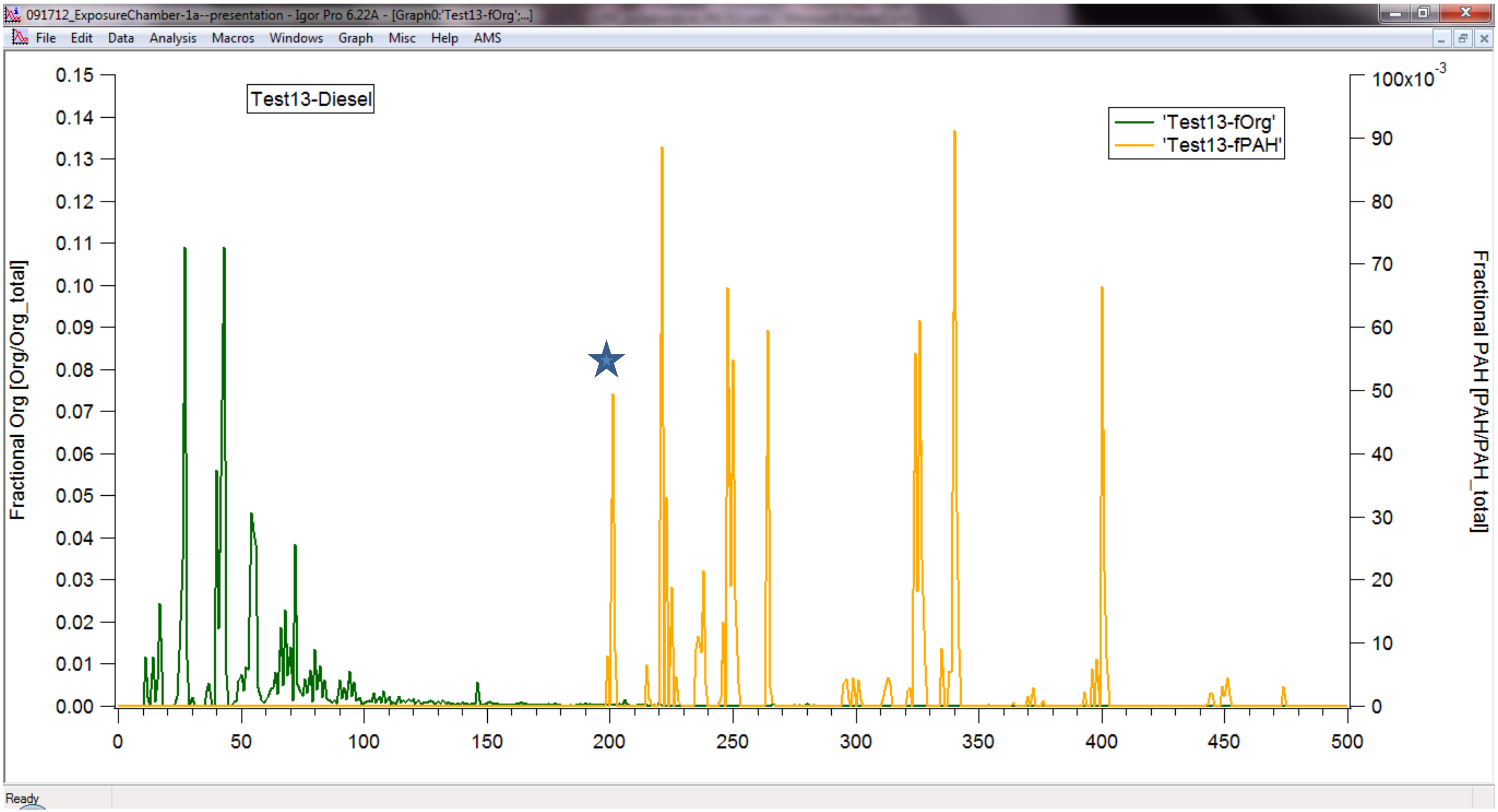
Test 13: **low PM concentration**, typical engine load



# AMS Data

Diesel exhaust fractional abundance of organic and PAH ions

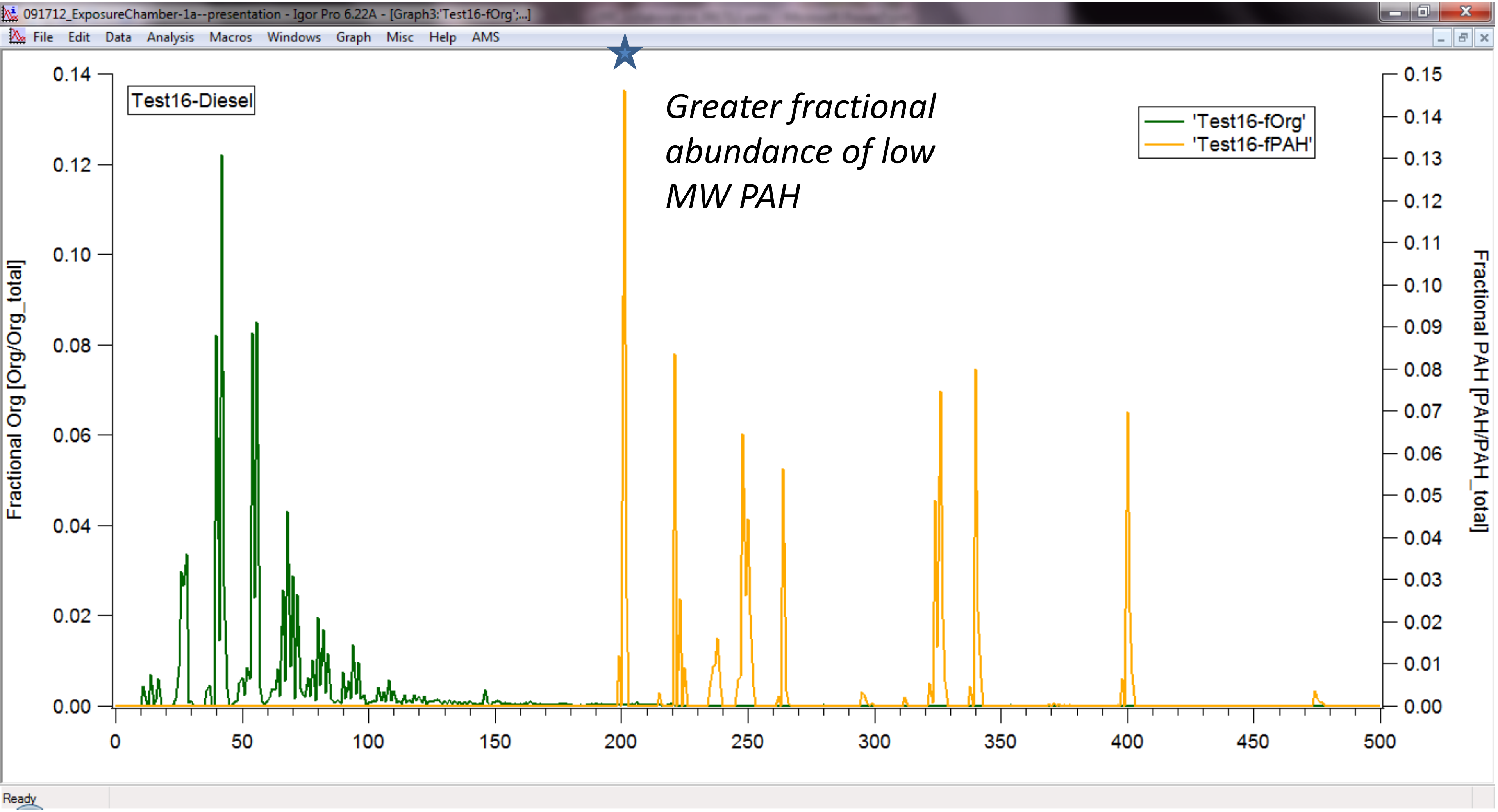
Test 13: **low PM concentration**, typical engine load



# AMS Data

<u>Diesel exhaust</u> fractional abundance of organic and PAH ions

Test 16: **medium PM concentration**, low engine load



# Comparing PM in Gasoline - Diesel Mixtures

| | Test05 | Test15 | Test24 |
|---|---|---|---|
| Filter: μg/m$^3$ | 12:370 $^{T:T}$ | 30:504 $^{H:L}$ | 35:269 $^{H:H}$ |
| AMS: μg/m$^3$ | Org: 74 (19%) | Org: 100 (19%) | Org: 130 (43%) |
| AMS: μg/m$^3$ | PAH: 0.085 | PAH: 0.14 | PAH: 0.11 |

→ **AMS measured <u>lower</u> organic mass for Test 15 (high PM) than Test 24 (medium PM).**

→ **indicates greater fraction of PM mass is soot at lower engine loads.**

# Summary / Status

1) VOC and IVOC data are being analyzed and QA / QC'd

2) AMS data has been worked up and calibration issue being sorted out (mass mode vs single particle mode)

3) Identifying lower molecular weight PAH compounds in AMS data likely possible given good signal-to-noise. This will aid quantification of G→P issue.

4) Just beginning to compare VOC / IVOC and AMS data.

5) Data will be examined to find evidence for gas-particle partitioning effects at high PM concentrations in the mixtures → do high concentration exposures accurately mimic ambient organic aerosol ?

# UW Center for Clean Air Research

# Project 2: Simulated Roadway Exposure Atmospheres for Laboratory Animal and Human Studies

Project 2: McDonald, Larson, Lund

www.LRRI.org

SCHOOL OF PUBLIC HEALTH
UNIVERSITY of WASHINGTON

THE UNIVERSITY of NEW MEXICO

WASHINGTON STATE UNIVERSITY

Lovelace™

# Objectives

- **Simulate ambient exposures in the laboratory**
  - Bridge these exposures to ambient measurements/modeling (Project 1)
- **Compare toxicity of exposures**
  - Use these results to determine mechanisms (Project 3) and to define priorities and atmospheres for human exposures (Project 4)

# Conceptual Paradigm: Exposures

**Background** + **Traffic Emissions**

$O_3$, $(NH_4)_2SO_4$, $NH_4NO_3$, VOC, NI, V

Tailpipe,
Evaporative,
Tire & brake,
Resuspended Dust

100 m 500 m 1 km ?? → **Exposures**

Distance From Roadway

**Chemical Transformation**

$OH^-$,
Sunlight

**Aging**

Nucleation,
Agglomeration

# Specific Aims

- Aim 1: Develop and characterize laboratory-generated exposure atmospheres simulating the key components of near-roadway exposures, including transformed emissions and co-exposures.
- Aim 2: Conduct inhalation exposures of laboratory animals.
- Aim 3: Conduct inhalation exposures of human subjects.

# Key *Initial* Research Questions

- Does agglomeration and physical transformation of particulate motor vehicle emissions alter their toxicity (does size matter)?
- Does chemical transformation, and formation of secondary organic aerosol from motor vehicle emission precursors, enhance or diminish the toxicity of roadway atmospheres?
- Do ozone and other background co-pollutants alter or exacerbate the toxicity of motor vehicle emissions?
- Does road dust, a significant non-tailpipe roadway emission, confer any cardiovascular toxicity that may confound associations with tailpipe emissions?

# Recommendations from ESAC

- Include PTR-MS and AMS Technology in Characterization of Exposure Atmospheres: Extend beyond characterization of irradiation atmospheres
- Apply Some Focus to further investigation of the gas-particle relationships that have been observed
- Consider composition differences among road dust samples prior to selection of final material.
- Consider impact of NOx on irradiation chamber atmospheres

# Principle Activities Since Last ESAC

- Development of Novel Atmospheres to Further Evaluate Gas-Particle Inter-Relationships
  - MVe combinations/load differences
  - MVe – all gases
  - Mve – Nox
- Characterize MVe Performance in the Irradiation Chamber
  - Participate/contribute to workshop on atmospheric transformation approaches
- Collaborate with Project 1 to Define/Bridge Atmospheres
- Evaluate MVe physical tranformation/size feasiblility
- Further analyze database on road dust composition (decision on which to use)
- Conduct of  acute (up to 7 days) and subchronic  (50 day) inhalation studies

# Methodology-Exposures to focus on Gas-Particle Interactions

- Laboratory generated simulated atmospheres this year
  - Gasoline + Diesel
    - Physical and/or Chemical Transformation
    - -NOx
    - -Gases
    - Load combinations
  - Study design defined in Project 3. Also included/leveraged additional study animals for ancillary investigations

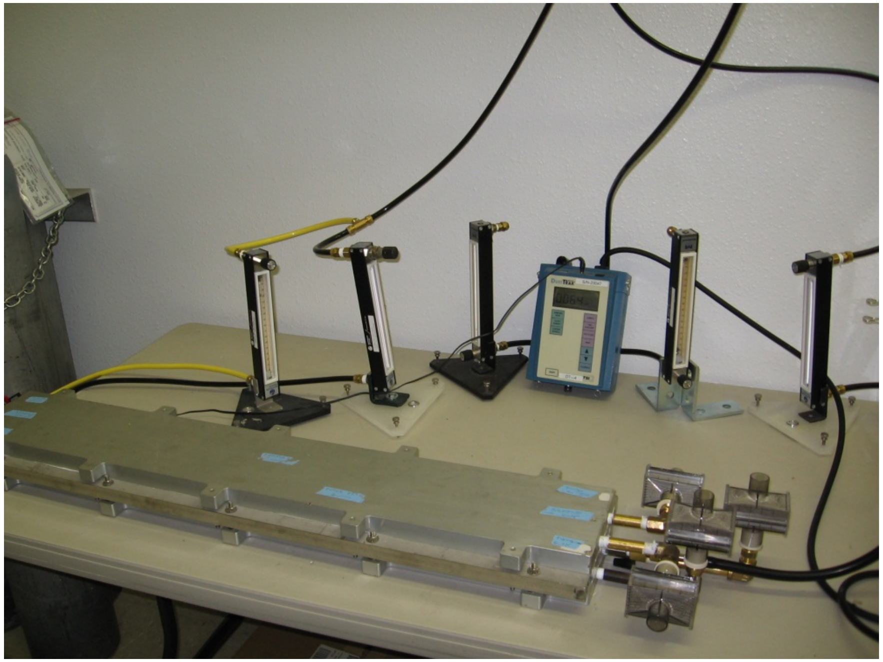
# DRI-Cobalt Oxide NOx Denuder

Cobalt oxide on firebrick substrate

# Denuders

DRI NOx Denuder

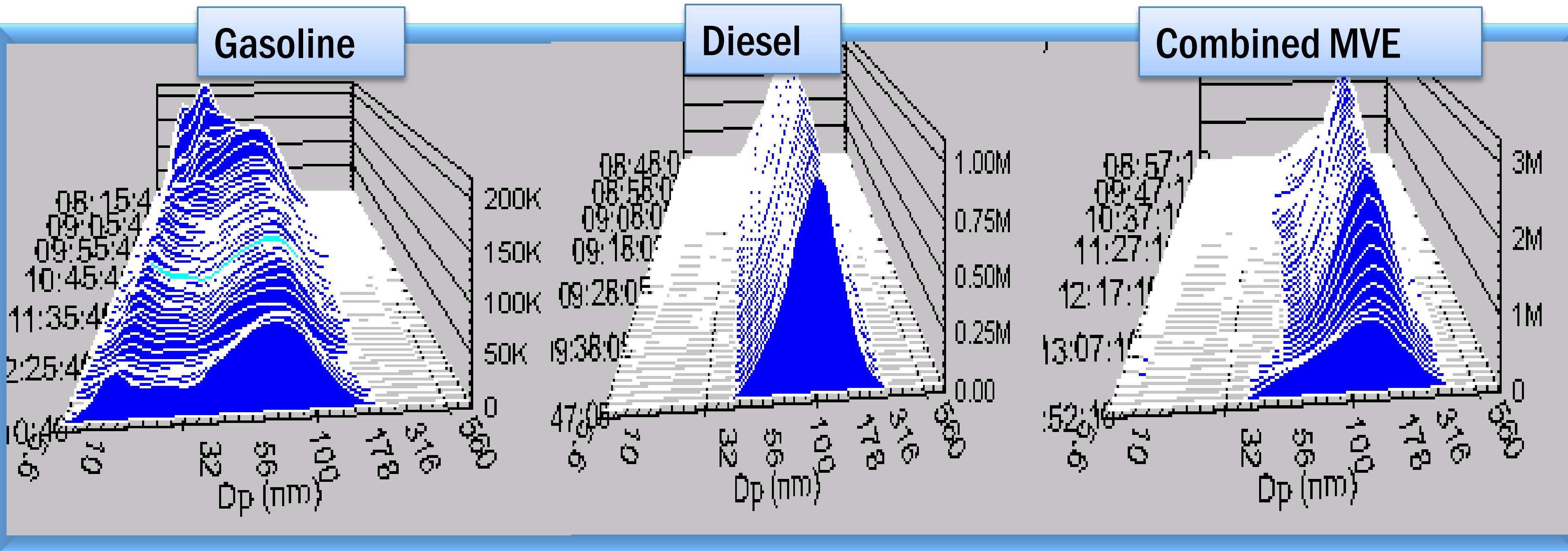
Harvard Gas Denuder



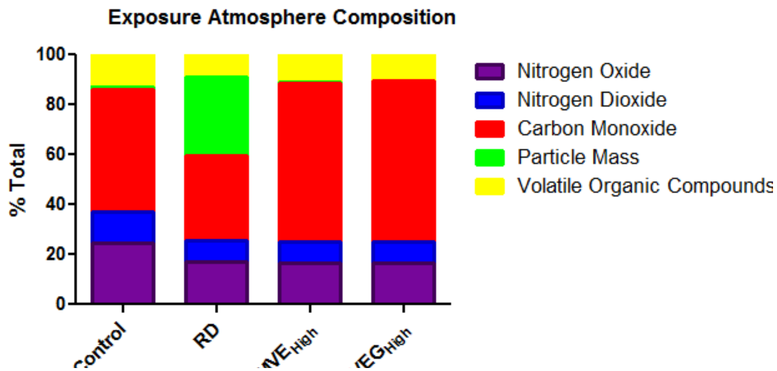
# Diesel and Gasoline Contributions

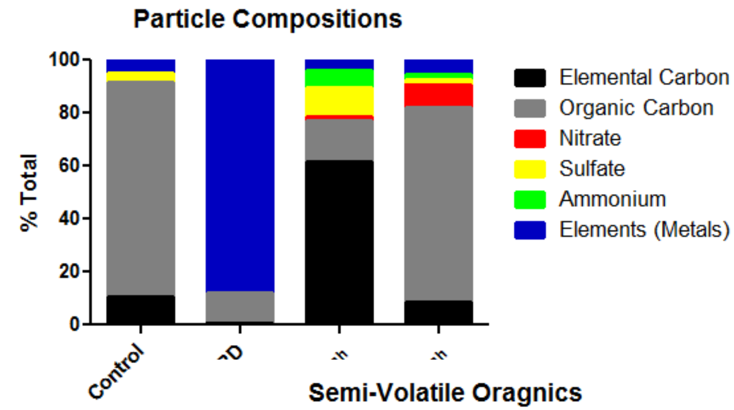
| | Diesel | Gasoline |
|---|---|---|
| Dilution factor | 10 | 10 |
| Total mass ($mg/m^3$) | 84 | 116 |
| **Particles** | | |
| Mass ($\mu g/m^3$) | 1005 | 60 |
| Number ($10^6$/cc) | 1.0 | 0.5 |
| Size (MMAD, μm) | 0.15 | 0.15 |
| %OC | 22 | 19 |
| %EC | 64 | 47 |
| %sulfate | 6 | 21 |
| %nitrate | 4 | 0.8 |
| %ammonium | 4 | 12 |
| %elements (ash) | 0.1 | 0.9 |
| **Gases & Vapors** | | |
| CO (ppm) | 30 | 80 |
| NO (ppm) | 45 | 18 |
| $NO_2$ (ppm) | 4 | 1 |
| $SO_2$ (ppm) | 0.4 | 0.6 |
| THC (ppm) | 2 | 12 |

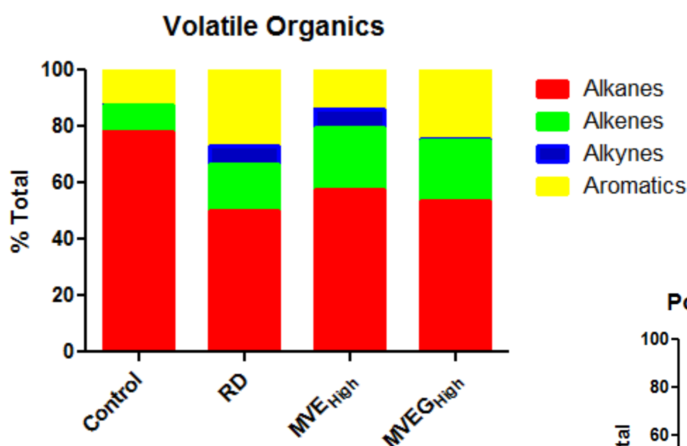
# Combining Motor Vehicle Atmospheres

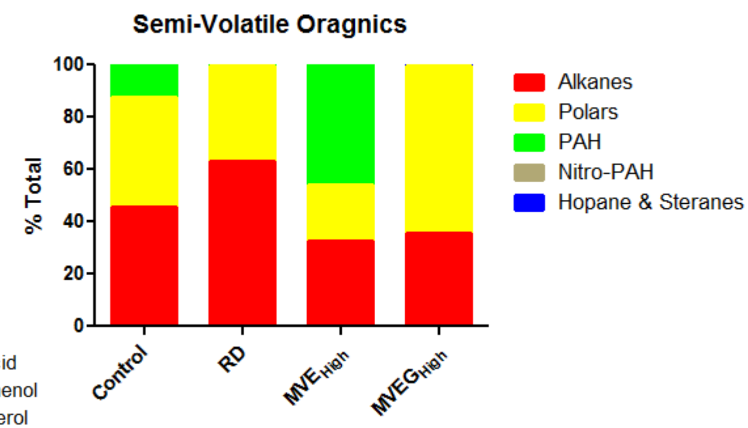


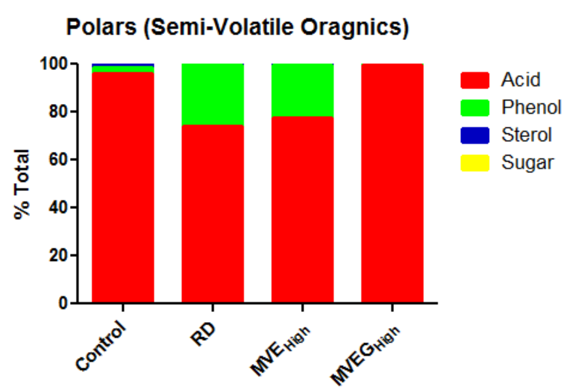
# Atmosphere Compositions



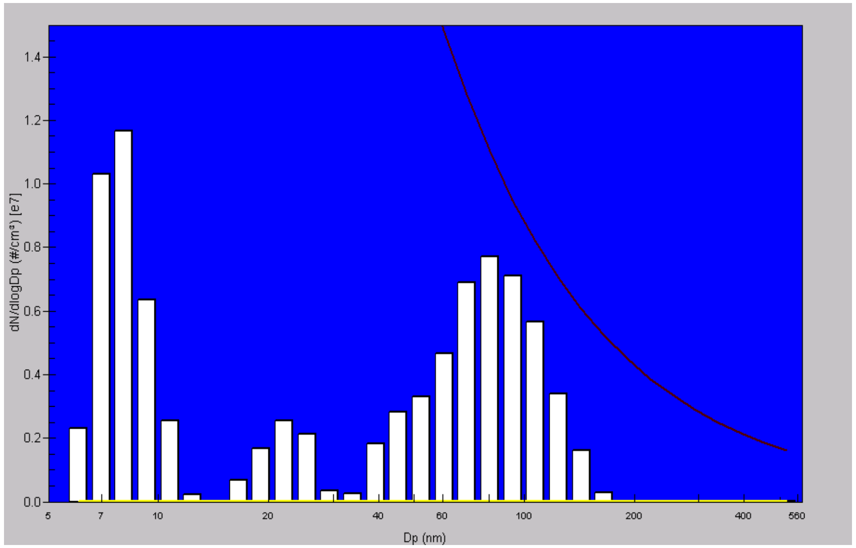



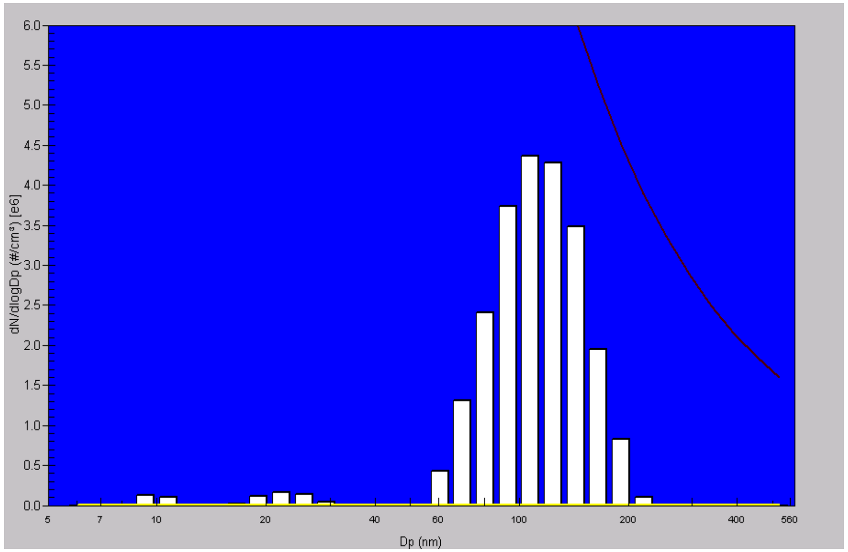



# Particle Number Size Distribution-Denuder

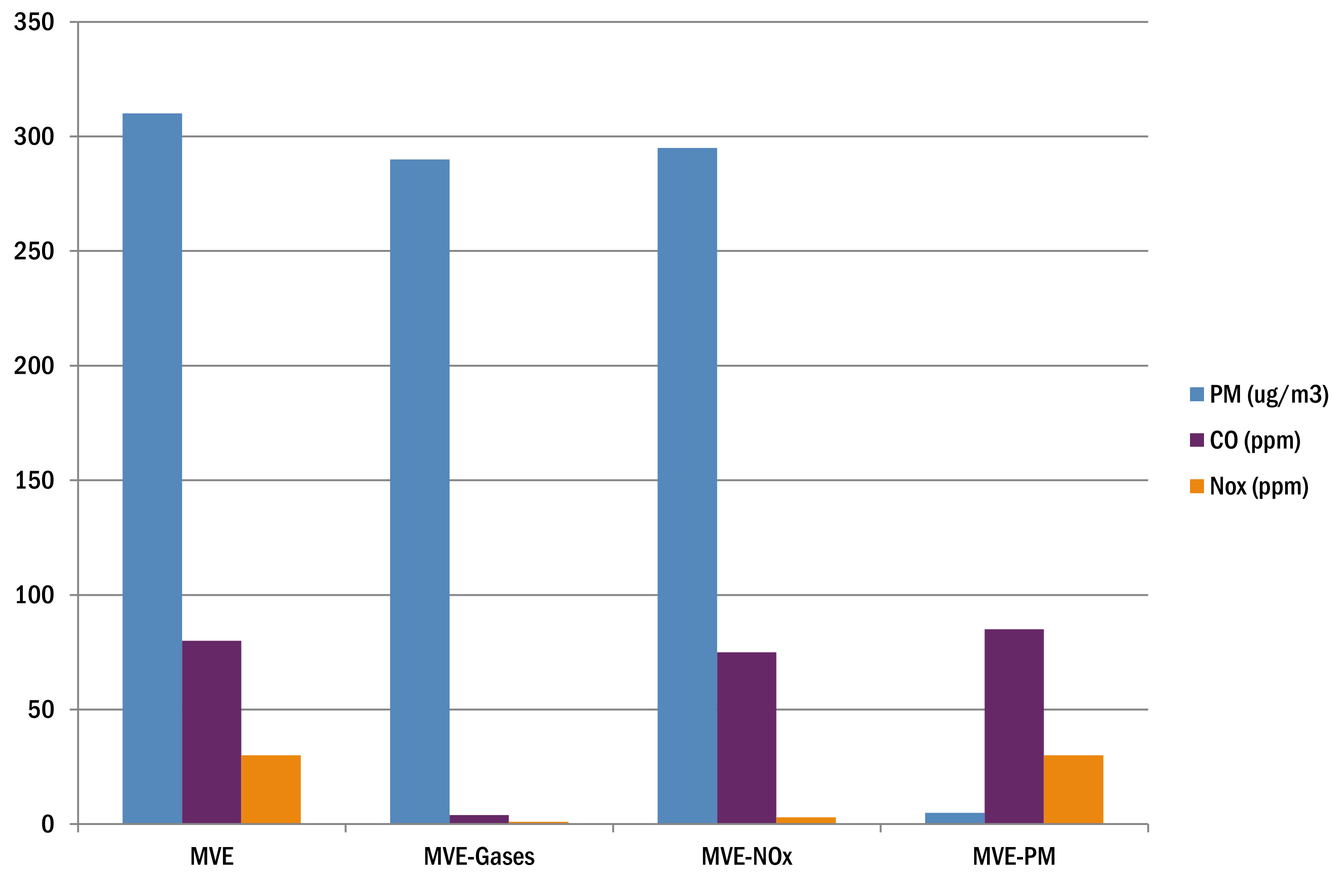



Mixed MVe




Mixed MVe Denuder

# Test Atmospheres for 50 Day Study



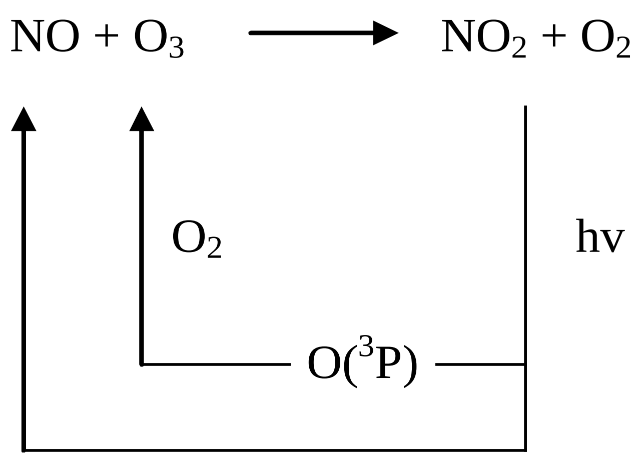

0000-15

# Snippets from Irradiation Chamber Workshop/Our Methods

- Atmospheric Transformation in Outdoor Chamber (Zielinska et al. 2007)
- Atmospheric Transformation in indoor continuous flow stir reaction chamber (McDonald et al., 2010; 2011; 2012; Campen 2010; Lund 2012)
- Simulation of atmospheric transformation products (e.g. for coal: McDonald et al., 2012)
- Collection of ambient PM and attributing SOA based on apportionment (Seagrave et al. 2010)

# Concerns – High NOx

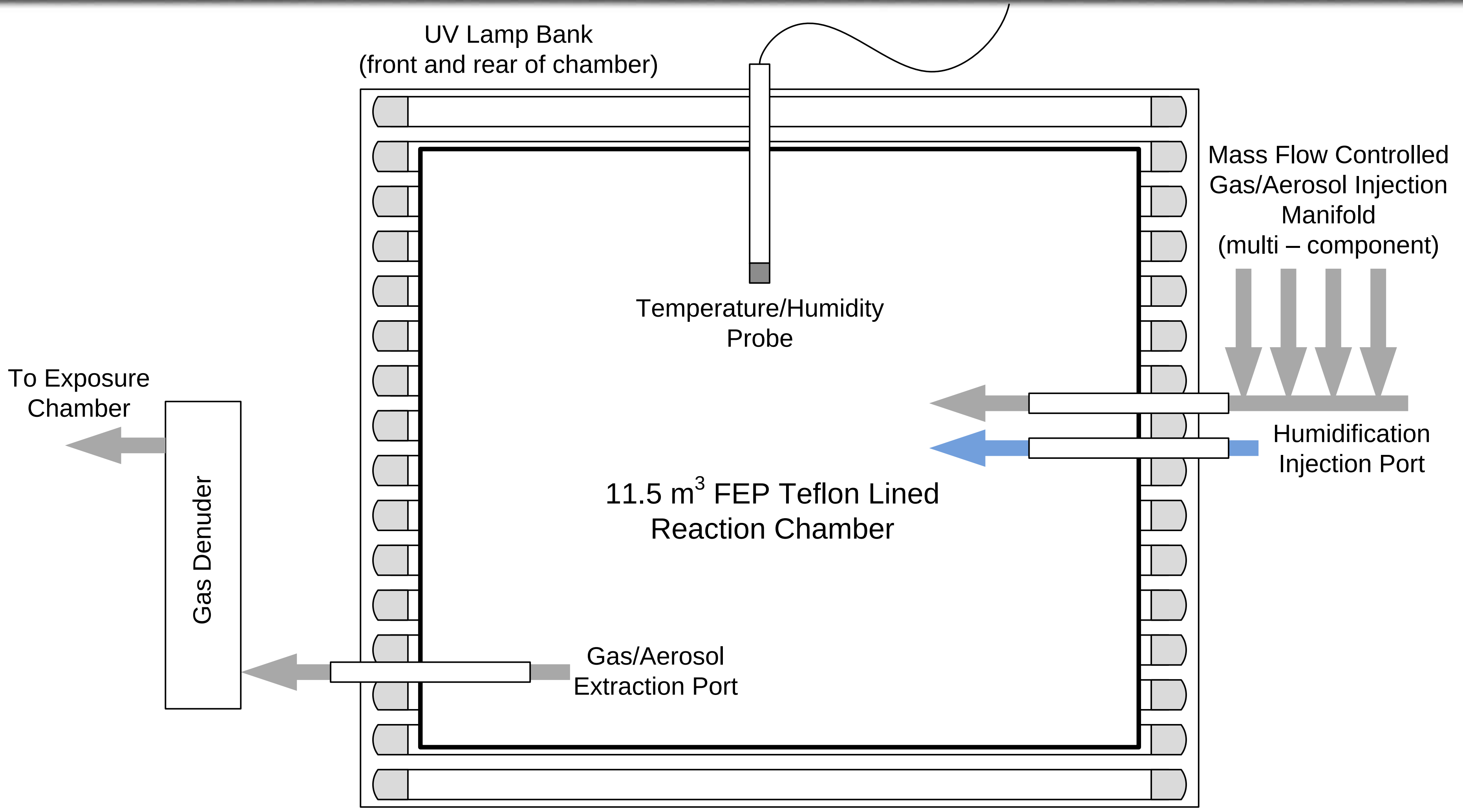
- **Modern diesel engine emits relatively high NOx (mostly NO) level (under our conditions app. 400 ppm) but low VOC and particulate matter**
- **This provides unrealistically high NOx level in the chamber and disturb the light exposure conditions (shuts down photochemical transformations of the exhaust)**



# Strengths, Limitations and Issues

- NOx Denuder:
  - Strengths
    - Reduction of NOx to more realistic NOX:Hydrocarbon ratio permits a better simulation of ambient chemistry
  - Limitations
    - Denuder not readily available/cumbersome
    - Small losses of ultrafine particles (not limited to this denuder technology)

# LRRI "Irradiation Chamber" and Exposure System

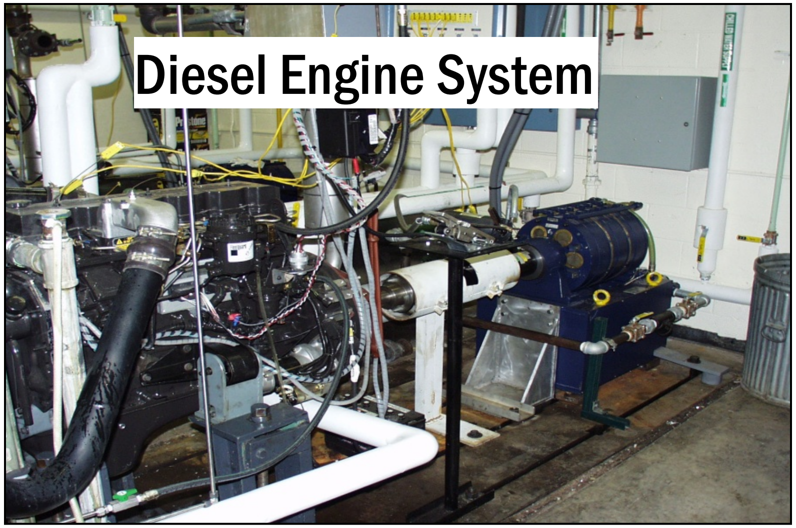


# Hardware

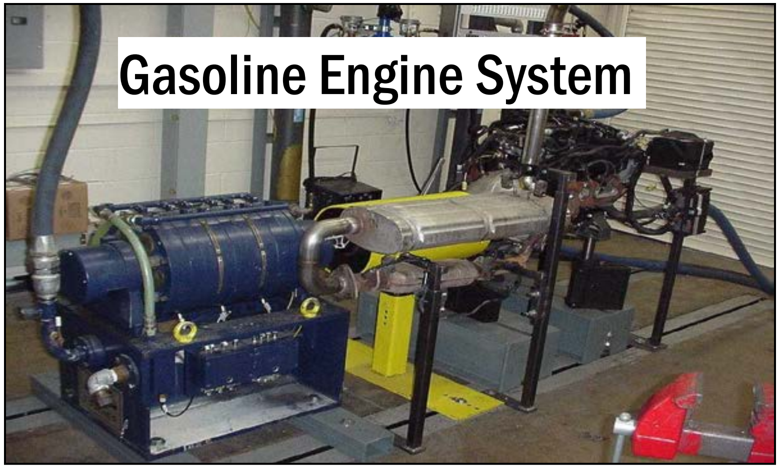
Lovelace

# Aerosol Generation Systems

Lovelace




Irradiation Chamber



# Strengths, Limitations and Issues

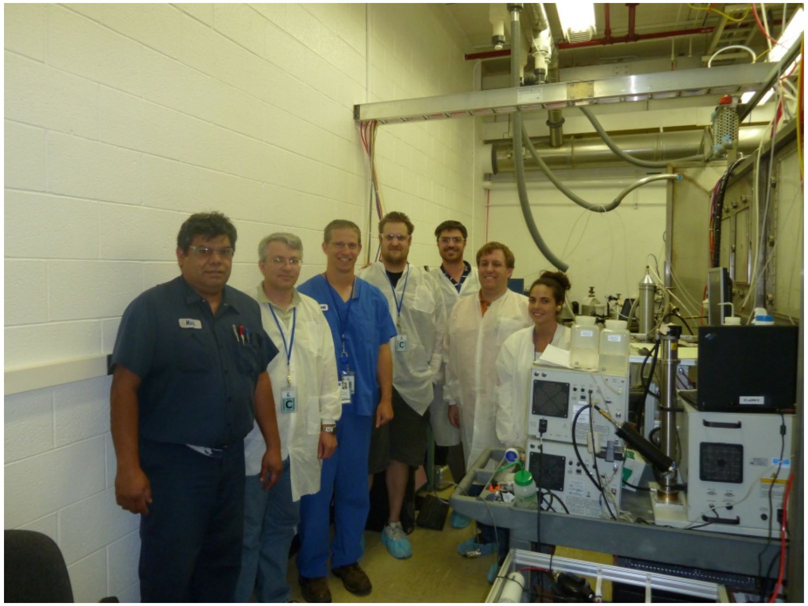
- Motor vehicle emissions:
  - Issues
    - VOC:NOx ratio is ~1:1 in the technology of emissions currently studied at LRRI. In modern technology ratio is 0.1:1 or lower
    - Target VOC:NOx ratio for 'typical' conditions and chamber work has been 10:1 (although 5:1 to 20:1 also used)
      - Impact of VOC:NOx ratio on chemistry
        - Read Johns book, chapter 5
        - Chemistry will occur in either condition: in general at low VOC:Nox levels OH is quenched by Nox and forms $HNO_3$ and less $RO_2$

# Strengths, Limitations and Issues

- Impact of VOC:NOx ratio on chemistry
    - Read Johns book, chapter 5
    - Chemistry will occur in either condition: in general at low VOC:Nox levels OH is quenched by Nox and forms $HNO_3$ and less $RO_2$
    - Low VOC:NOx, all RO2 react with NO
    - Higher VOC:NOx: RO2 radicals more abundant
- Another issue: expense of fuel in operating continuously
- Strength of LRRI system: can control gasoline/diesel contributions
    - ➢ Weakness: limited to our hardware, reactants.
    - ➢ Low SOA yield

# Data on Irradiation of Mve

# Project 1-2 Integrated Characterization Team



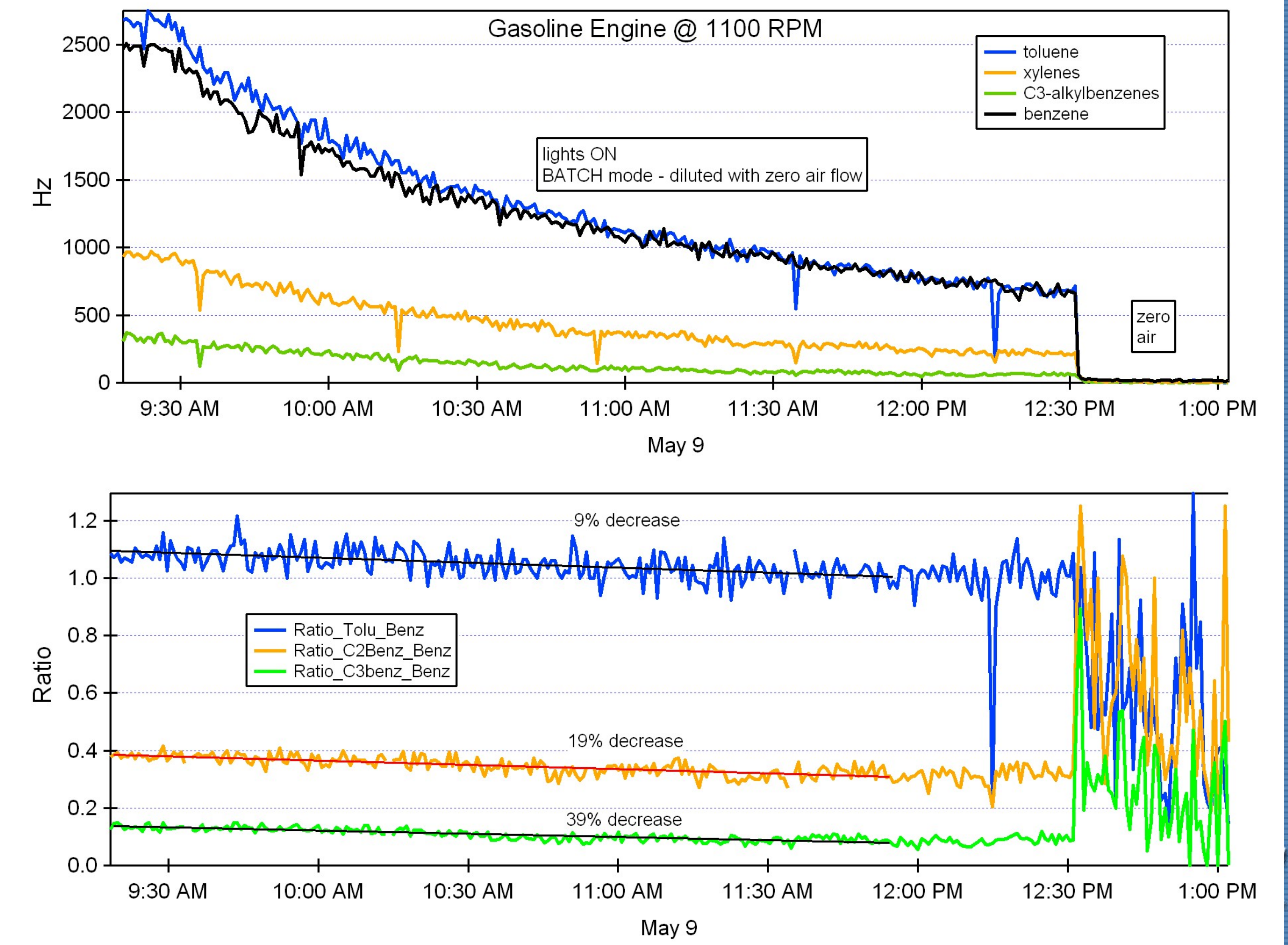
# Irradiation Chamber Batch Mode

Gasoline engine exhaust only
engine at 1100 rpm
added NO

Initial NOx ~ 400 ppbv
Initial Toluene ~ 100 ppbv

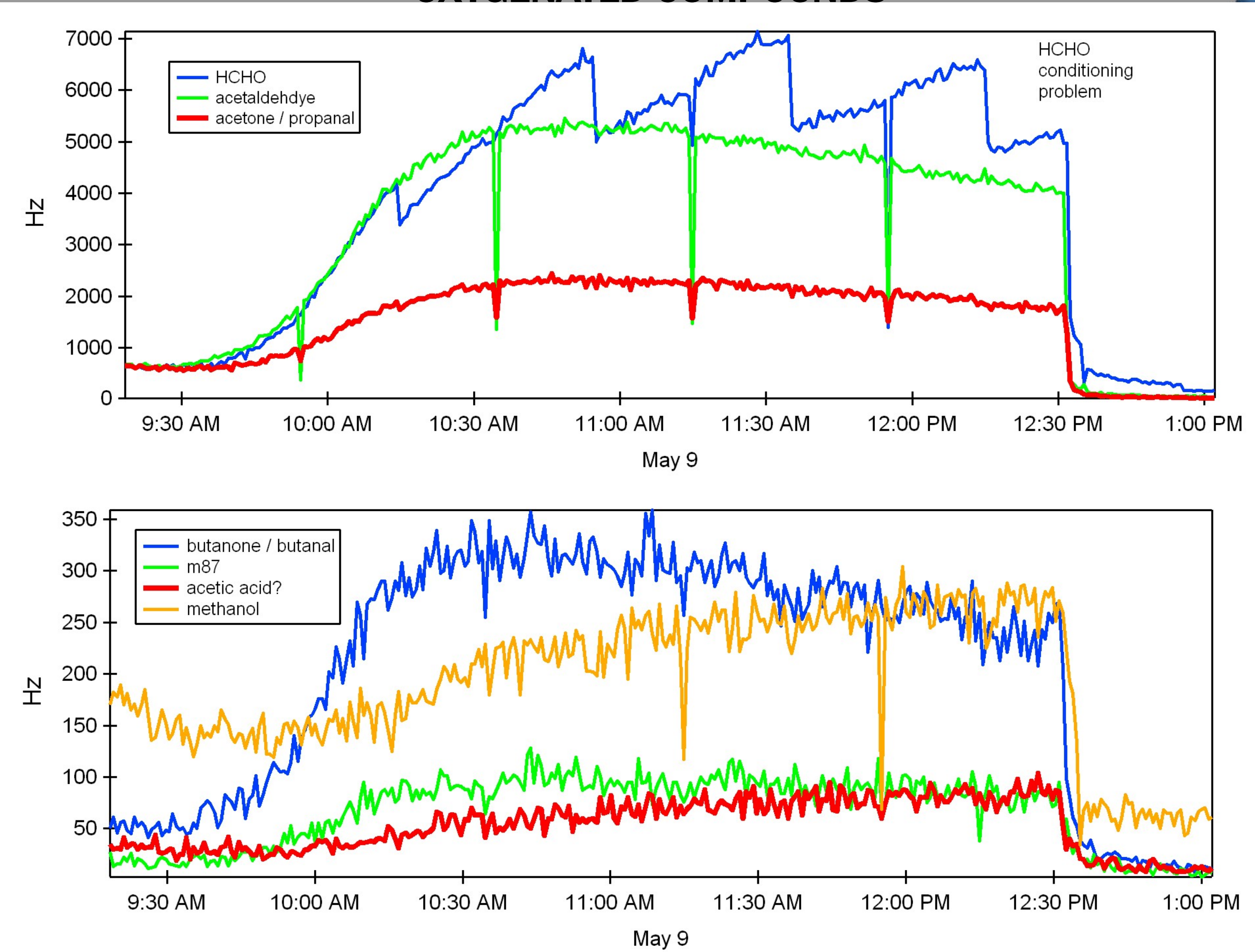
STUDIES CONDUCTED TO ASSESS SMOG CHAMBER PERFORMANCE AND BRIDGE CHARACTERIZATIONS TO PROJECT 1

# AROMATICS




**Changes in relative abundance of aromatics indicate photochemical oxidation**

# OXYGENATED COMPOUNDS

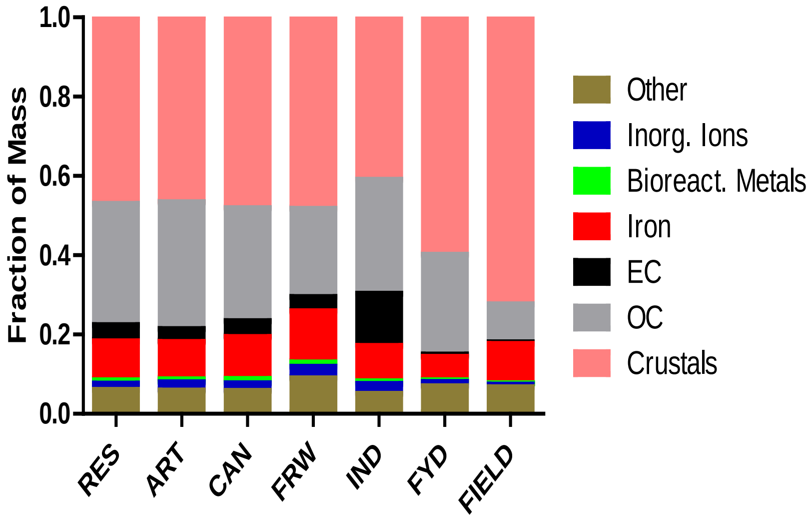


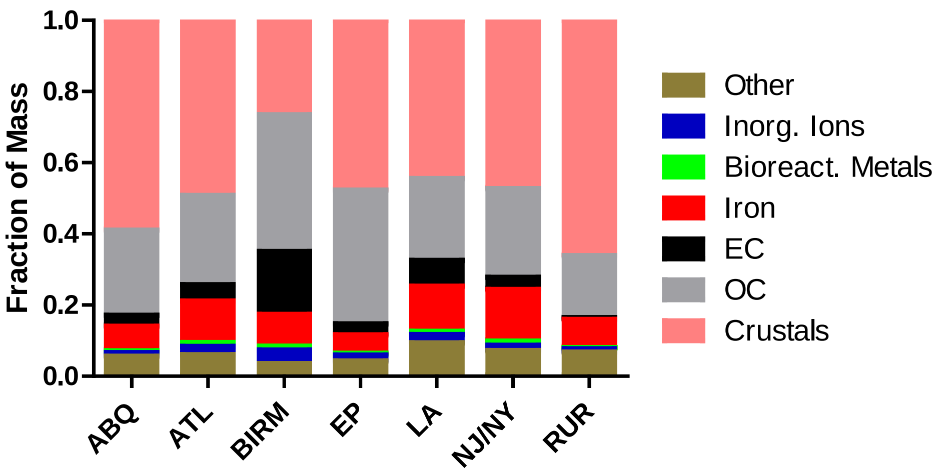

**Are m33 (methanol) & m61 (acetic acid) evidence of radical + radical products at low NO?**

# Challenges Encountered

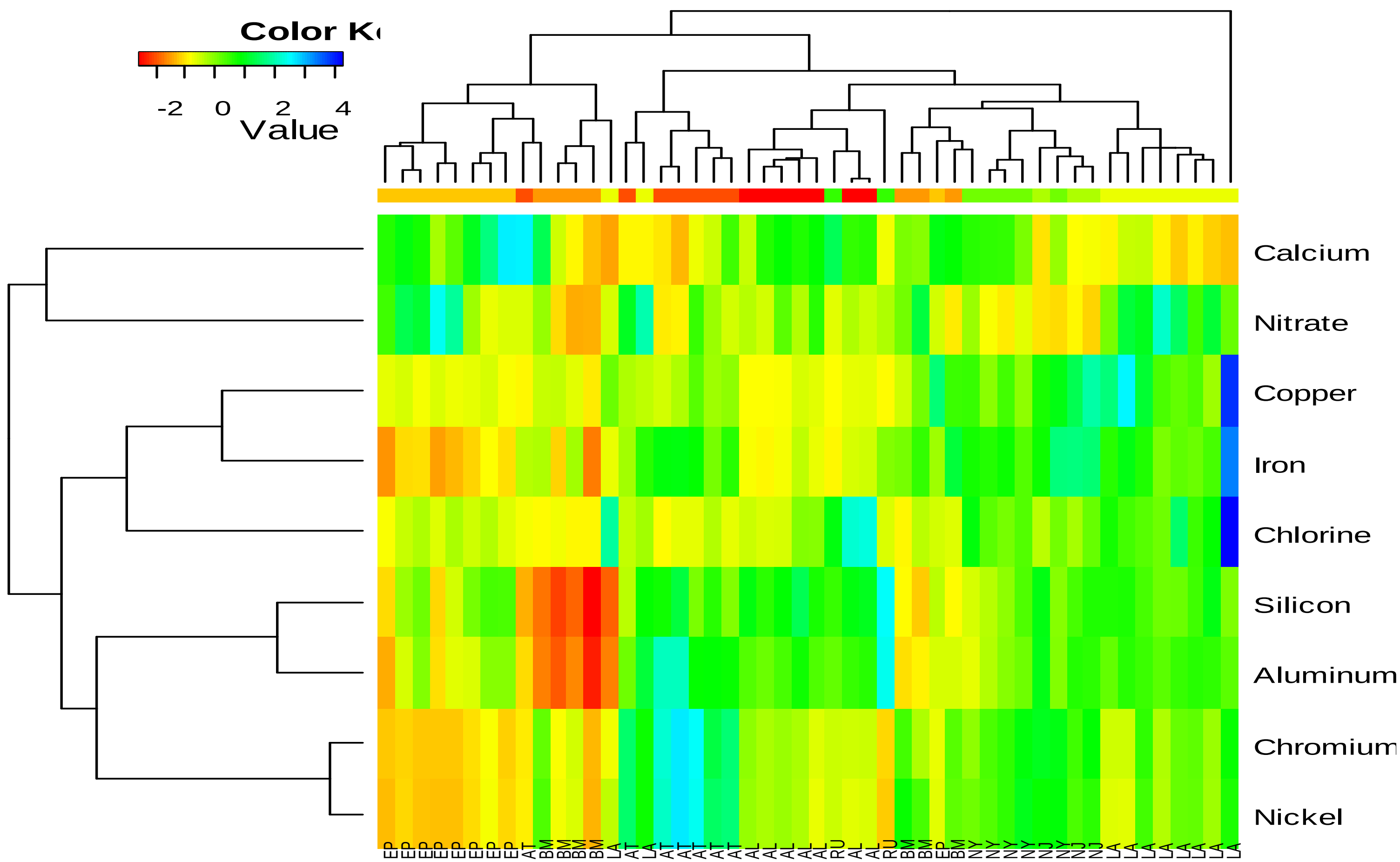
- SOA yield from gasoline engine exhuast is low; ie 10 x lower then alpha pinene atmosphere with similar precursors
- SOA yield from diesel engine exhaust is even lower
- Solution: need to add reactants to create stronger source of OH.  Current efforts focus on HONO and formaldehyde.

# Considerations on Road Dust (ESAC Recommendation)



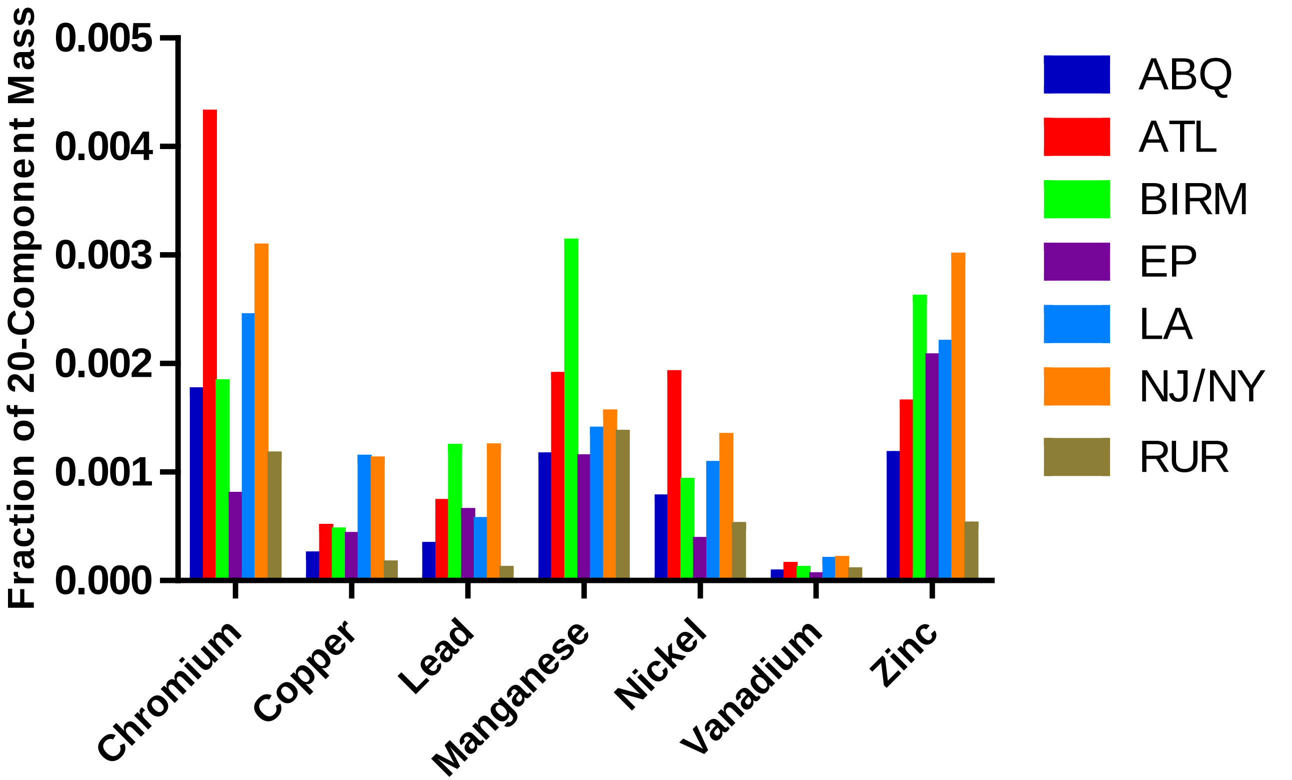



# Most Important Contributors to Sample Differences




Southwest Southeast Northeast LA

# Are the magnitude of these differences important?



# Questions/Discussion

## Project 3: Cardiovascular Consequences of Immune Modification by Traffic-Related Emissions

Campen, Rosenfeld, Lund, McDonald

# Project 3 Aims

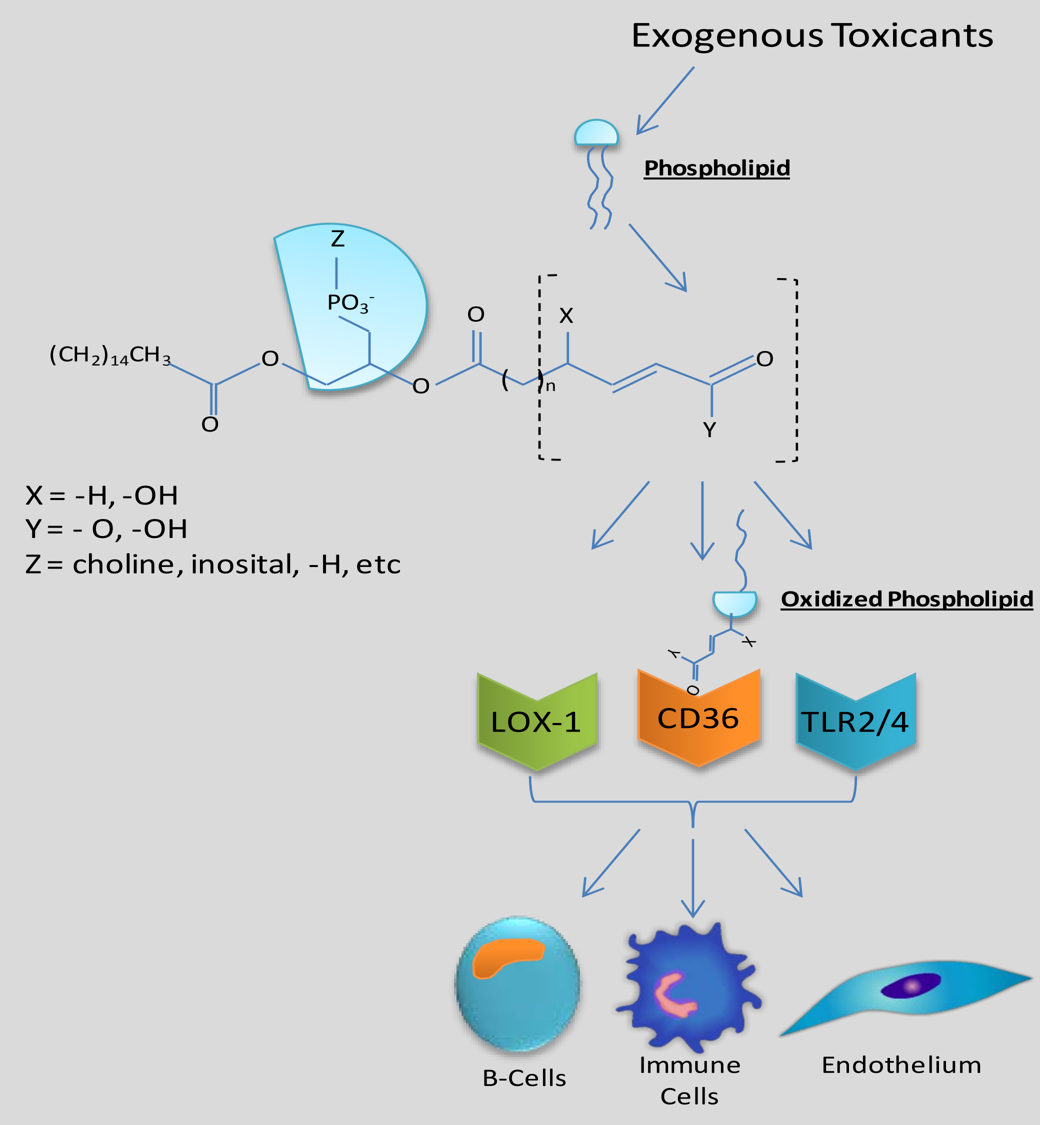
- **Aim 1**, we will ascertain the potentiating effects of physical and photochemical aging on fresh emissions, in terms of driving this vascular oxidative stress**.**

- **In Aim 2**, we will examine effects of the emissions-induced oxidative modifications to endogenous phospholipids, in terms of activating immune-modulating receptors such as LOX-1, CD-36, TLR-2, and TLR-4.

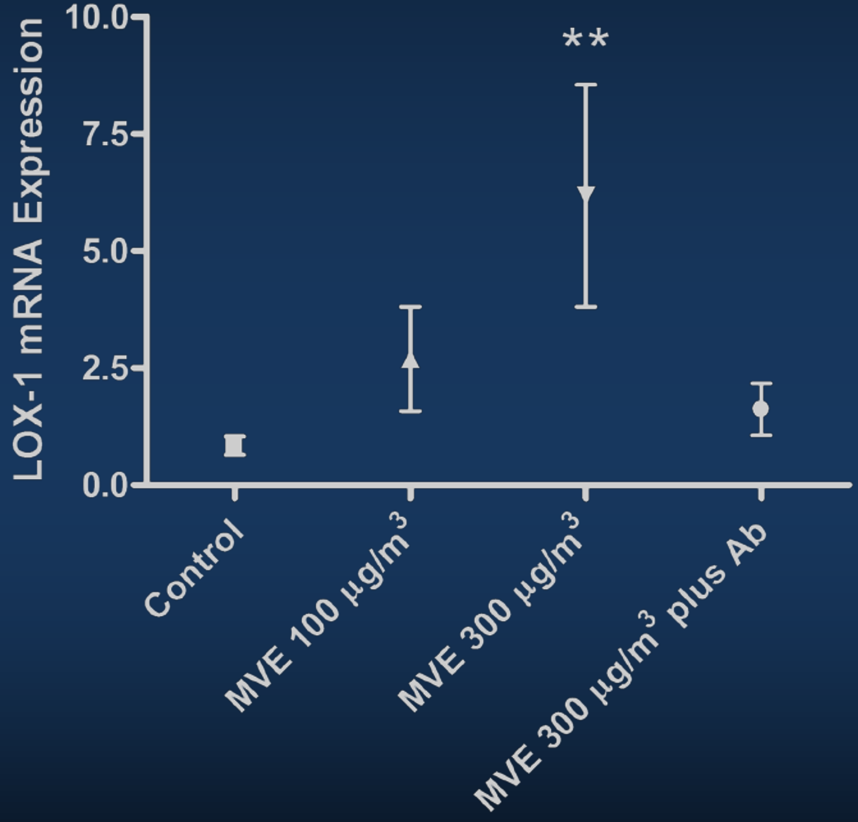
- **Aim 3**, we will further explore the role of specific immune cell populations as participants in the innate and adaptive responses to emissions-induced phospholipid modifications.

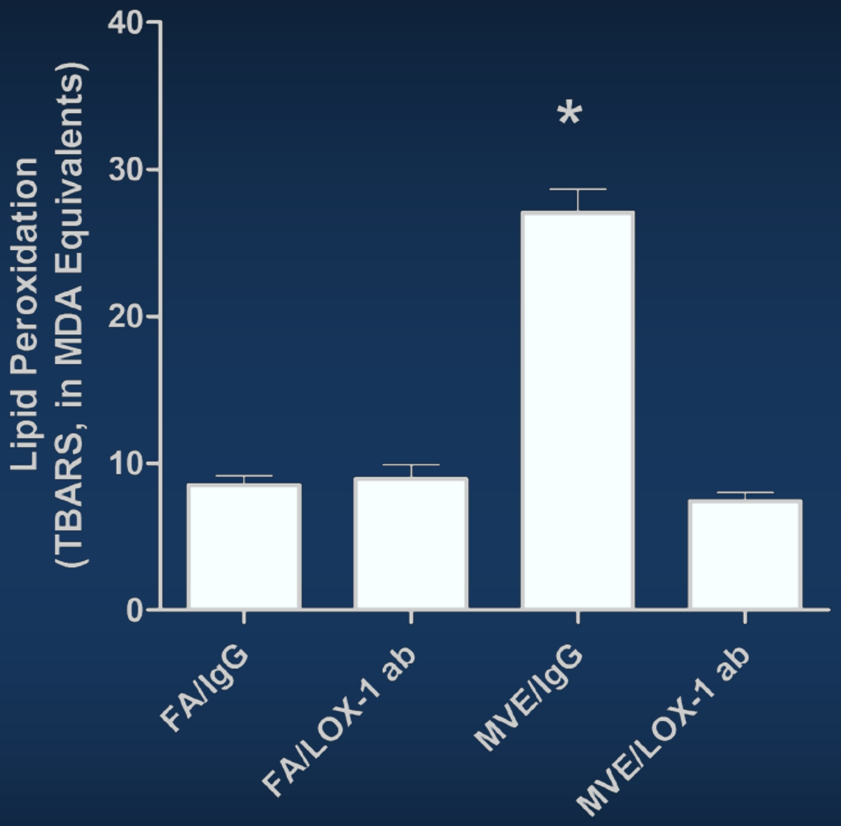
# Hypothesis: Chemical modification of phospholipids ^*and/or proteins* leads to altered biological signaling

Specifically, we suspect that reaction by-products from the lung enter the circulation to drive <u>endothelial cell activation</u> via cell surface receptors, especially pattern recognition receptors such as CD36, TLR4, and LOX-1



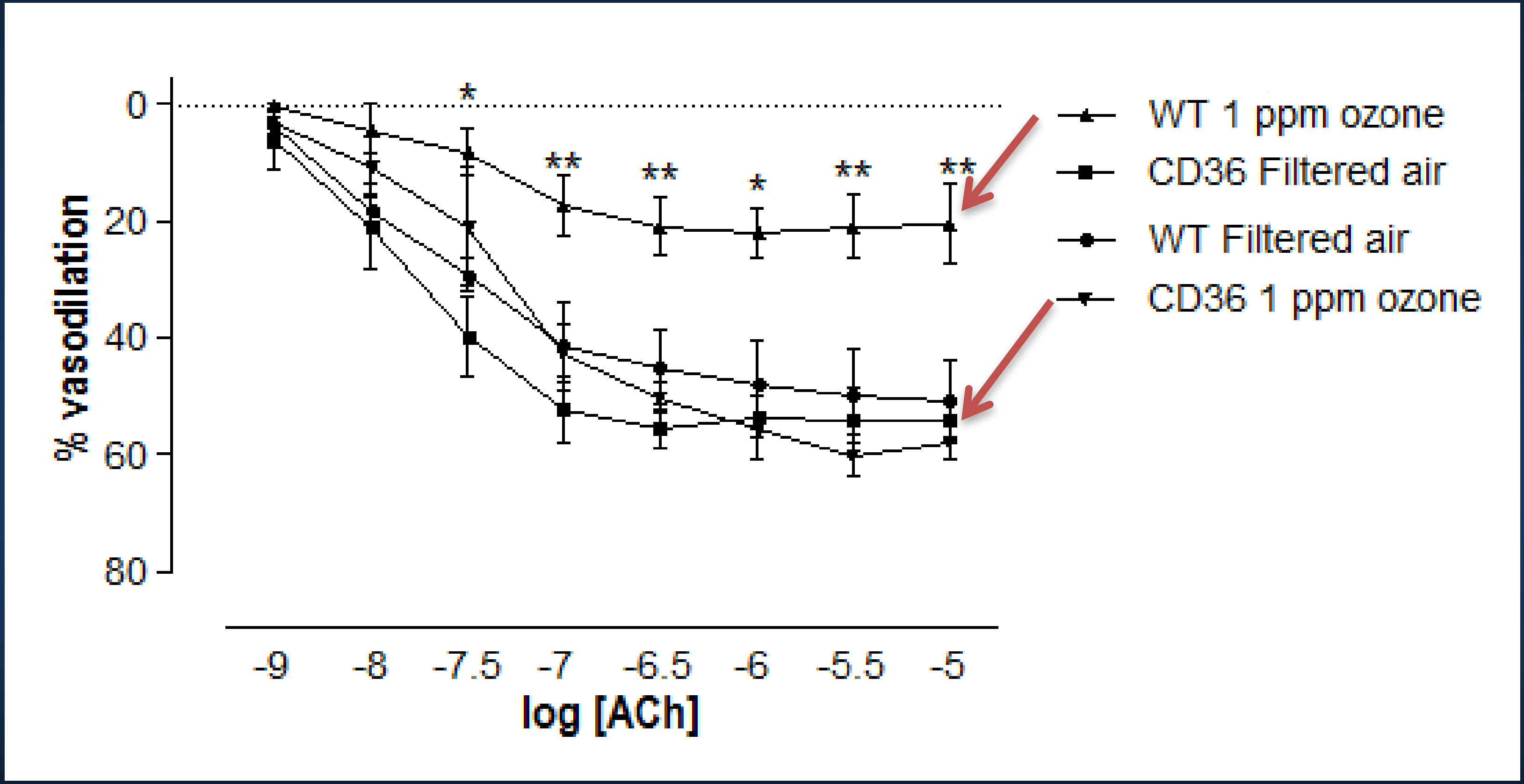
# LOX-1 Inhibition Reduced Aortic TBARS Following a 7-d MVE Exposure




Lund et al AJRCCM 2011

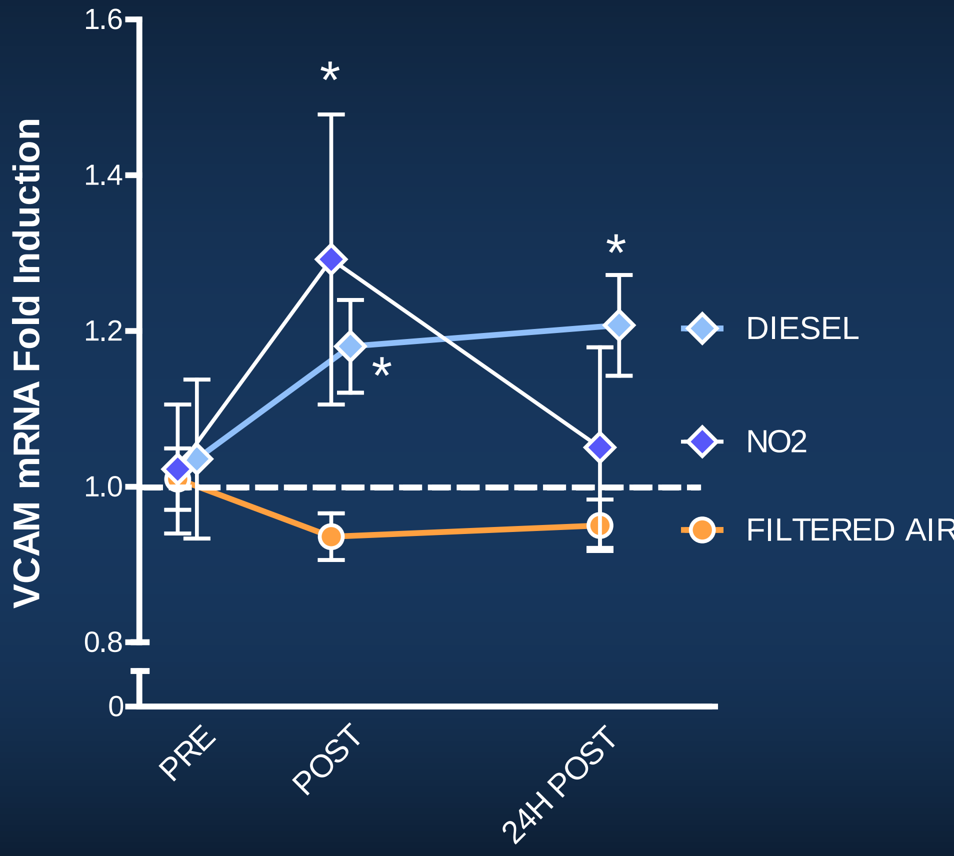
# CD36 Is Necessary for Endothelial Dysfunction Following Ozone Exposure




Courtesy of Sarah Robertson

# Evidence that the signal is blood-borne:

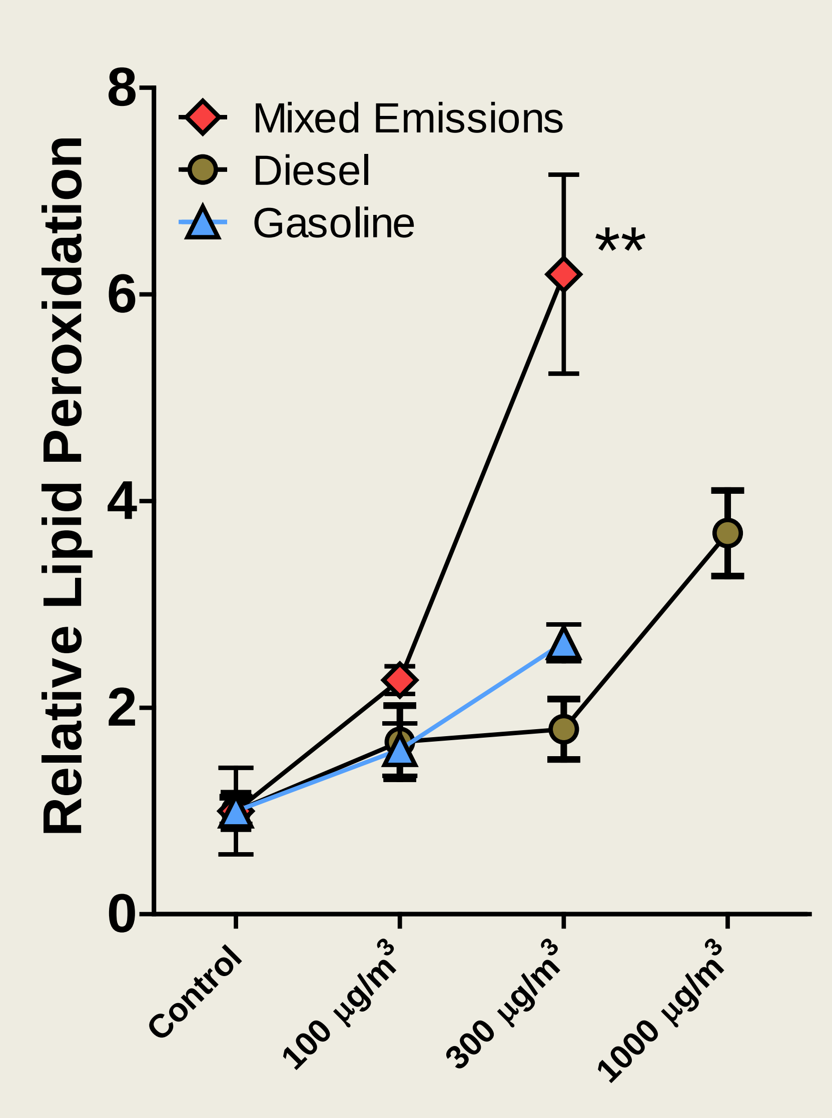
- Plasma from humans exposed to $NO_2$, Diesel, or filtered air (control) for 2 h
- Incubated with primary human coronary artery endothelial cells at 10% in media
- Plasma after exposures induced ICAM, VCAM, P-selectin and IL-8




Channell et al., Tox Sci, 2012

# Vascular Lipid Peroxidation from Mixed Gasoline and Diesel Emissions

Compared to gasoline or diesel alone, even at considerably greater concentrations, the combined gasoline-diesel emissions had a synergistic increase in systemic vascular lipid peroxidation.

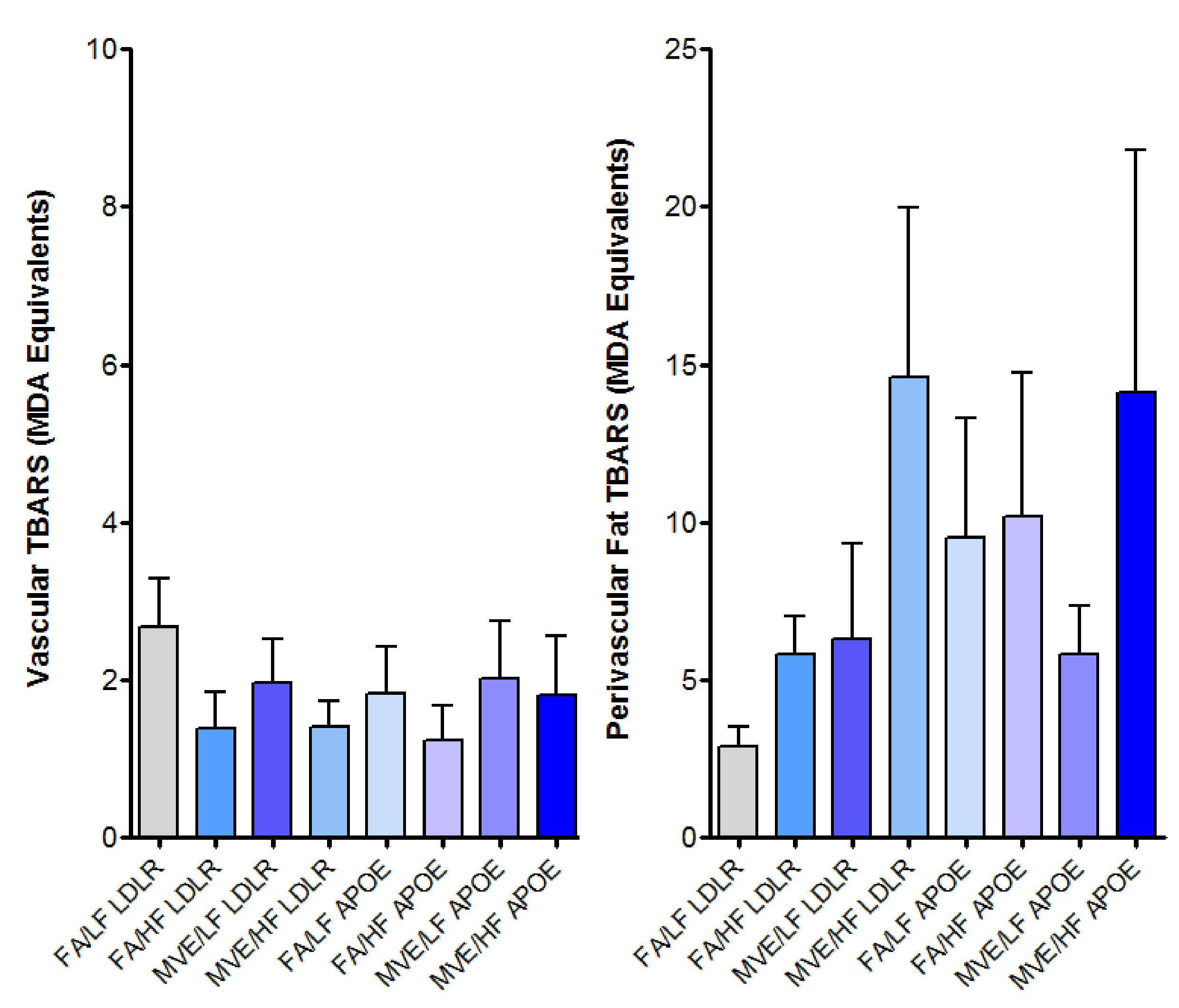


# Aim 1 Studies to date

- First, we wanted to test 2 key factors with regard to their sensitivity to vascular response to mixed vehicle emissions (MVE)
  - Strain (LDLR v ApoE)
  - Diet (normal v high fat)
- Also wanted to compare vascular wall vs perivascular adipose contribution to response
- Conducted 2 x 1 week-long exposures to MVE
  - 6 h/d at 100 and 300 $\mu g/m^3$
  - At 100 $\mu g/m^3$ we saw nothing at 7 days

# 7-d Exposure to MVE: Vascular TBARS (Lipid Peroxidation)

- 300 µg/m³
- Only slight changes in TBARS, mostly seen in perivascular fat, not aorta



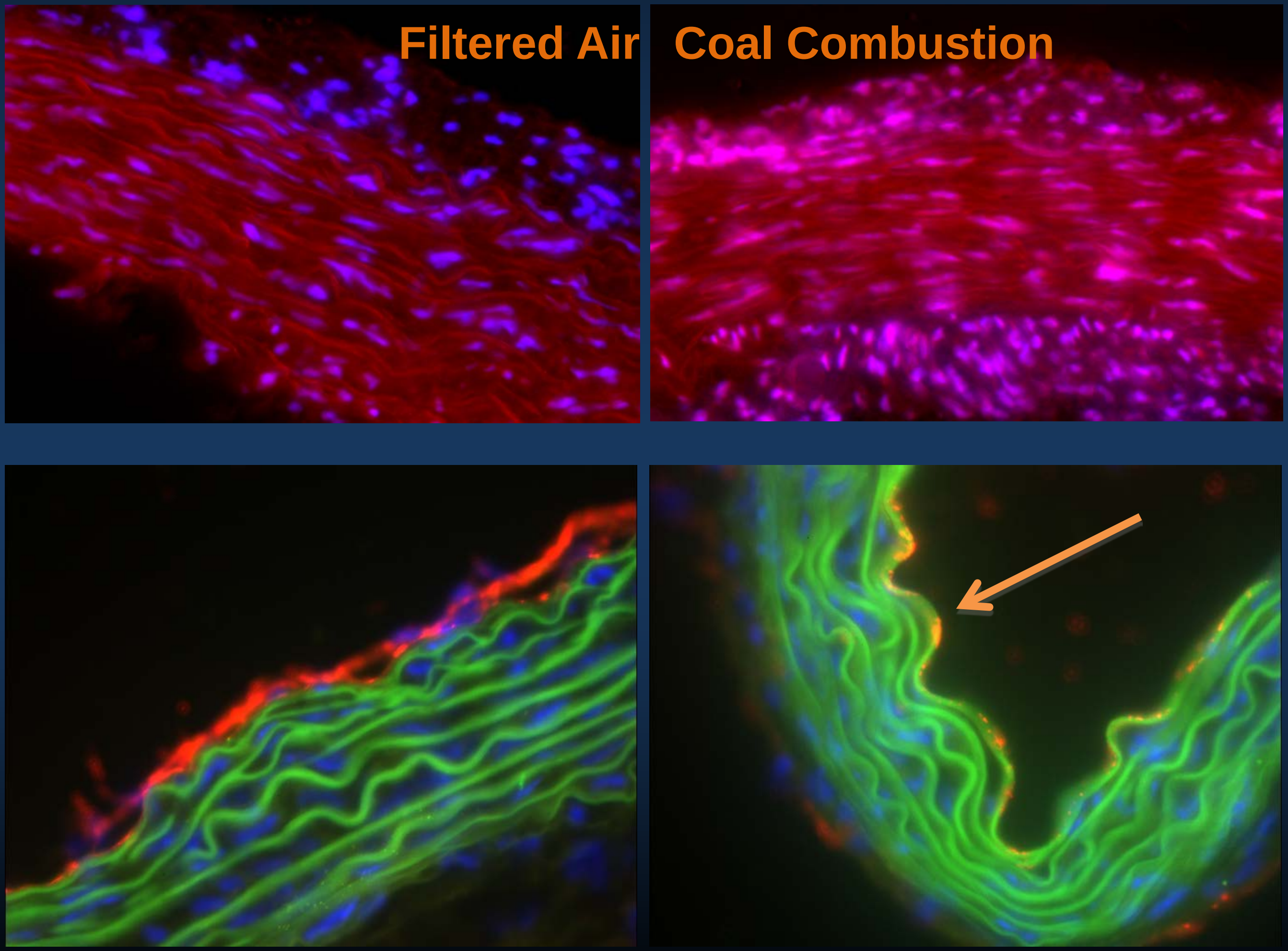
# Next Steps

- Clarity (signal:noise) of responses in the 7-day exposure is low compared with what we have seen in the past
  - Refine model and outcomes
- Compare aged emissions with 50 day ApoE on normal and high fat chow model
  - Physical aging
  - Photochemical Aging (upcoming study)

# Immunohistochemical methods to assess vascular oxidative stress

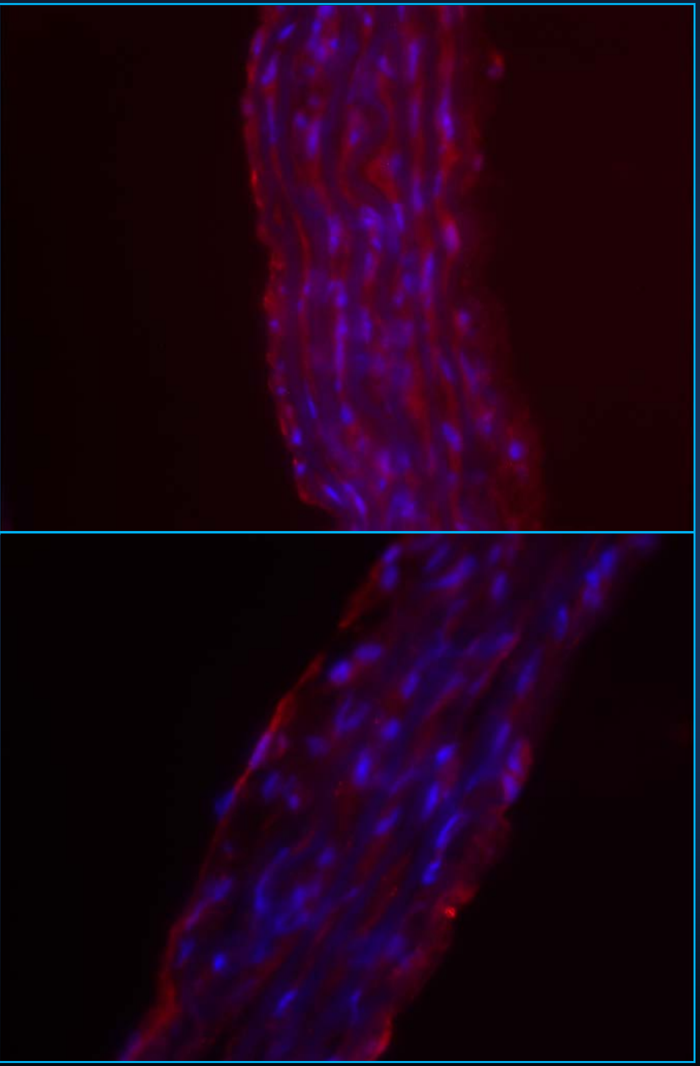
Dihydroethidium
For superoxide

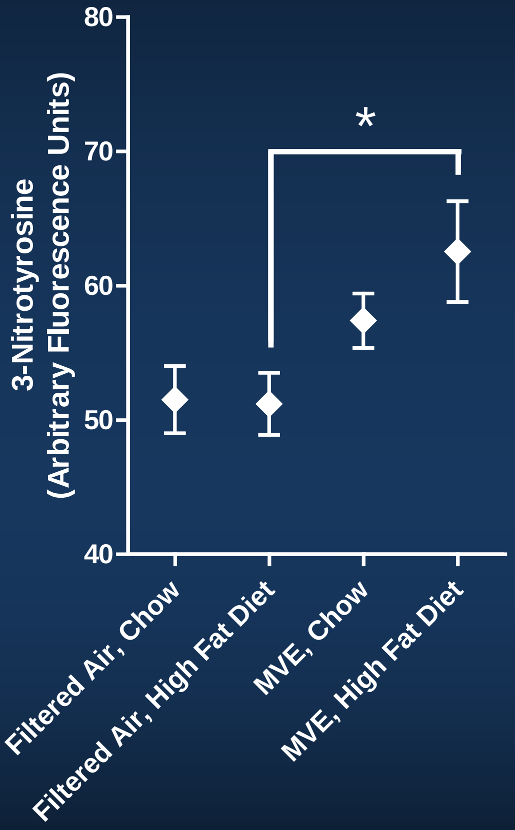
3-nitrotyrosine
for peroxynitrite



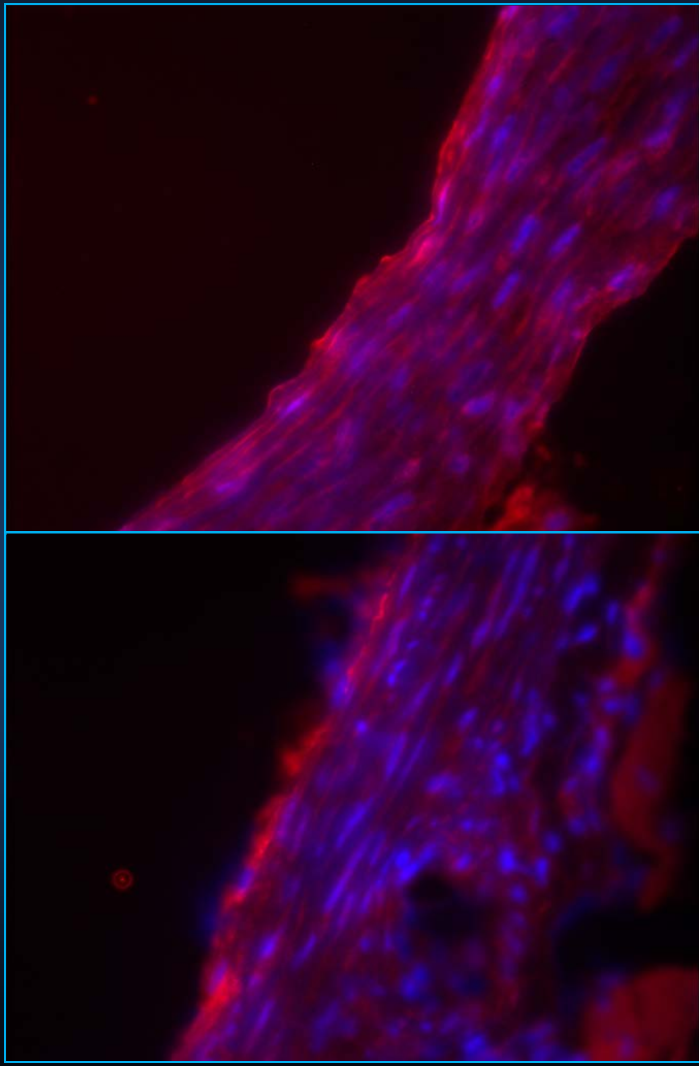
# 3-Nitrotyrosine staining

Control

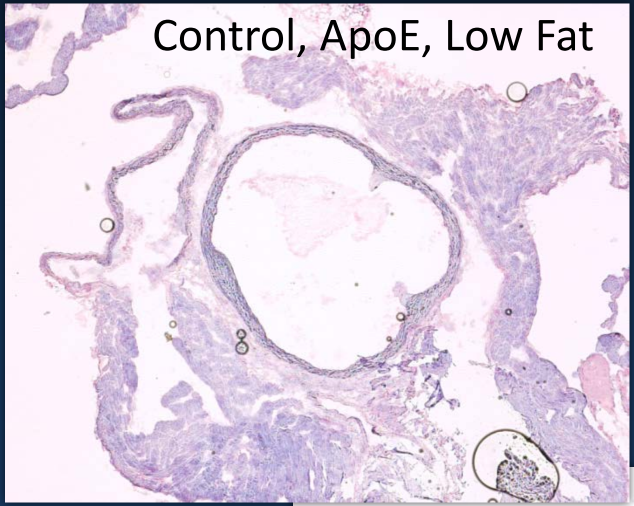


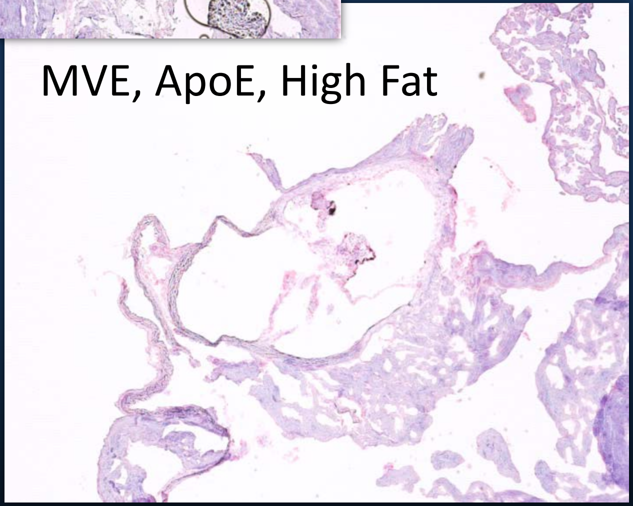


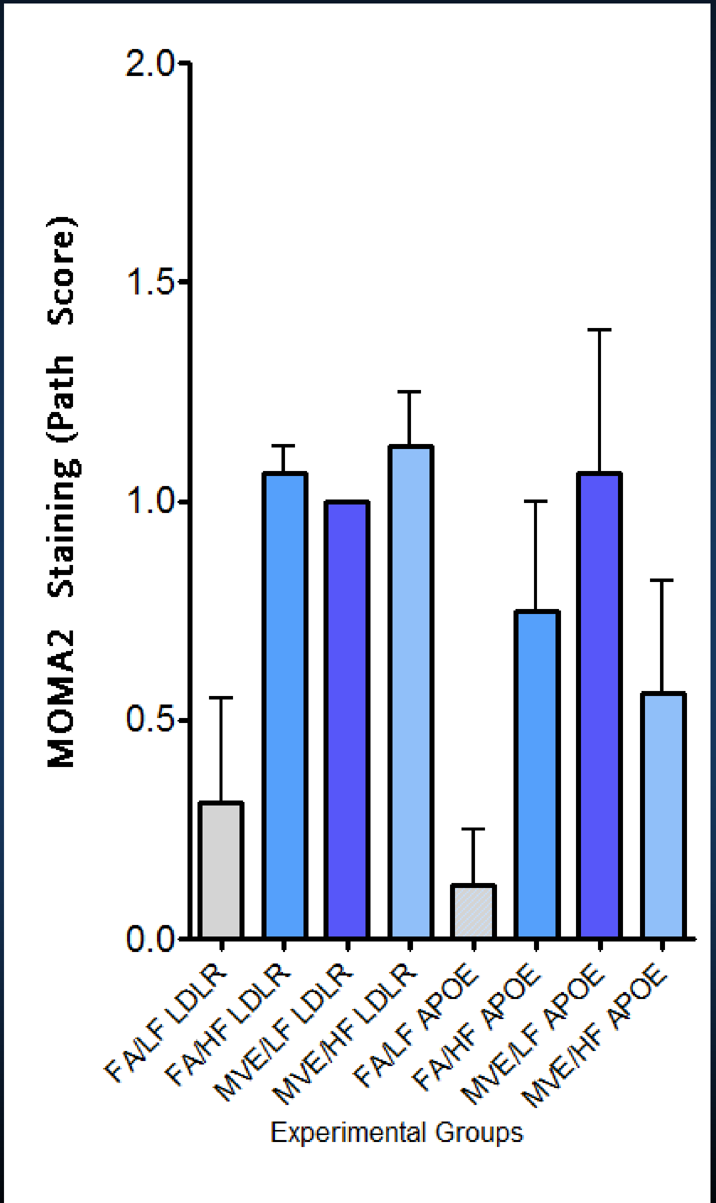

Mixed Vehicle Emissions

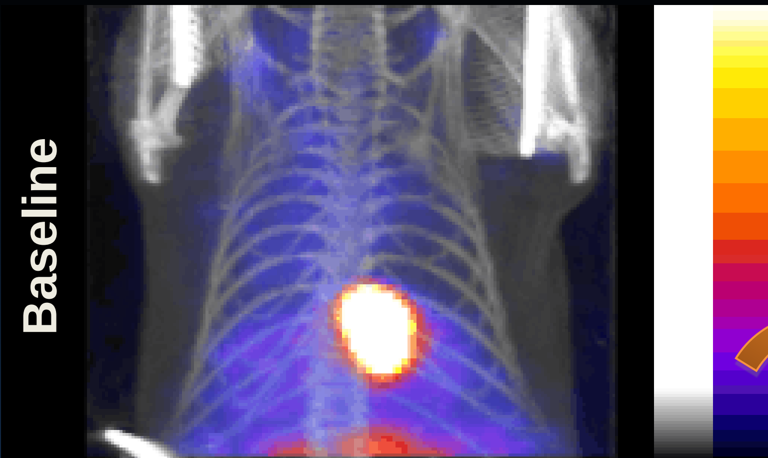


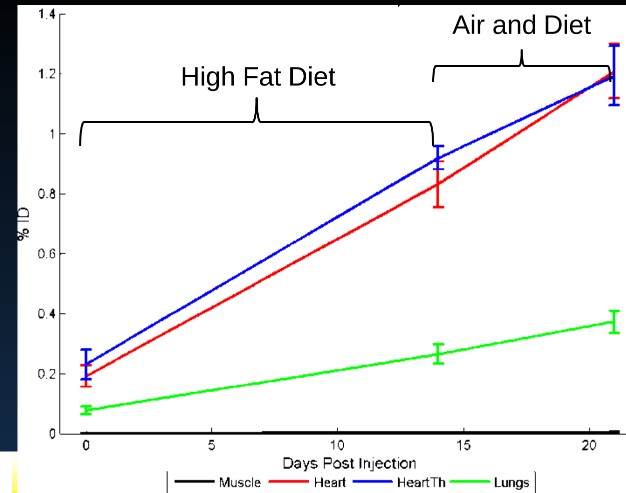
# Macrophage Staining in Aortic Outflow Tract

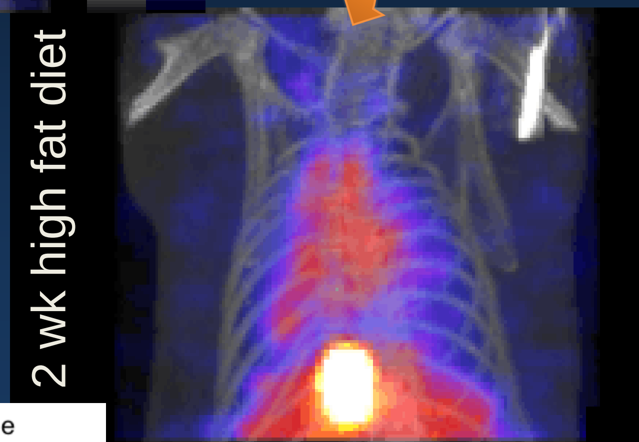


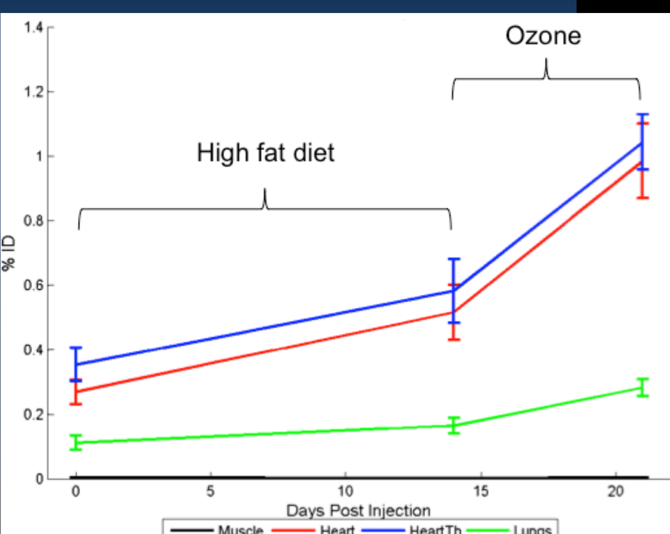



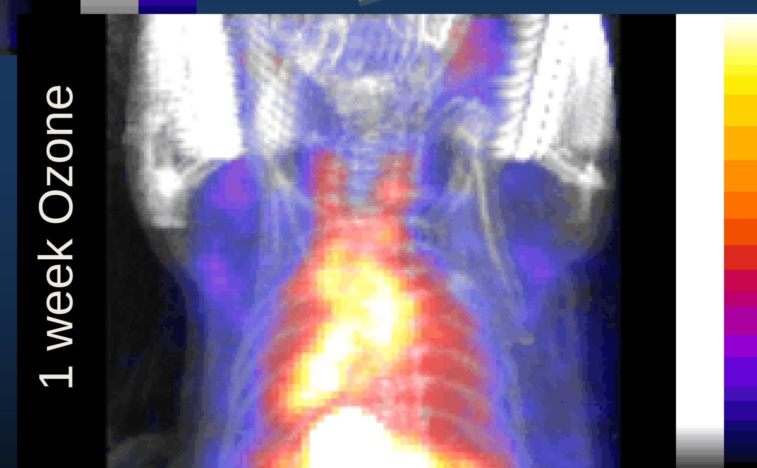



Imaging of Vascular Inflammation using $^{111}$In-LFA1-Norbirt

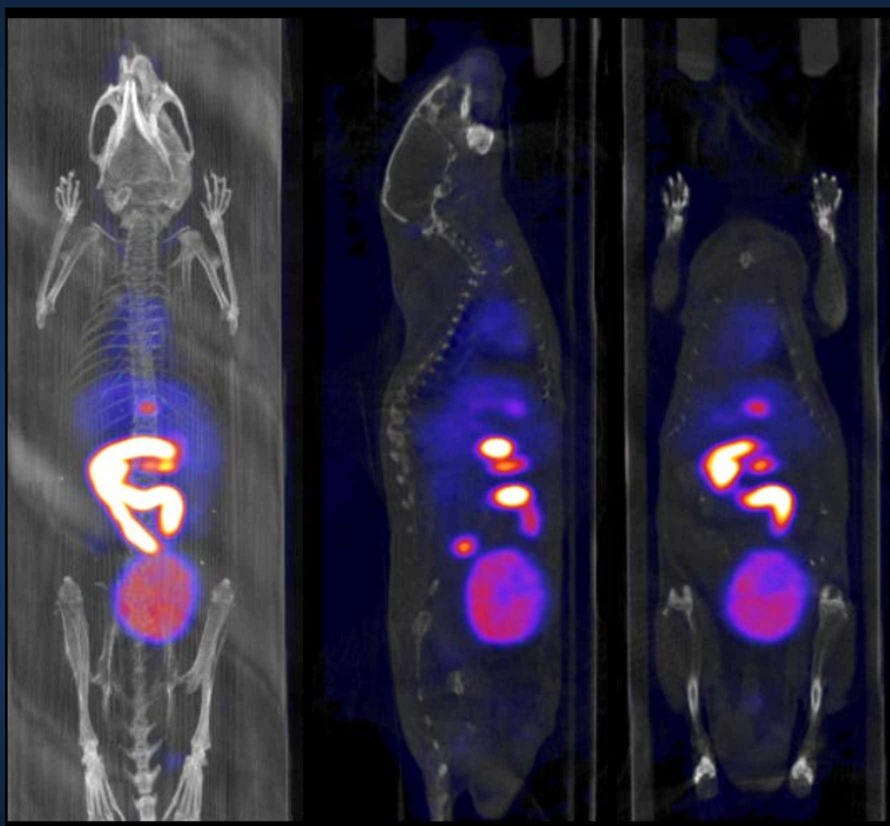


# Latest Round of Exposures

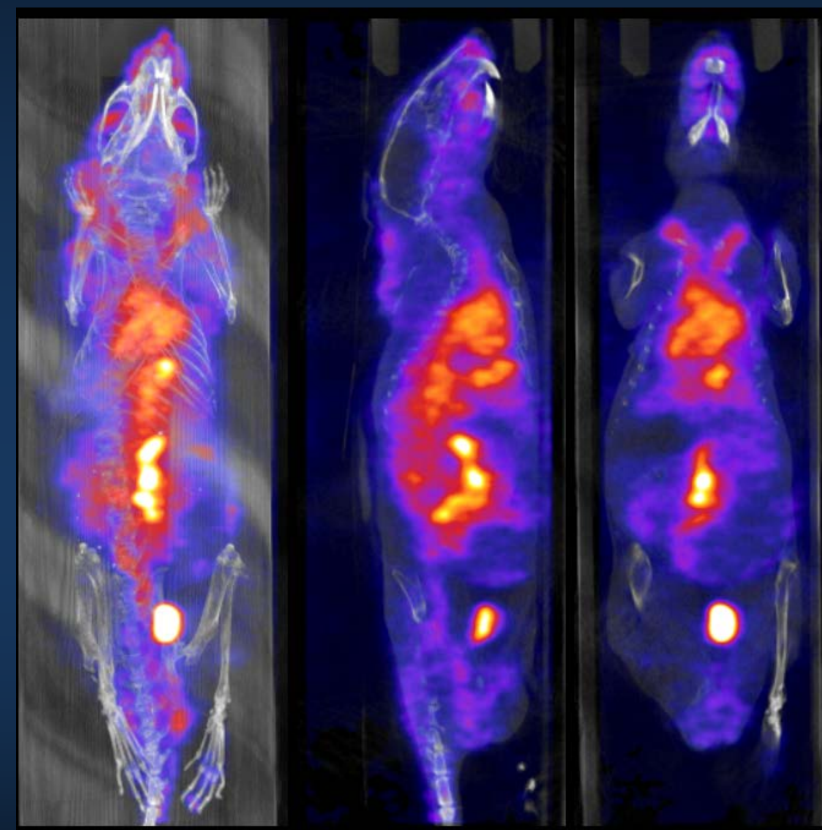
- Mixed vehicle emissions
  - Whole
  - Without Nox
  - Without gases
  - Without PM
- ApoE mice: vascular oxidative stress, histopath
- Young versus old mice (2 v 18 month) for cardiac function, inflammation by SPECT/CT

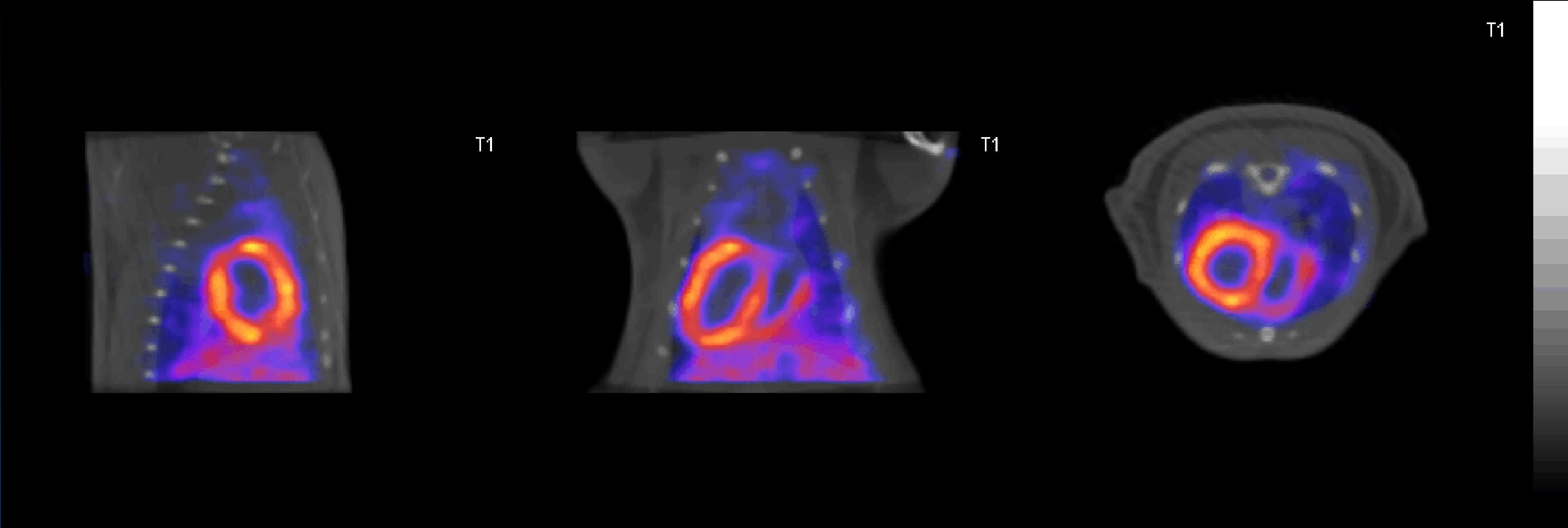
# Mixed Vehicle Emissions Exposures in Older Mice (18mo)

Control



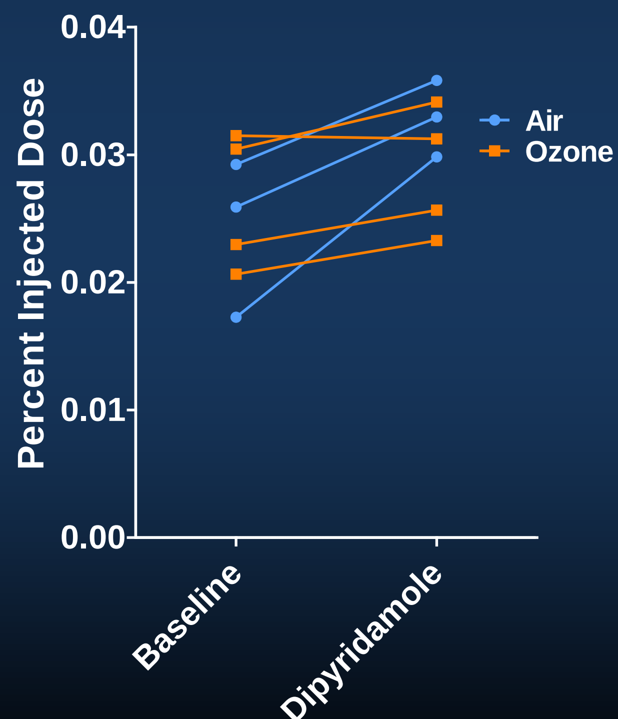
Mixed Vehicle Emissions

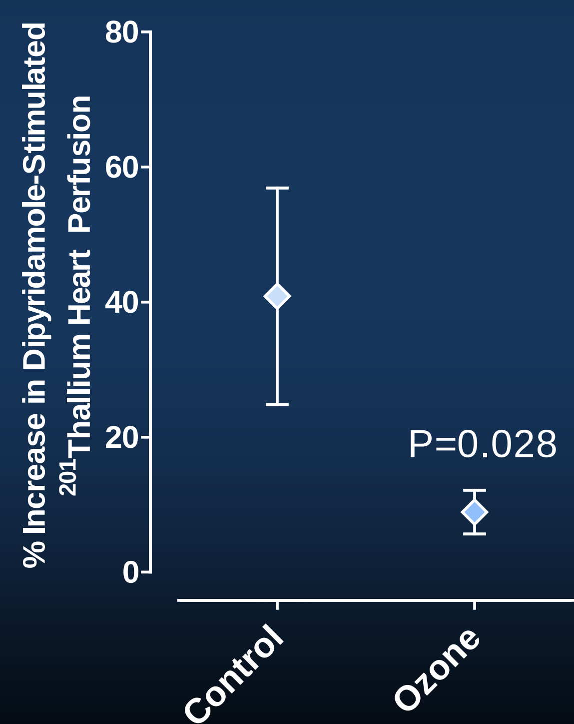





# Cardiac perfusion and function by ECG-gated $^{201}$Thallium imaging

Stress testing via persantine or dobutamine



# Next Steps: Aims 2 and 3

- Expose TLR2/4-null and LOX-1-null (on ApoE background) mice to "raw" MVE for 50 days
  - Ongoing short-term work with CD36$^{-/-}$ mice can be extended
- Conduct SCID mouse adoptive transfer protocol, as proposed

CENTER FOR CLEAN AIR RESEARCH

UNIVERSITY *of* WASHINGTON

# Project 4

## Vascular Response to Traffic-Derived Inhalation in Humans

## “Human Clinical Studies”


**Joel Kaufman**

**Jacob McDonald**

**Amie Lund**

CENTER FOR CLEAN AIR RESEARCH

UNIVERSITY *of* WASHINGTON

# Project 5: Effects of Long-Term Exposure to Traffic-Derived Particles and Gases on Subclinical Measures of Cardiovascular Disease in a Multi-Ethnic Cohort

PI: Joel Kaufman

# Aims

- Aim 1: To build a multi-pollutant exposure model for traffic-derived air pollutants for use in epidemiological analysis
  - Using the data collected in Project 1 to model TRAP along roadways
  - Modeling efforts part of the biostats core

# Aims

- Aim 1: To build a multi-pollutant exposure model for traffic-derived air pollutants for use in epidemiological analysis
- Aim 2: To determine the effect of time-in-transit on personal exposure in this cohort
  - Achieve this through a combination of personal, residential and in-vehicle monitoring and location tracking
  - Goal of understanding measurement error in previously administered questionnaires *and* understanding relative importance of the vehicle as an exposure “compartment”

# Aims

- Aim 1: To build a multi-pollutant exposure model for traffic-derived air pollutants for use in epidemiological analysis
- Aim 2: To determine the effect of time-in-transit on personal exposure in this cohort
- Aim 3: To estimate the effect of individual-level exposure to traffic-derived air pollution on subclinical cardiovascular disease in MESA Air
  - This aim will integrate the two exposure pieces above into health effects analyses

# Current Focus is on Planning for Field Work

- Aim 1: To build a multi-pollutant exposure model for traffic-derived air pollutants for use in epidemiological analysis
- **Aim 2: To determine the effect of time-in-transit on personal exposure in this cohort**
- Aim 3: To estimate the effect of individual-level exposure to traffic-derived air pollution on subclinical cardiovascular disease in MESA Air

# Individual Exposure Estimation in MESA Air

$$E^{\mathrm{A}} = \alpha\, C^{A} = [f^{\,\mathrm{o}} + (1 - f^{\,\mathrm{o}}) F_{\mathrm{inf}}]\, C^{A}$$

$f^{\,\mathrm{o}}$ Time outdoors, assumed to be at home

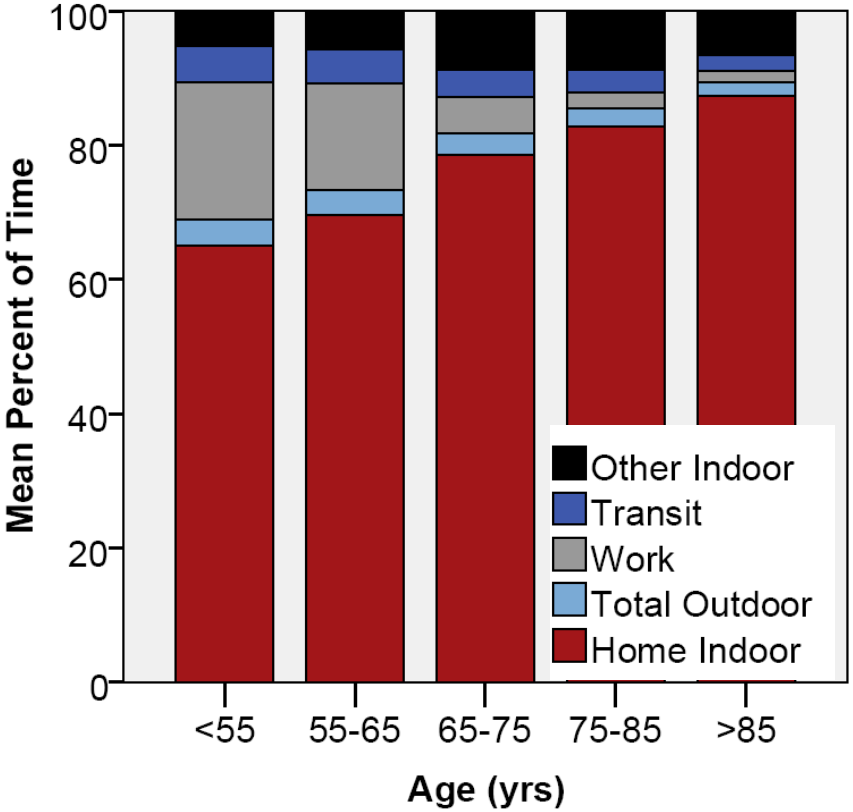
$(1- f^{\,\mathrm{o}})$ Time indoors, assumed to be at home

$F_{\mathrm{inf}}$ Infiltration factor for the participant's home

$C^{A}$ Outdoor exposure concentrations at home

# Just Two Compartments?

- Still an advance over previous studies that have assumed all time was spent outside
  - (by assuming ambient concentration = exposure)
- Most MESA Air participants spend the majority of their time at home
- We are still missing potentially important exposure "compartments"
  - Work
  - **Time in transit**
  - Other indoor locations
  - Other outdoor locations



# MESA Air Questionnaire Traffic Questions

The next few questions will ask about your travel time during the day.

**3.** On average, how many hours each day do you spend doing the following during your travel time:

a. walking or biking ☐☐ hours ☐☐ minutes

b. in a private car or taxi ☐☐ hours ☐☐ minutes

c. on a bus ☐☐ hours ☐☐ minutes

d. on a train or subway ☐☐ hours ☐☐ minutes

e. other ☐☐ hours ☐☐ minutes please specify: ☐

**4.** On average, what percent of your travel time do you spend on or next to:

○ **Participant does not leave home in a typical week (Skip to Question 6)**

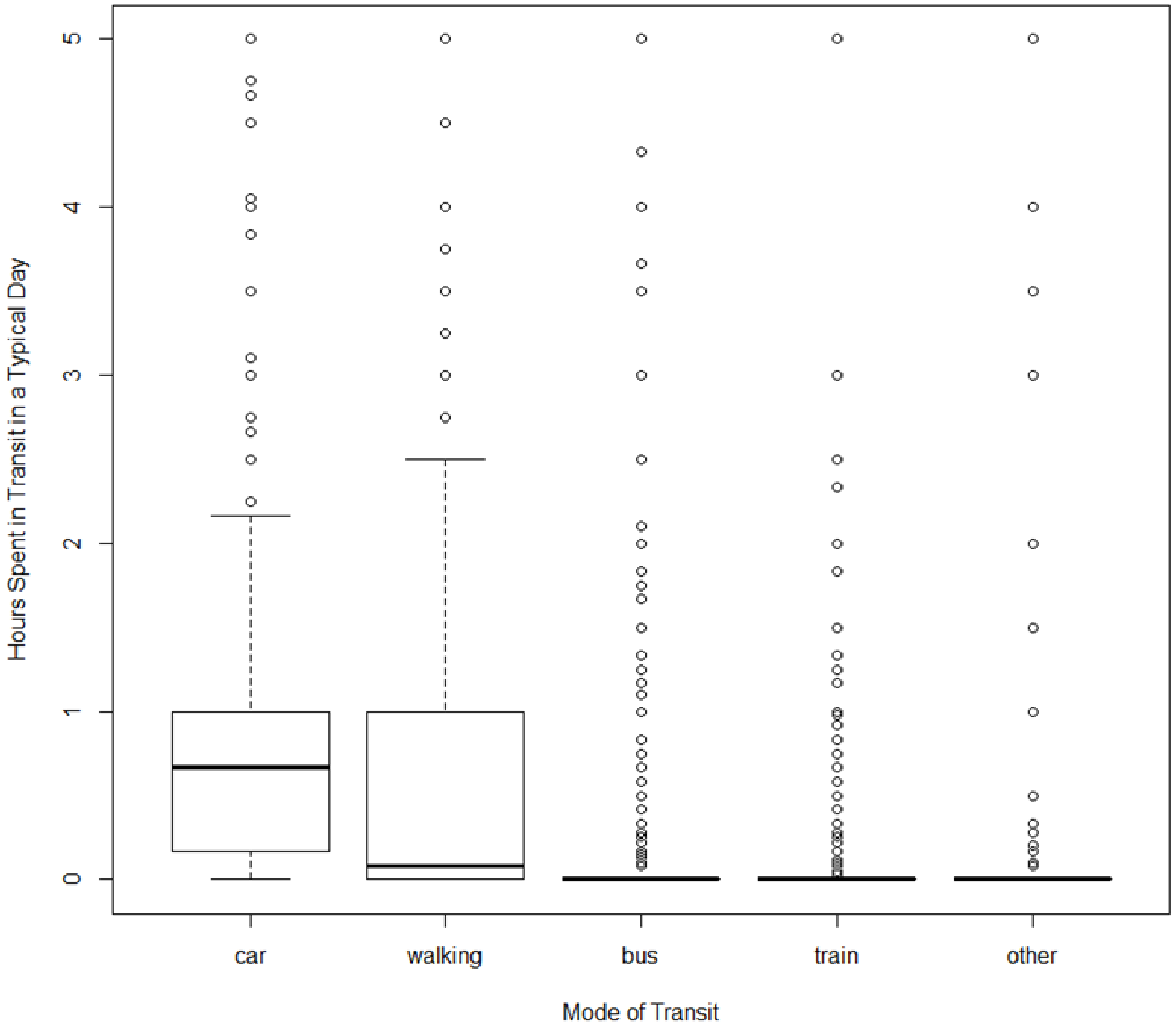
Freeways, expressways, highways, toll roads, etc. ☐☐☐ %

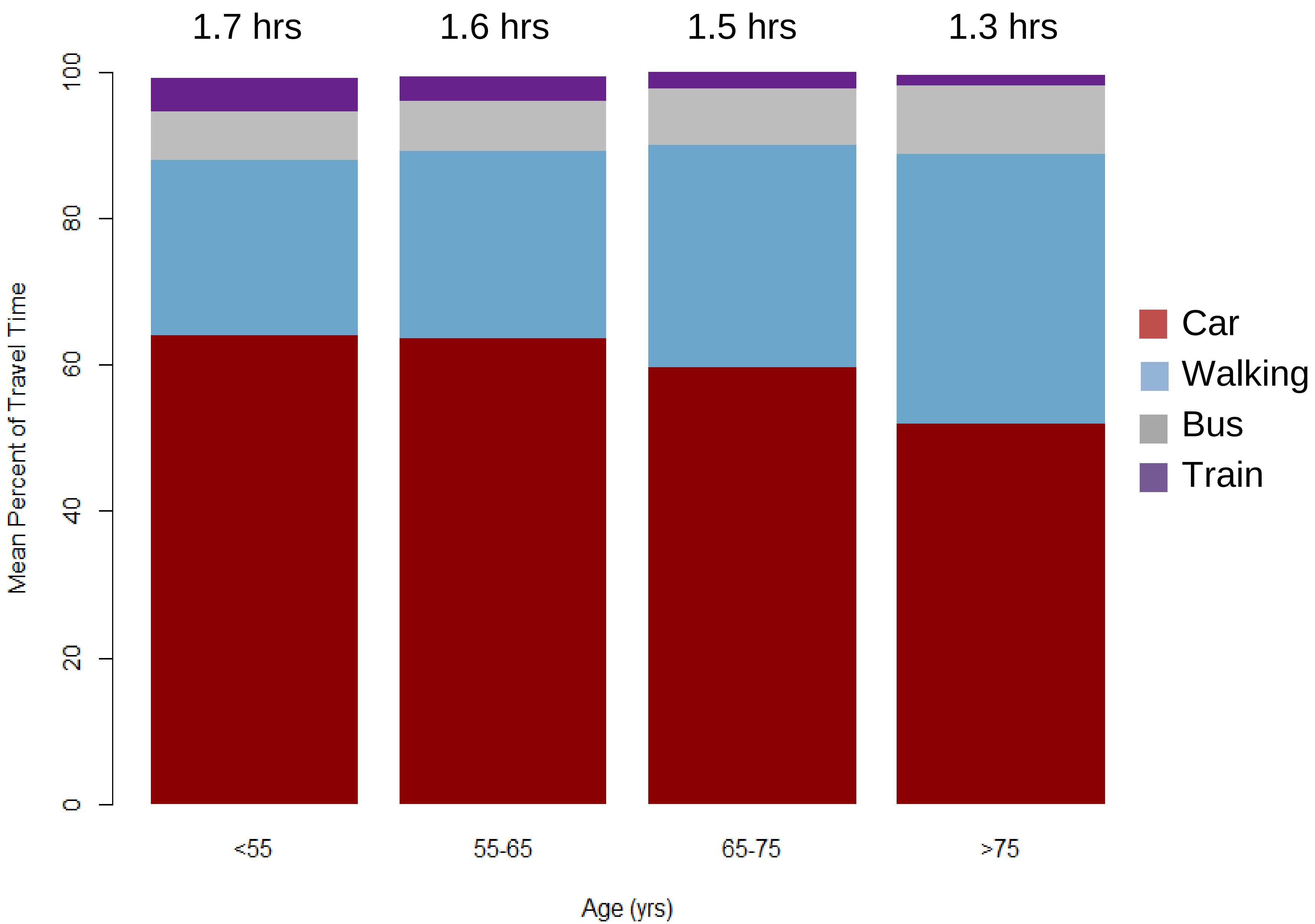
Other major, heavily traveled roads or streets ☐☐☐ %

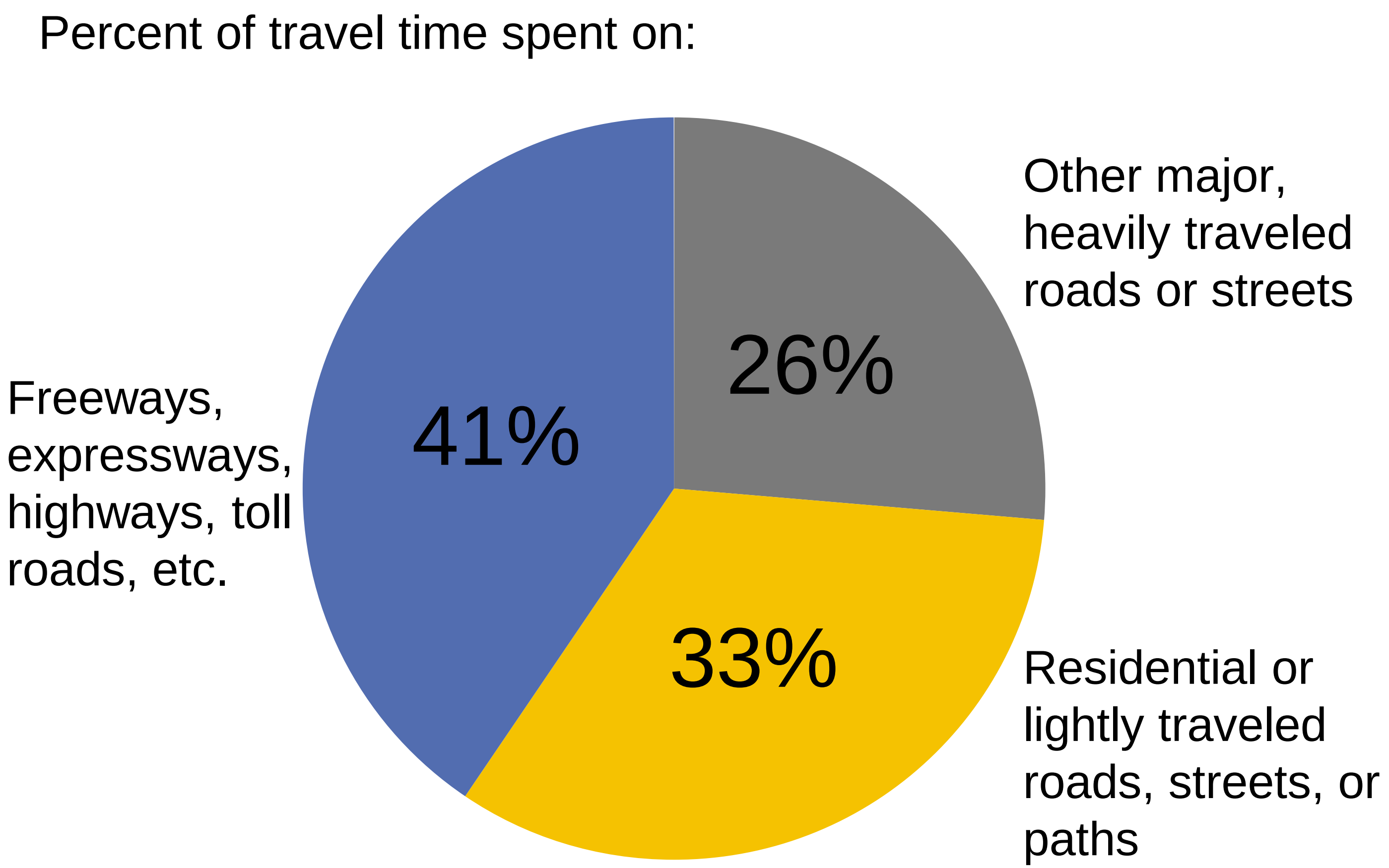
Residential or lightly traveled roads, streets, or paths ☐☐☐ %

**Most participants do not frequently travel by bus, train, or other mode of transit.**

**On average, most participants spent about 1.5 hrs in transit, about 60% of which is in a car and the majority of the rest is walking.**




1.7 hrs
1.6 hrs
1.5 hrs
1.3 hrs
Mean Percent of Travel Time
0
20
40
60
80
100
<55
55-65
65-75
>75
Age (yrs)
Car
Walking
Bus
Train


Percent of travel time spent on:
Other major, heavily traveled roads or streets
26%
Freeways, expressways, highways, toll roads, etc.
41%
33%
Residential or lightly traveled roads, streets, or paths

# Focusing on In-Vehicle Exposures

- Studying actual travel patterns
  - GPS trackers and proximity sensors provide gold standard
  - Can be combined with more specific self-reported time-location diary data
  - Can then be compared with data acquired for summer and winter from the MESA Air Questionnaire on the entire cohort

- Measuring concentrations of TRAP in vehicles
  - Goal to determine importance of the in-vehicle “compartment”
  - Determine whether we need to add an “in-vehicle” component to MESA Air individual exposure model

# Monitoring Campaign

- Two-week duration
- Sample ~50 participants in each of two cities (Winston-Salem and Los Angeles) in each of two seasons in 2013
  - January (Winston-Salem) and February (LA)
  - June (LA) and August (Winston-Salem )
- Location logging
  - GPS tracking unit
  - Proximity monitor
  - Self-reported time-location diary
- Passive monitoring
  - Ogawas
  - Organic Vapor Monitor

# Participant selection criteria

- Previously consented to be approached about participation in a personal monitoring study
- Own and travel in a personal vehicle as primary mode of transportation
    - Ok if multiple vehicles; monitoring equipment will be transferable
- Living at primary residence during the sampling period
- Non-smoking and not living with a smoker

# Select sample based on:

- A range of reported time spent in transit in personal vehicles
- A range of reported road types traveled
- Select participants to match the demographics of the MESA participants

# Location Logging

- GPS trip recorder
  - Intended to track travel routes
  - Will be used to determine total time traveling from place to place and road type traveled
- Proximity sensors (2)
  - 1) distinguish time indoors at home from time outdoors
  - 2) to clock time in vehicle
- Self-reported time-location diary

~100 participants in Project 5 monitoring

- Air Questionnaire time-location data
  - Provided previously by all MESA Air participants
  - Will be compared with sampling specific time-location diary information from Project 5 subset

Entire MESA Air cohort

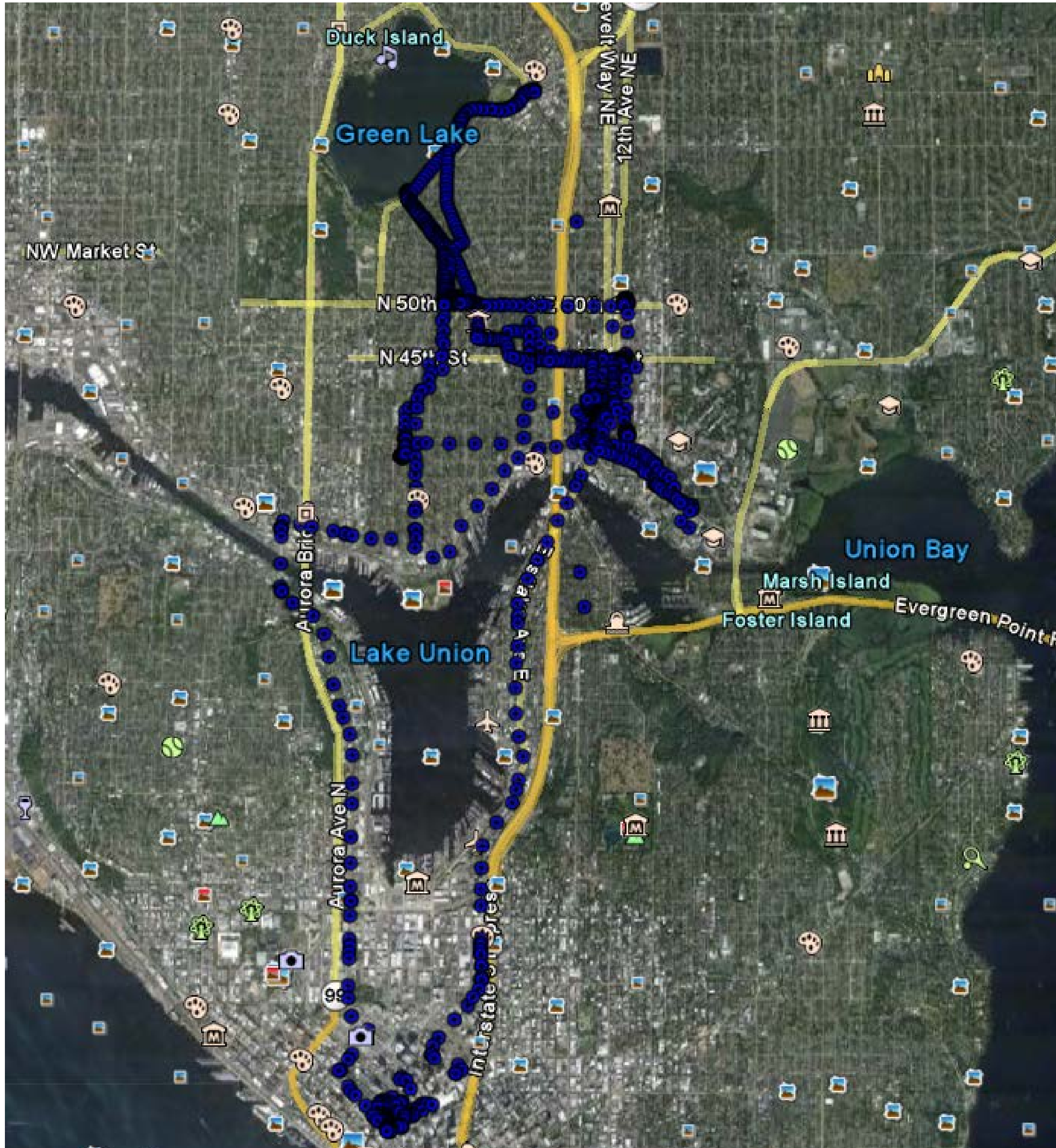
| Device Name | Memory Length (# waypoints) | Percentage of points within 10 m of true path | | Weight (grams) | Cost ($) |
|---|---|---|---|---|---|
| | | In car | Walking | | |
| **747ProS [1]** | **250,000** | **84** | **79** | **65** | **99** |
| **Adapt AD-850[2]** | **120,000** | **77** | **88** | **55** | **129** |
| Garmin Oregon 550[2] | SD card | 79 | 97 | 191 | 300 |
| TracKing Key Pro[2] | 360,000 | 89 | 88 | 226 | 249 |
| WBT-201[3] | 131,000 | 82 | 40 | 48 | 94 |
| VGPS-900[3] | SD card | 79 | 57 | 55 | 95 |
| BT-Q1000x[3] | 200,000 | 78 | 55 | 65 | 95 |
| GPhone[3] | SD card | 88 | 57 | 128 | 99 |
| E71 cell phone[3] | SD card | 88 | 23 | 126 | 345 |
| BT-335[3] | 60,000 | 81 | 40 | 75 | 63 |
| DG-100[3] | 60,000 | 83 | 58 | 227 | 70 |

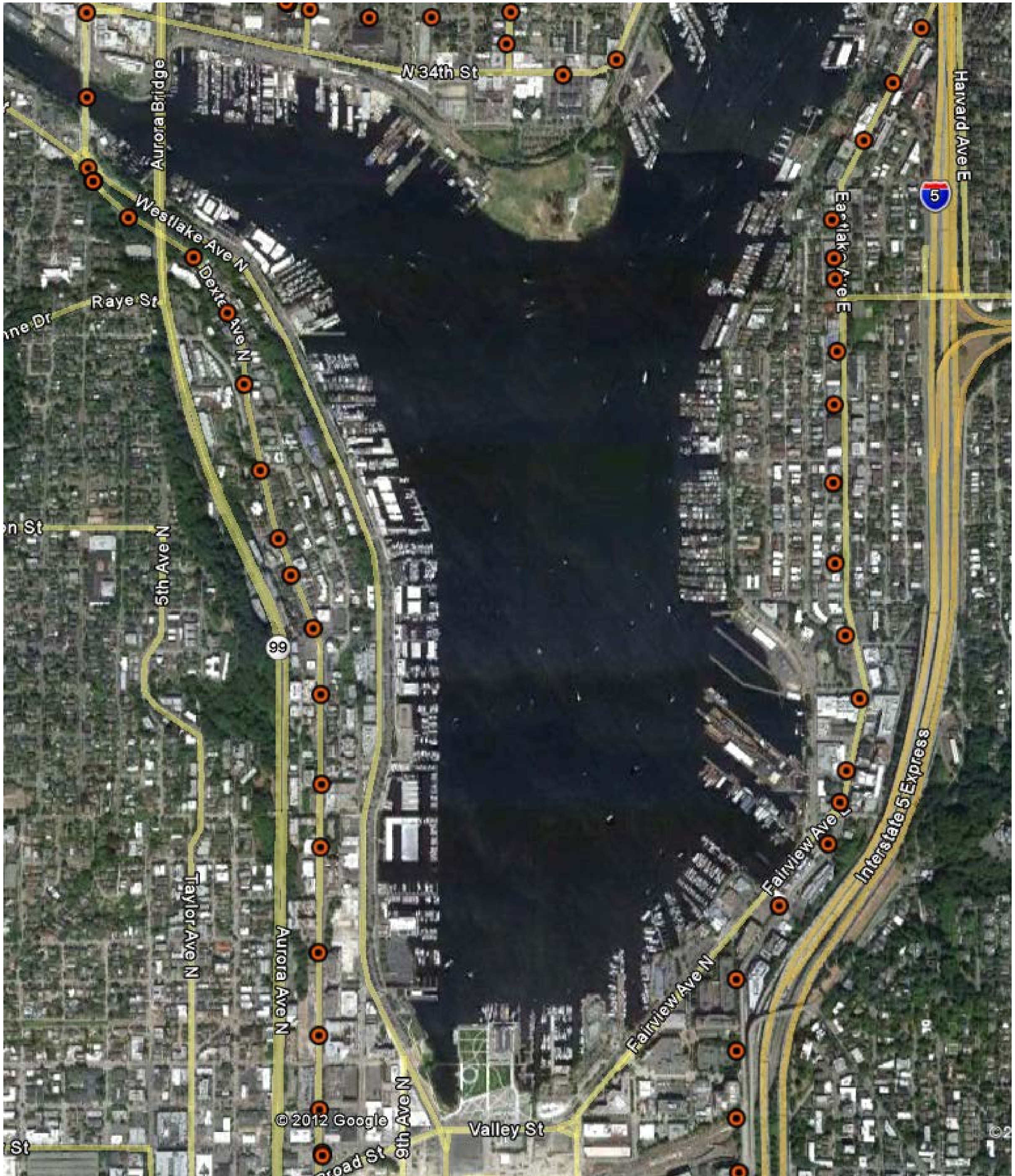
References: 1. Pilot testing at the University of Washington; 2. Beezkhuizen et al., JESEE, epub ahead of print; 25 July 2012; 3. Wu et al., Environ Health Insights, 2010, 4: 93-108.

# 747ProS Trip Recorder



# Pilot testing the 747ProS Trip Recorder





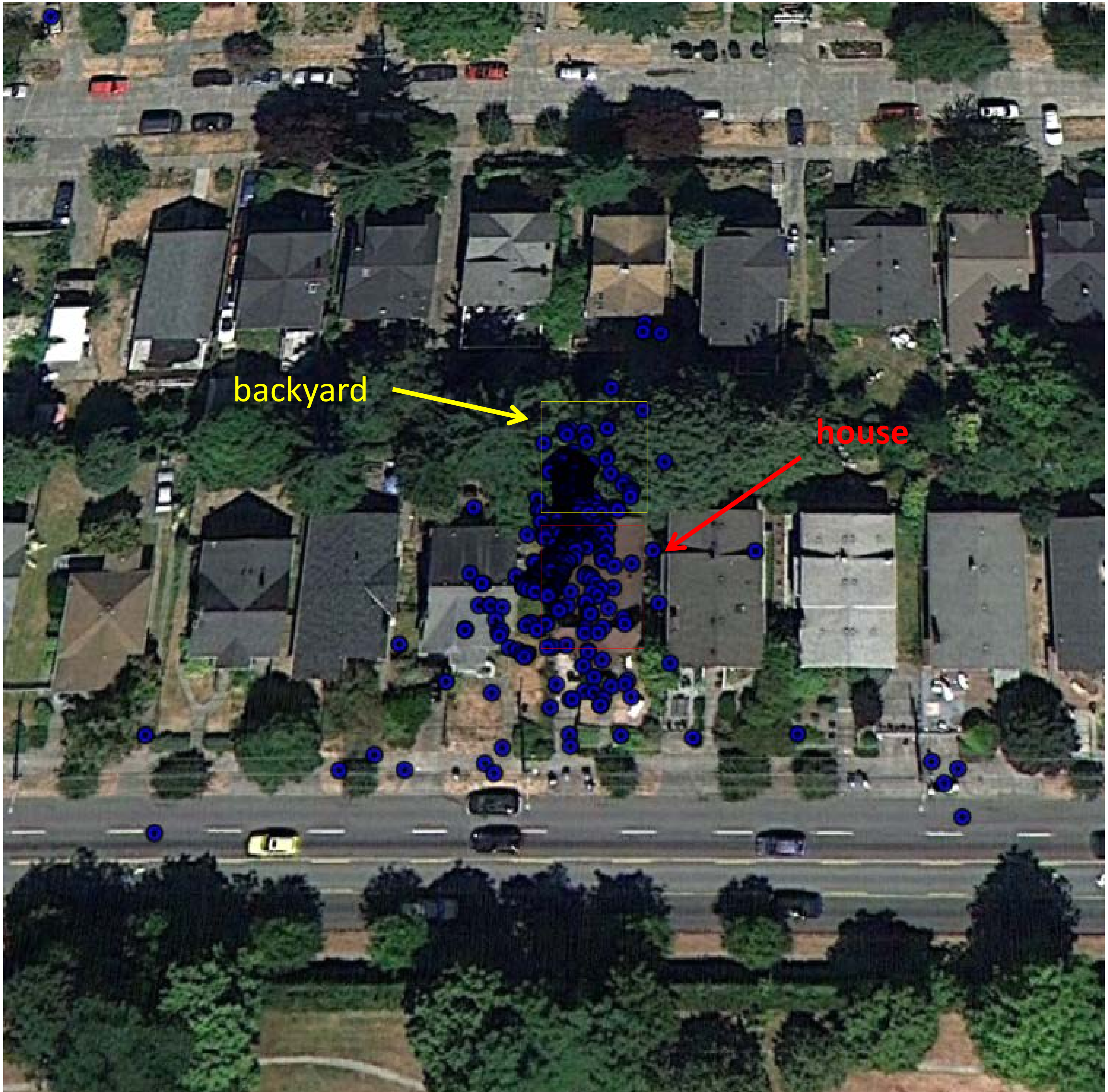
N 34th St
Aurora Bridge
Harvard Ave E
Westlake Ave N
Dexter Ave N
Raye St
Eastlake Ave E
5
5th Ave N
99
Interstate 5 Express
Fairview Ave E
Taylor Ave N
Aurora Ave N
Fairview Ave N
9th Ave N
Valley St
Broad St
© 2012 Google

# 747ProS Trip Recorder Pilot Test Results

- With added battery pack, battery life is sufficient for *at least* <u>21 days</u>
  - Additional battery pack added 385 g; next generation will be smaller
- Waypoint frequency sufficient to track routes; current settings for acquisition rate dependent on speed
  - <3 km/hr logs data point every 30 sec
  - 3 - 20 km/hr logs data point every 15 sec
  - >20 km/hr logs every 5 sec
- Waypoint memory sufficient for at least 21 days
- Spatial accuracy sufficient to allow determination of travel routes
- Small and inexpensive

# Determination of time indoors and outdoors

- GPS trackers were not accurate enough to determine whether we were indoors or outdoors at a given location
- In pilot studies, the sheer number of datapoints collected while we were at home created a “cloud” around the home


backyard
house

# Proximity Sensor

- Plan to include with the indoor sampling set up a small “proximity sensor”
  - Activated by a magnet embedded in the GPS case
  - Participants will be asked to store their GPS trackers at the sampling set up when they are indoors at home, activating a light, a beep, and a timer
- A second proximity sensor will be included with the in-vehicle sampling equipment
- Used to calculate time spent indoors at home and in vehicle
- Will be compared to the self-reported time-location diary data and to the data collected in the Air Questionnaire

# Time-location diary

- Participants will also complete a time-location diary to aid interpretation of GPS-based route and indoor/outdoor time distribution

- Diary modeled after the one used in the MESA Air personal monitoring efforts in Exam 4 and found to be useful and acceptable to participants

| Time | LOCATIONS (minutes) | | | | |
| --- | --- | --- | --- | --- | --- |
| | Home | | Other | | Motorized Vehicle |
| | In | Out | In | Out | |
| 12-1 AM | | | | | |
| 1-2 AM | | | | | |
| 2-3 AM | | | | | |
| 3-4 AM | | | | | |
| 4-5 AM | | | | | |
| 5-6 AM | | | | | |
| 6-7 AM | | | | | |
| 7-8 AM | | | | | |
| 8-9 AM | | | | | |
| 9-10 AM | | | | | |
| 10-11 AM | | | | | |
| 11-12 AM | | | | | |
| 12-1 PM | | | | | |
| 1-2 PM | | | | | |
| 2-3 PM | | | | | |
| 3-4 PM | | | | | |
| 4-5 PM | | | | | |
| 5-6 PM | | | | | |
| 6-7 PM | | | | | |
| 7-8 PM | | | | | |
| 8-9 PM | | | | | |
| 9-10 PM | | | | | |
| 10-11 PM | | | | | |
| 11-12 PM | | | | | |

| Travel | | |
| --- | --- | --- |
| Vehicle | Traffic conditions | Notes |
| | | |
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# Passive monitoring

- Personal monitoring plus three “compartments”
  - Indoor
  - Outdoor
  - In-vehicle
- In-vehicle monitoring set up will be portable
  - Participants will be asked to take it with them if they travel in other personal vehicles
  - Participants will be asked to open and close lid at beginning and end of their trips
  - Will also include a proximity sensor, a timer, and a temperature and humidity logger

# Four Sets of Passive Badges Deployed per Home

- Indoor, outdoor, in-vehicle and on the participant
- Ogawas samplers: measurements of $NO_X$, NO, $NO_2$, $SO_2$, $O_3$
- Organic Vapor Monitors: measurements of benzene, isoprene, toluene, n-decane, n-nonane, 2-methylpentane, m-xylene, undecane, i-pentane, n-pentane, o-xylene



# Pilot Testing Underway

1. Testing the battery life and memory of the GPS tracking unit
2. Blank testing the in-vehicle monitoring set up
3. Determining the limit of detection (in terms of hours per road type) of the in-vehicle monitors
4. Evaluating the accuracy of the in-vehicle monitors by comparison with measurements obtained by Project 1 monitors

# Next Steps

- Coordination with the field centers
- Continuing pilot testing
- Human subjects approval
- Recruitment scripts, forms and protocols
- Participant selection lists

- Recruitment beginning in December 2012 in Winston-Salem

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# Biostatistics Core Update

UW CCAR

27 September 2012

# Major Activities

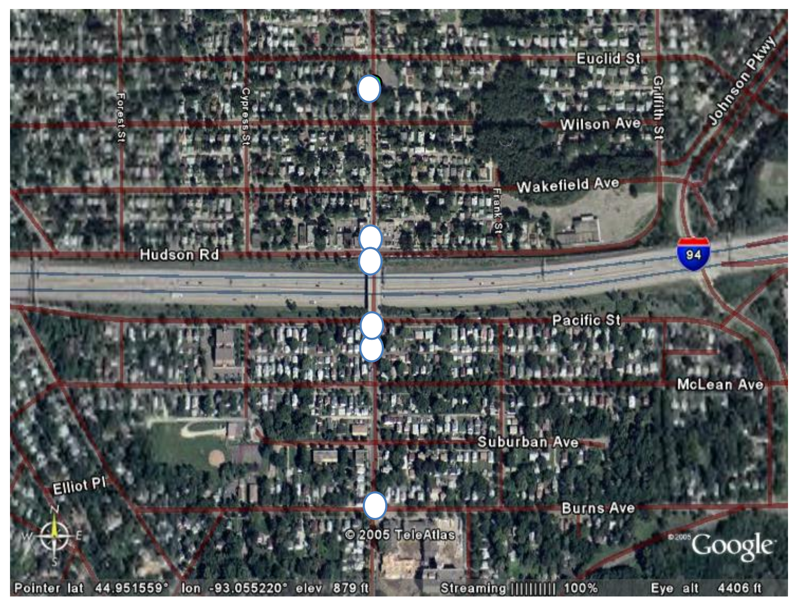
- Support Project 1
  - Design (select fuzzy point locations)
  - Data management
  - Data analysis
- Develop Collaborative Proposals
- Methods Research

# Support Project 1 – Data Management

- **Combine** mobile monitoring **data** from multiple instruments and times into a single coherent dataset
  - Original plan was two data files per day (one per platform)
  - Data and instrument issues have resulted in **many** files per day
- **QC system** to give feedback to the field team
  - Identify instrument problems during deployment
- Develop **standardized** data creation and storage **procedures**
- **Incorporate fuzzy point locations** into the dataset
  - Filter data by geographic location and time to identify observations the vehicle is traveling in the fuzzy points

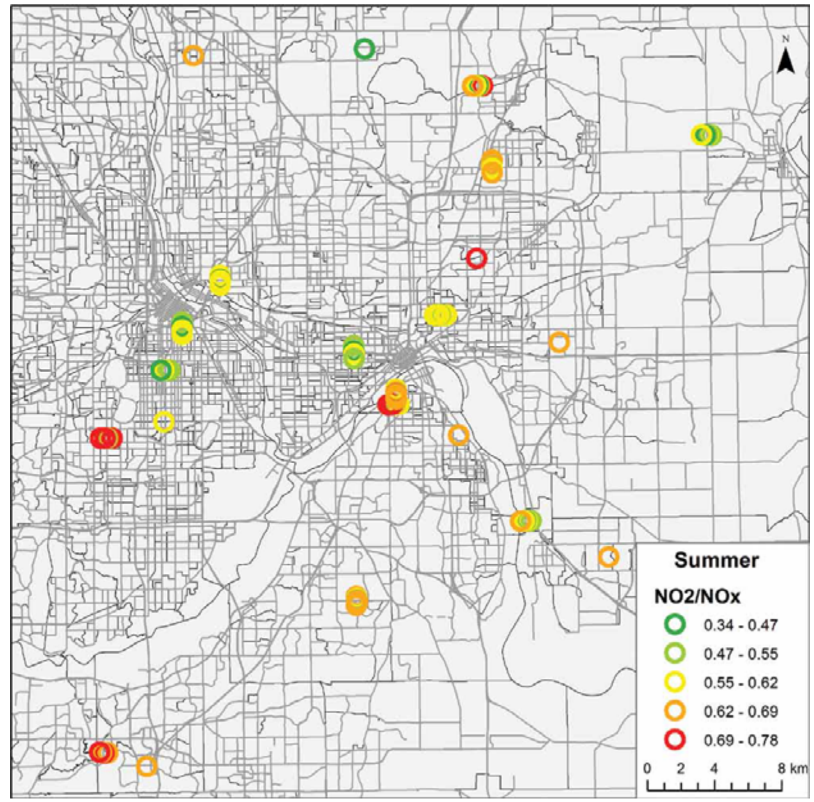
# Support Project 1 – Data Analysis

- Descriptive summaries
  - Time adjust measurements
    - Smooth the mobile data using 30-minute median of fixed site data
  - Fuzzy point estimates of central tendency
    - Median of the median from each pass through a fuzzy point
- Analysis of $NO_2/NO_x$ ratio
  - Proxy for pollutant aging?
  - Data from the MESA Air snapshot campaign
    - Minneapolis-St. Paul
  - Data in 3 seasons at ~100 locations:
    - 15 clusters – traffic gradient sites
    - 8-12 individual sites



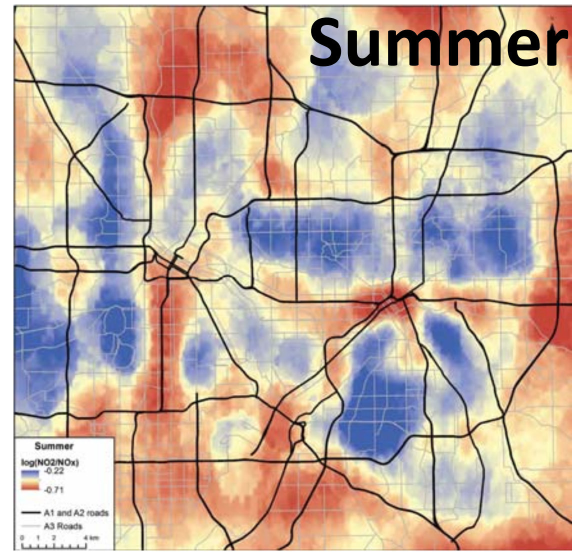
# Log($NO_2$/$NO_x$) Modeling

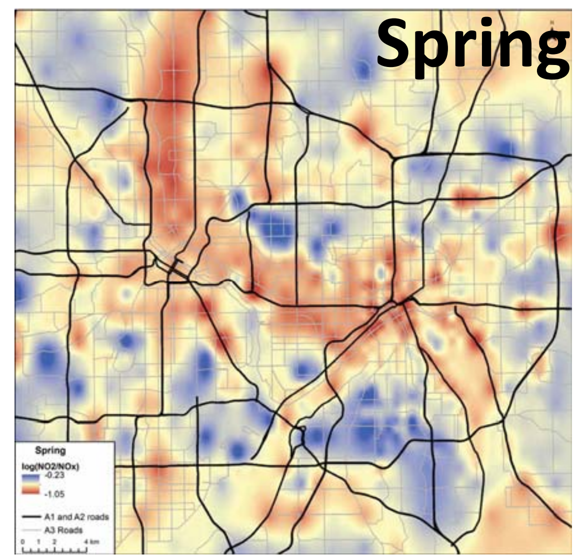
- **Rationale:** Pollutants undergo physical and chemical reactions as they move away from roads
  - Oxidation of NO to $NO_2$ is one reaction in the pollutant aging process
- **Scientific questions**: Is there spatial structure in this ratio?
  - How does it vary over space?
    - Is there seasonal dependence?
  - What geographic features are predictive?



# Log($NO_2$/$NO_x$) Results

- Fair cross-validated $R^2$ estimates
  - .36 winter; .56 spring; .58 summer
  - Less accurate than predictions from single-pollutant models (NOx, $NO_2$)
- Relatively less $NO_2$ near busy roads and in the city center
  - Open land use and multiple traffic covariates were included in the models
  - Results varied by season
- Future analyses may need to control for ozone




Key: Fresh (low $NO_2$) → Aged (high $NO_2$)

# Collaborative Proposals

- Background / context (Vedal)
- Biostatistics Core collaborations
  - Satellite data
  - Measurement error

# Exposure Estimation Collaboration

- **Title**: Ambient $PM_{2.5}$ Estimation Inter-Comparison
- **Purpose**: Evaluate the performance of various $PM_{2.5}$ exposure models including satellite-driven models and CMAQ $PM_{2.5}$ simulations
- **Goals**: Compare & summarize results; identify directions for future development; consider applications to various population-based health effects studies
- **Data**: EPA data in North Carolina modeling domain (2006-8)
- **Candidate models** to be evaluated:
  1. Mixed effect models (Harvard, Emory)
  2. Multi-level model (Harvard)
  3. Spatial downscaler (Emory)
  4. **Spatiotemporal model (UW)**
  5. CMAQ $PM_{2.5}$ simulation (Georgia Tech)

# Measurement Error Collaboration

- **Title:** Measurement error for air pollution cohort studies: application and comparison of several statistical methods to Georgia birth cohort data
- **Data:** On-going study of maternal exposure to air pollution and fetal growth in Georgia
  - Predicted exposure metrics at maternal residences
  - Exposures with different averaging times
- **Approach:** Develop methods and examine PM2.5 linear associations between birth outcomes and predicted exposure:
  1. **Parametric/parameter bootstrap (UW)**
  2. Regression calibration and simulation extrapolation (Harvard)
  3. Bayesian modeling (Emory)

# Methods Research

- Conceptual framework:
  - CLARC Biostatistics Workshop presentation (Sampson)
  - Review & status update  (Szpiro)
- Start-up activities:
  - Identified and obtained permission to use a “testbed” dataset
  - Methodological development in a single-pollutant context
  - Preliminary analyses of $PM_{2.5}$ components :  National single pollutant prediction models and health effect analyses with measurement error correction (Bergen)
- Recruitment:
  - Postdoctoral fellow Roman Jandarov

# “Testbed” Data

- **Exposure data**:  EPA network of PM components + gases
  - Focus on 15-20 reasonably well-measured pollutants that are plausibly related to health outcomes
    - E.g., S, Si, EC, OC, Ni, Cu, Cr, $SO_2$, $SO_4$, NOx, $NO_2$, $O_3$, CO
  - 250-400 locations across the US
    - Not all locations have all measurements
- **Health data**:  NIEHS Sister Study cohort
  - Large prospective cohort study
  - Designed to investigate environmental and other risk factors for breast cancer
  - >50,000 women from across the U.S.

# Methodological Approach

- **Goal**: Develop a comprehensive statistical framework for assessing the health effects of long-term exposure to multi-pollutant mixtures of pollutants. Steps:
    1. **Dimension reduction** of the multi-pollutant exposure surface based on monitoring data
    2. **Spatial prediction** of the multi-pollutant exposure surface
    3. **Health effect inference** that accounts for the uncertainty from prediction and dimension reduction in the first two steps
- **Evaluation**:
    - Preliminary analyses using single pollutant models
    - Simulation studies
    - Data analysis using “testbed” dataset

# A national prediction model for components of $PM_{2.5}$ and measurement error corrected health effect inference.

Silas Bergen

Sept 27, 2012

# Introduction

- 2-stage approach to assessing long-term impact on health of pollution exposure:
    - Build exposure models to assign individual-level exposures
    - Use predictions in regression analyses to get $\hat{\beta}_X$, the health effect estimate
- Separate analyses of multiple pollutants:
    - Exposure modeling approach should not be labor intensive
    - Important to understand relationship between exposure surface characteristics and measurement error in health analyses

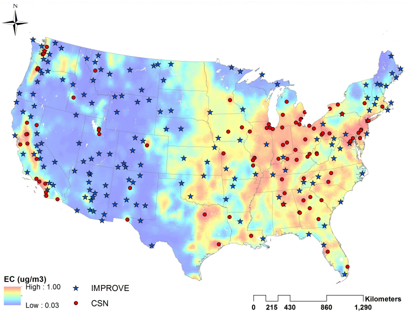
# Introduction

In our analysis:

- Health outcome is carotid intima-media thickness (CIMT) for 5,501 participants in the MESA study
- Exposures are four $PM_{2.5}$ components:
    - Elemental carbon (EC)
    - Organic carbon (OC)
    - Sulfur (S)
    - Silicon (Si)
- Exposure model:
    - National prediction model
    - Combination of partial least squares (PLS) and universal kriging
    - Can efficiently make predictions on national scale

# Monitoring data

- Observed exposures are annual averages from $\sim 250$ EPA regulatory monitors
- Chemical Speciation Network (CSN): mostly urban areas
- Interagency Monitoring for Protected Visual Environments (IMPROVE): rural areas, especially state/national parks



# Exposure model

Let $X$ denote true unobserved exposure; $X^*$ true exposure at monitoring locations. Assume that $X$ and $X^*$ are jointly modelled as:

$$\begin{pmatrix} X \\ X^* \end{pmatrix} = \begin{pmatrix} S \\ S^* \end{pmatrix} \alpha + \begin{pmatrix} \eta \\ \eta^* \end{pmatrix}$$

- $S$ and $S^*$: $N \times k$ and $N^* \times k$ matrices of covariates (often geographic covariates)
- $\alpha$: $k \times 1$ vector of *unknown* coefficients
- $\begin{pmatrix} \eta \\ \eta^* \end{pmatrix} \sim N\left(0, \Sigma_{(\eta\eta^*)}(\theta_\eta)\right)$; $\theta_\eta$ vector of *unknown* parameters; $(\sigma^2,\ \phi, \tau^2)$ in a universal kriging framework

$$Cov(X_i, X_j) = \begin{cases} \sigma^2[e^{-(d/\phi)}] & d > 0 \\ \sigma^2 + \tau^2 & d = 0 \end{cases}$$

# PLS

- For $S$ and $S^*$, have $\sim 150$ geographic covariates (some possibly collinear)
- Building 4 prediction models
- Variable selection approaches time-consuming, require decision making for each pollutant
- Partial least squares: reduces dimension of geographic covariate set to small number (2 or 3) of PLS scores
- Use these scores as new $S$ and $S^*$ in exposure model in place of the geographic covariates
- Can also look at predictions using derived from fitting ordinary least squares using PLS scores as covariates (analogous to land-use regression)

# 10-fold Cross-validation

- Used to determine optimal number of PLS scores to use in prediction
- Compares effects of using PLS only and PLS in conjunction with kriging

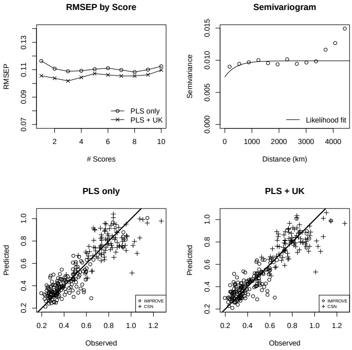



Figure: 10-fold CV results: EC

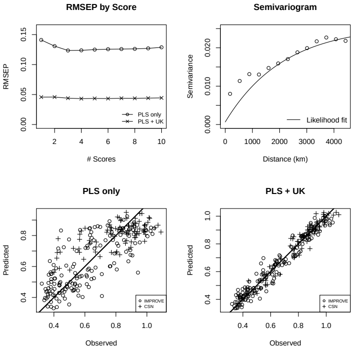
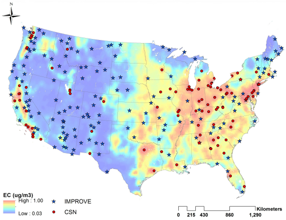
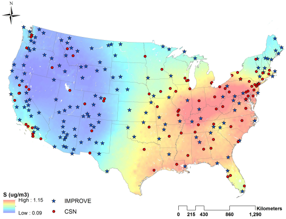



Figure: 10-fold CV results: Sulfur

- EC, OC:
    - Very little large-scale spatial structure
    - Predictions derived mostly from PLS alone
- Si and especially S showed much greater spatial structure




| | | $R^2$ | | RMSEP | | Est. UK pars | | | |
|---|---|---|---|---|---|---|---|---|---|
| Pollutant | # Scores | PLS only | PLS+UK | PLS only | PLS+UK | $(\tau^2)^a$ | $(\sigma^2)^b$ | $(\phi)^c$ | $\tau^2/\sigma^2$ |
| EC | 3 | 0.79 | 0.82 | 0.11 | 0.10 | 0.0074 | 0.0025 | 413 | 2.96 |
| OC | 2 | 0.60 | 0.69 | 0.22 | 0.20 | 0.0251 | 0.0199 | 304 | 1.26 |
| Si | 2 | 0.36 | 0.62 | 0.10 | 0.08 | 0.0043 | 0.0086 | 2789 | 0.50 |
| S | 2 | 0.63 | 0.95 | 0.13 | 0.05 | 0.0007 | 0.0251 | 2145 | 0.03 |

[a] Nugget used in kriging
[b] Partial sill used in kriging
[c] Range used in kriging

# 2-stage modeling: Stage 2

Interested in estimating health effect via linear regression, specifically, the effect of $X$ on $Y$ (here, $Y$ denotes IMT; $X$ the *true* long-term EC, OC, Si or S exposure):

$$Y = \beta_0 + X\beta_X + Z\beta_Z + \epsilon$$

- $Y$ denotes CIMT
- $X$ denotes *true* long-term EC, OC, Si or S exposure
- $\beta_X$ is the regression coefficient of interest
- $Z$ is a vector of possible confounders

Actual fitted model is

$$Y = \beta_0 + \hat{W}\beta_X + Z\beta_Z + \epsilon$$

- $\hat{W}$ denotes predicted individual-level exposure

# Measurement error

The measurement error can be decomposed as follows. Let $W$ be the predictions made if the exposure model parameters were known.

$$X - \hat{W} = (X - W) + (W - \hat{W}) = U_{BL} + U_{CL}$$

- $U_{BL}$: Berkson-like error
  - Error from smoothing (in this case, kriging)
  - Does not bias $\hat{\beta}_X$
  - Inflates SE of $\hat{\beta}_X$
  - Berkson-"like": $W$ is not fixed; $U_{BL}$ not independent across locations
- $U_{CL}$: Classical-like error
  - Error from estimating spatial parameters
  - Can induce bias in $\hat{\beta}_X$
  - Inflates SE of $\hat{\beta}_X$
  - Classical-"like": Not independent across locations; not strictly independent of $Y$
- Correct for both using the bootstrap methods of Szpiro *et al.* (2010)

## Bootstrap methods

Account for Berkson-like and classical-like measurement error by assessing variability in exposure model parameters and smoothing exposure surface

- **Parametric bootstrap:**
  - Simulate new observed and unobserved exposures
  - Re-estimate exposure model parameter from simulated data
  - Predict at unobserved locations
  - Calculate $\hat{\beta}_X$ using predictions as plug-ins; estimate bias, SE
- **Parameter bootstrap:**
  - Eliminates time-consuming re-estimation of exposure model parameters
  - Estimate sampling distribution for exposure model parameters
  - Predict at unobserved locations with exposure model using sampled parameters
  - Can be used to see how bias varies as function of classical-like error by sampling exposure model parameters from sampling density with increasing variance
- **Partial parametric bootstrap:**
  - Accounts only for Berkson-like error
  - Hold exposure model parameters fixed; predict at unobserved locations

# Results

| | EC | | OC | | Si | | S | |
|---|---|---|---|---|---|---|---|---|
| | $\hat{\beta}_X$ | $\hat{SE}(\hat{\beta}_X)$ | $\hat{\beta}_X$ | $\hat{SE}(\hat{\beta}_X)$ | $\hat{\beta}_X$ | $\hat{SE}(\hat{\beta}_X)$ | $\hat{\beta}_X$ | $\hat{SE}(\hat{\beta}_X)$ |
| Naïve | 0.001 | 0.014 | 0.025 | 0.008 | 0.401 | 0.082 | 0.055 | 0.017 |
| Parametric | 0.000 | 0.015 | 0.026 | 0.008 | 0.400 | 0.134 | 0.055 | 0.025 |
| Parameter | 0.000 | 0.016 | 0.025 | 0.009 | 0.397 | 0.141 | 0.054 | 0.025 |
| Partial Parametric | 0.001 | 0.016 | 0.025 | 0.008 | 0.401 | 0.134 | 0.055 | 0.025 |

Table: Point estimates and standard errors for the different pollutants, using naïve analysis and with bootstrap correction for measurement error in covariate of interest

# Discussion

- National prediction model provides nearly automated approach applicable to multiple pollutants, and is effective
  - PLS alone works well to predict EC and OC
  - Exploiting the spatial structure in the residuals after using PLS improves Si and S predictions; EC and OC improvements are negligible
- Measurement error has different implications for different pollutants
  - The spatial structure in S, Si induces Berkson-like error that is highly correlated in space; not appropriately accounted for by naïve methods
  - EC, OC exposure models are almost entirely explained by PLS; Berkson-like error is nearly pure Berkson error (independent across locations) and is properly accounted for by naïve SE estimation
- Implies careful attention should be given to exposure model characteristics when performing 2-stage analyses

# SIMEX version of parameter bootstrap

- Integration of method by Stefanski *et al.* into parameter bootstrap
- Previously described bias corrections assume bias is linear
- SIMEX extension of parameter bootstrap: can sample $\hat{\alpha}_j$, $\hat{\theta}_{\eta,j}$ from a probability distribution with variance inflated by factor of $\lambda$
- Plotting estimated biases as function of $\lambda$ gives representation of how classical-like measurement error induces bias
- Can extrapolate to hypothetical setting where variance of measurement error is zero to get alternative bias estimate

# SIMEX results

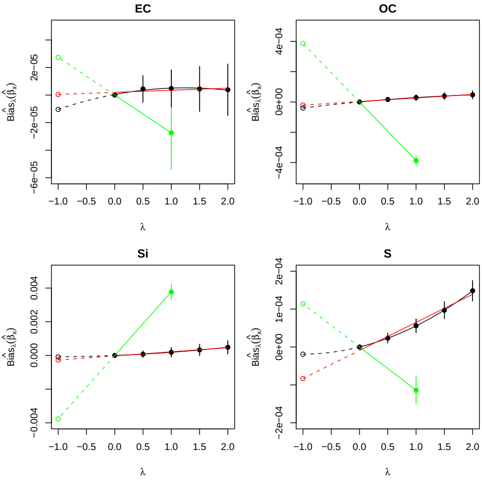



Figure: Means of bootstrapped $\hat{\beta}_{X,j}$ estimated from exposure models with increasing exposure model parameter covariances

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# Strategies for Multipollutant Exposure Modeling and Health Analysis

UW CCAR

27 September 2012

# Methodological approach

- **Goal**: Develop a comprehensive statistical framework for assessing the health effects of long-term exposure to multi-pollutant mixtures of pollutants. Steps:
  1. **Dimension reduction** of the multi-pollutant exposure surface based on monitoring data
  2. **Spatial prediction** of the multi-pollutant exposure surface
  3. **Health effect inference** that accounts for the uncertainty from prediction and dimension reduction in the first two steps

# Overview of plans

- NIEHS Sisters Study for development and initial application
  - Clear linear model air pollution effect in a large national cohort
  - Spatially misaligned multi-pollutant data is a springboard to Project 1 mobile monitoring
  - Health and monitoring data available, clean, and and in-hand now!
- Refined *eigenpollutant* methods for dimension reduction
  - Enforce sparseness to improve interpretability
- Staged development plan
  - Start with relatively straightforward multi-step analysis
  - Integrate dimension reduction + spatial prediction
  - Propagate uncertainty in health analysis (i.e., measurement error)

# Sisters Study

- Strong evidence of association between $PM_{2.5}$ and elevated systolic blood pressure (Van Hee et al, in preparation)
  - A 10 $\mu g/m^3$ increase in $PM_{2.5}$ was associated with a 1.2 mmHg increase in SBP (95%CI: 0.5, 1.8; $p < 0.001$)
  - $PM_{2.5}$ based on national spatial model using AQS monitor data
  - Evidence of a similar association with $NO_2$ exposure
- CSN/IMPROVE networks provide national monitoring data for >20 components, trace metals, and gaseous pollutants
  - Some of these were modeled in NPACT study
- Goal: Identify multi-pollutant mixtures and/or components that are responsible for the observed associations

# Need for dimension reduction

- Say we have $m$ reasonably well-measured pollutants that are plausibly related to health outcomes
- General disease model not practical

$$Y = \beta_0 + \sum_{l=1}^{m} \beta_l P_l + interactions + \cdots$$

- Too many main effects + interactions to estimate or interpret
- Our solution
  - Characterize contrasts with a small number of eigenpollutants
  - Sparseness within eigenpollutants will improve interpretability
- Other CLARCs are using clustering
  - May try this if eigenpollutants don't work out and/or for comparison

# What findings *might* look like

- Consider SBP and exposure to pollutant mixtures, e.g.,
  - $P_1 = \mathrm{EC},\ P_2 = \mathrm{OC},\ P_3 = \mathrm{SO_2},\ P_4 = \mathrm{NO_x}$, etc.
- Identify 2-dimensional eigenpollutant space
  - $E_1 = (0.9, 0.8, 1.1, 0.7, \dots, 0.9)$; dense eigenpollutant ; aggregate air pollution
  - $E_2 = (1.0, 0.8, 0, 0, \dots, 0)$; sparse eigenpollutant ; carbon species
  - $X = (X_1, X_2)$; projections of $P$ onto $E_1$ and $E_2$
- Health model $Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + (interactions?\,)$ …
  - A 1 IQR increase in the average exposure to all pollutants was associated with a $\hat{\beta}_1 = 1$ mmHg increase in SBP
  - Independent of overall pollution, a 1 IQR increase in exposure to carbon species was associated with a $\hat{\beta}_2 = 0.5$ mmHg increase in SBP

# Data availability and needs

- Cohort study subjects
  - Health data
  - Subject-specific covariates
  - Geographic covariates (GIS, long, lat)
- Exposure monitors
  - Pollutant concentrations ($m$-dimensional)
  - Geographic covariates
- Need to derive *new exposures* at *new locations*
  - Sparse eigenpollutants profiles ($k < m$ components)
  - Eigenpollutant scores at *subject* locations

# Three step sequential procedure

High dimensional monitoring data → Eigenpollutant profiles + scores at monitor locations → Eigenpollutant scores at subject locations → Health effect analysis

1. Sparse PCA

2. Multivariate spatial prediction modeling (**low dimensional**)

3. Linear regression (with measurement error correction)

- Initially carry out the steps in this approach sequentially
- Refinements once we have all the pieces working
  - Combine steps 1 and 2 to improve efficiency
  - Propagate uncertainty with measurement error correction in step 3
- Alternative approaches
  - Reverse order of steps 1 and 2 (high-dimensional spatial model)
  - Combine steps 1-3 (joint exposure and health model)

# Sparse PCA (step 1)

High dimensional monitoring data → Eigenpollutant profiles + scores at monitor locations → Eigenpollutant scores at subject locations → Health effect analysis

1. Sparse PCA

2. Multivariate spatial prediction modeling

3. Linear regression (with measurement error correction)

- Sparse principal components analysis (PCA) to define eigenpollutants from monitoring data
- Search for small number of vectors that account for most variability in matrix of pollutant data from all locations
- Similar to standard PCA, except use an $L^1$ penalty to encourage zeros in individual components
- At least three published approaches (Shen and Huang 2008, Witten et al. 2009; Joliffe et al. 2003; Zou et al. 2006)

# Multivariate spatial prediction (step 2)

High dimensional monitoring data → Eigenpollutant profiles + scores at monitor locations → Eigenpollutant scores at subject locations → Health effect analysis

1. Sparse PCA

2. Multivariate spatial prediction modeling

3. Linear regression (with measurement error correction)

- Multivariate spatial modeling for $k < m$ eigenpollutants much more manageable than for all $m$ pollutants
  - Lower dimensional
  - Eigenpollutants expected to be nearly independent of each other
- Mean model options
  - PLS or variable selection
- Spatial structure options
  - Independent kriging models / co-kriging
  - Independent low-rank spline models / correlated spline coefficients

# Measurement error correction (step 3)

High dimensional monitoring data → Eigenpollutant profiles + scores at monitor locations → Eigenpollutant scores at subject locations → Health effect analysis

1. Sparse PCA

2. Multivariate spatial prediction modeling

3. Linear regression (with measurement error correction)

- Initially propagate uncertainty from spatial modeling only (not sparse PCA)
- Parametric bootstrap methods can be extended to multi-pollutant, if we believe exposure model
- Currently working on single pollutant methods with misspecified exposure model; will extend to multi-pollutant
- Early findings for misspecified exposure model may inform how we carry out steps 1 and 2 (next few slides)

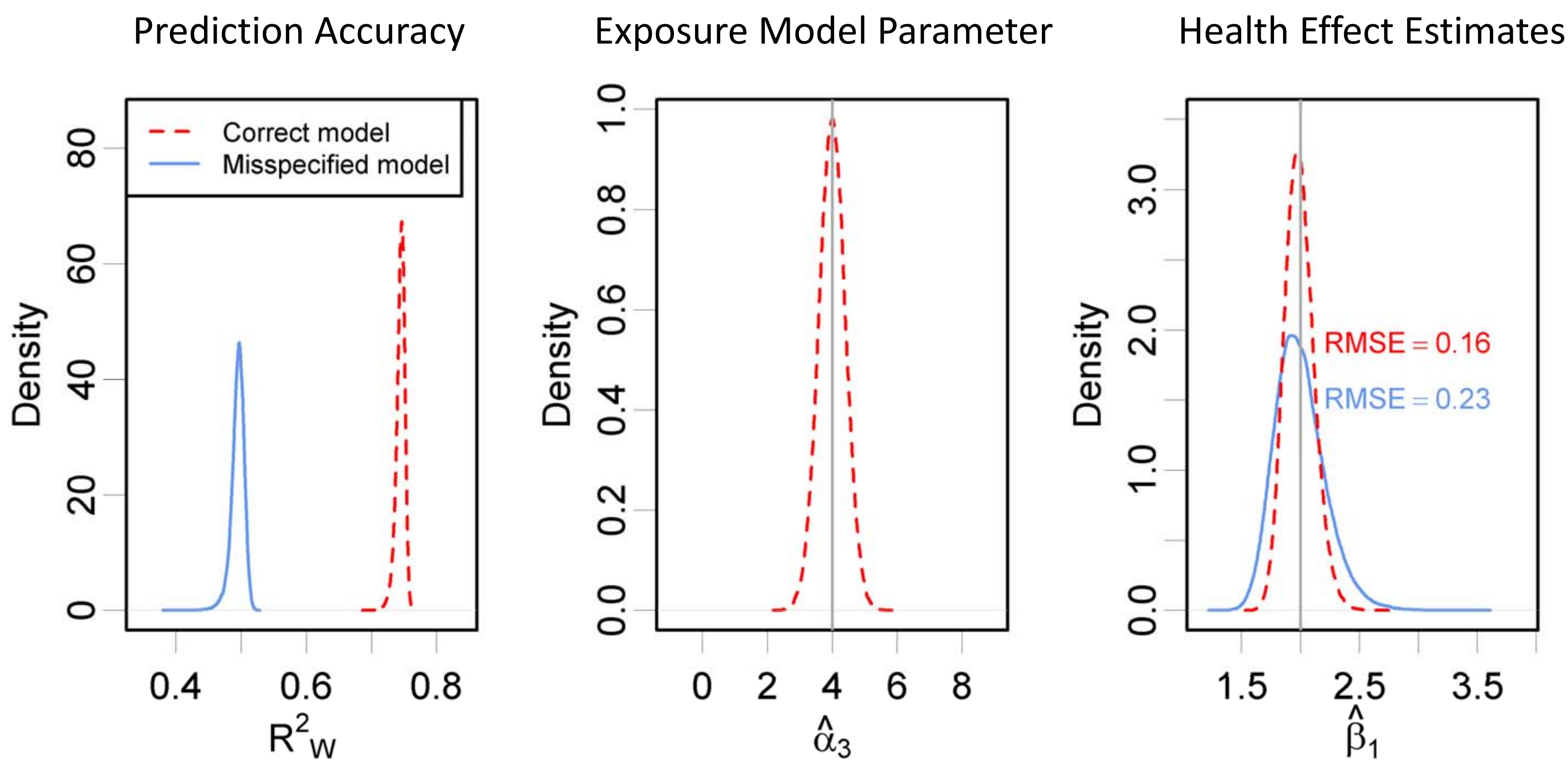
# Do better exposure predictions improve health effect estimation?

- Exposure models typically designed to maximize prediction accuracy
  - Key is selecting covariates and/or spatial smoothing parameters
  - Leaving out covariates introduces model misspecification, but this is not always bad
  - Bias/variance tradeoff is on the scale of exposure predictions
- **Do better exposure predictions necessarily improve health effect estimation?**
  - Not as obvious at it seems because there are two types of measurement error (Berkson-like and classical-like)
  - Is there a different bias/variance tradeoff on the scale of health effect estimates?

# Simulation scenario

- Subject data (don't observe the exposures $x_i$)
  - $y_i = \beta_0 + x_i\beta_1 + \epsilon_i$
  - $x_i = \gamma_0 + R_{1i}\gamma_1 + R_{2i}\gamma_2 + R_{3i}\gamma_3 + \eta_i$
  - $R_1, R_2, R_3 \sim N(0,1)$
- Exposure monitoring data
  - $x_k^* = \gamma_0 + R_{1j}^*\gamma_1 + R_{2j}^*\gamma_2 + R_{3j}^*\gamma_3 + \eta_i^*$
  - $R_1^*, R_2^* \sim N(0,1),\ R_3^* \sim N(0, \sigma^2)$ $\sigma^2 = 0.1$ or $1.0$
- Use either full or truncated model exposure prediction model
  - Correct model: $\hat{w}_i = \hat{\gamma}_0 + \hat{\gamma}_1 R_{1i} + \hat{\gamma}_2 R_{2i} + \hat{\gamma}_3 R_{3i}$
  - Misspecified model: $\hat{w}_i = \hat{\gamma}_0 + \hat{\gamma}_1 R_{1i} + \hat{\gamma}_2 R_{2i}$

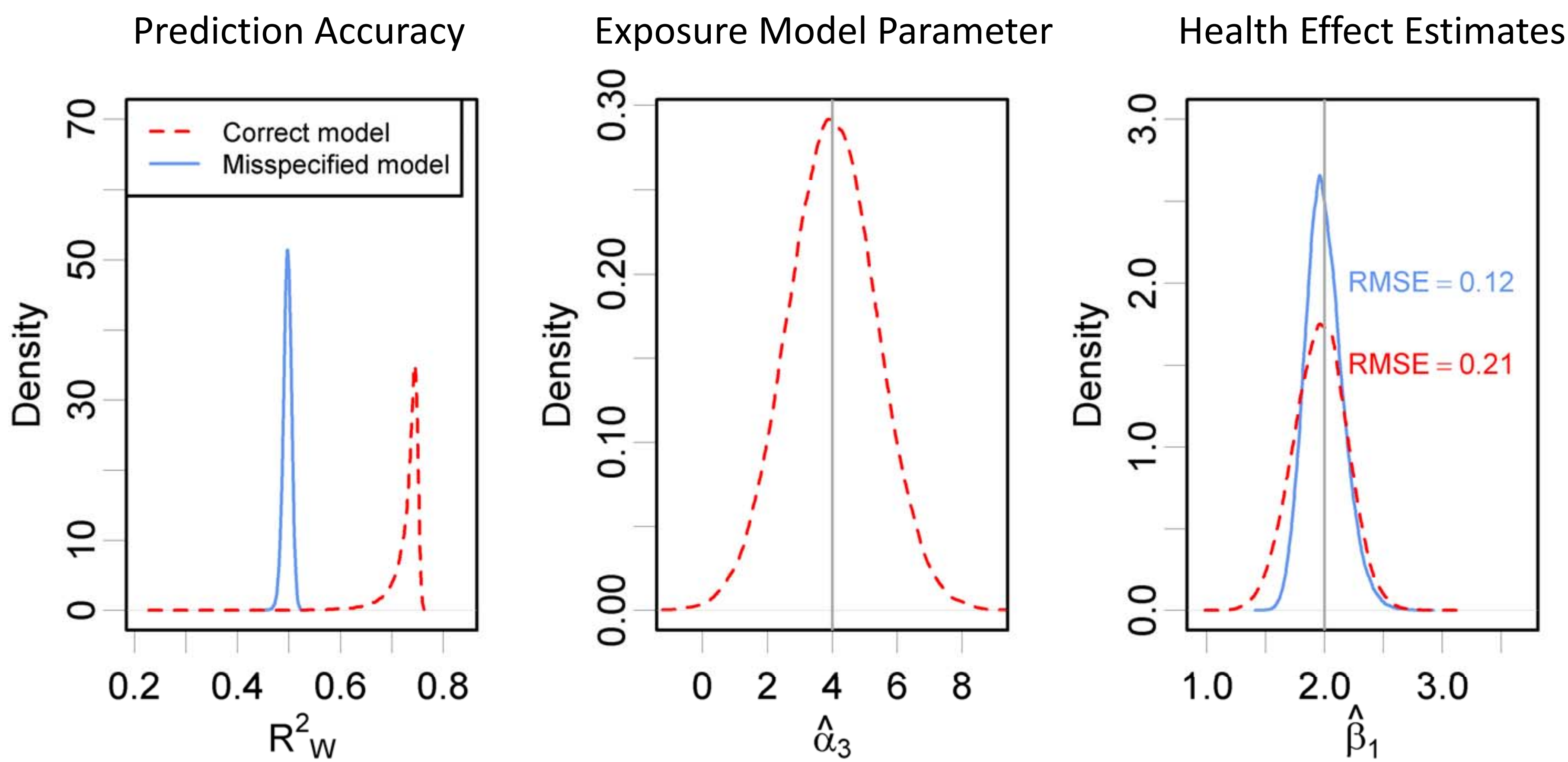
# Do better exposure predictions improve health effect estimation? *Often, yes*




- $\sigma^2 = 1$ (full range of covariates in monitoring data)
- $N$ = 10,000 subjects • $N^*$ = 100 monitors

Szpiro et al., *Epidemiology* (2011)

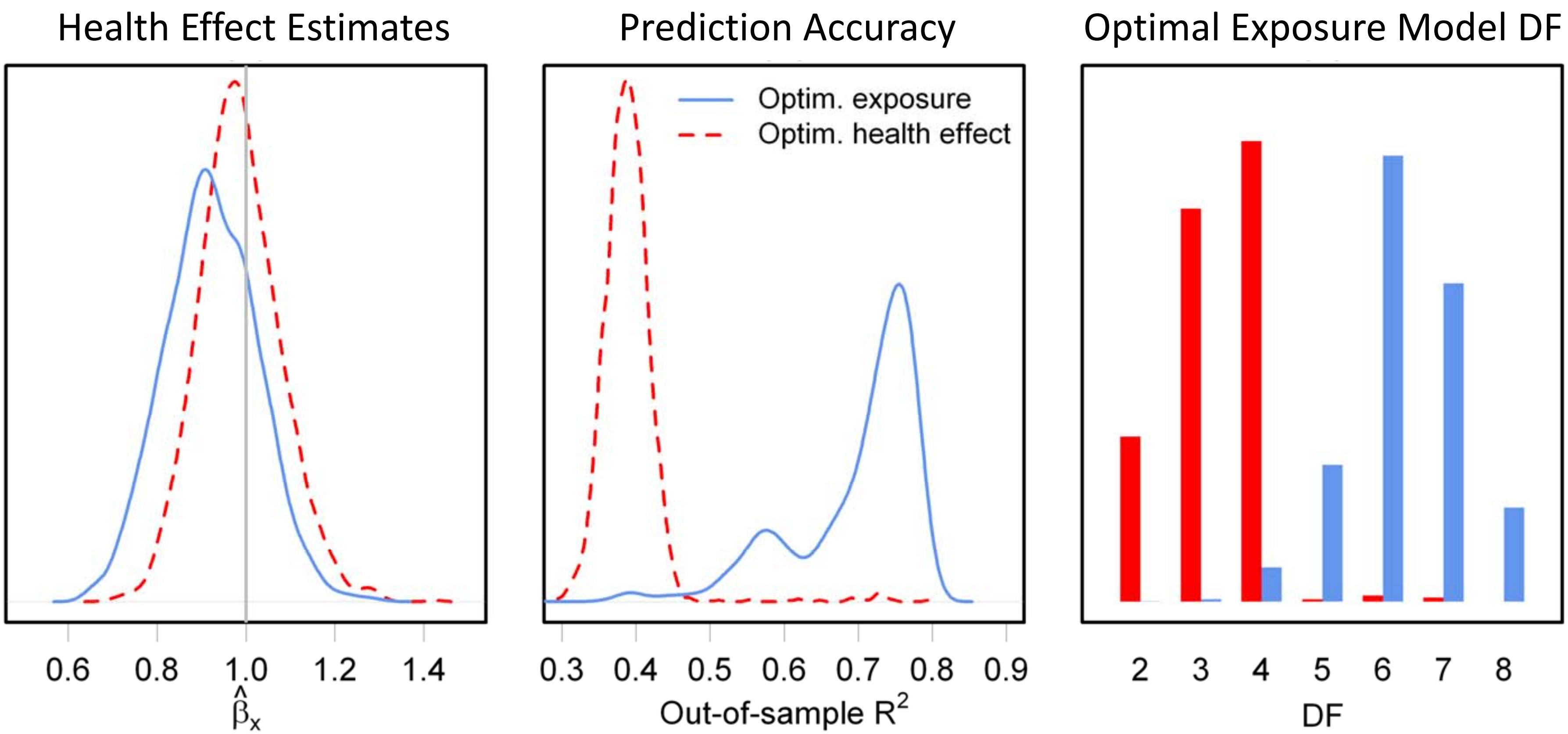
# Do better exposure predictions improve health effect estimation? *Not always*




- $\sigma^2 = 0.1$ (limited range of covariates in monitoring data)
- $N$ = 10,000 subjects
- $N^*$ = 100 monitors

Szpiro et al., *Epidemiology* (2011)

# Model selection example




- Correctly specified exposure model has 8 covariates
- Variable selection approach: LASSO pre-screening of low-rank regression splines

# Back to 3-step procedure: combining steps 1 and 2

High dimensional monitoring data → Eigenpollutant profiles + scores at monitor locations → Eigenpollutant scores at subject locations → Health effect analysis

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# Integrating sparse PCA and spatial exposure model ("spatial sparse PCA"?)

- Objectives of each step separately
  - Sparse PCA: describe most of the variability in $m$-dimensional monitoring data as linear combinations of $k$ sparse eigenpollutants
  - Multivariate spatial model: accurately predict as much of the $m$-dimensional multi-pollutant exposure surface as possible
- Combined objective
  - Accurately predict as much of the $m$-dimensional multi-pollutant exposure surface as possible as linear combinations of $k$ sparse eigenpollutants
- Could design a joint statistical model for steps 1 and 2
  - Not clear exactly what form this will take (is there a likelihood?), but knowing what we are trying to optimize is a great start
  - Interesting feature is that geographic covariates and monitor locations will contribute to specification of eigenpollutants

# Summary of our plans

- *Ultimately*, we plan to exploit mobile monitoring data (Project 1) to analyze MESA Air cohort (Project 5)
  - Very complex spatio-temporal monitoring data a major challenge on top of dealing with multi-pollutant mixtures
- *Initially*, we will work in a simpler setting where we can observe long-term averages at monitor locations (purely spatial exposure data) and don't have to worry about multiple cities
  - NIEHS Sister Study + CSN/IMPROVE monitoring data; data available now!
  - First implement three-step sequential procedure without propagating uncertainty
  - Improve methodology by combining sparse PCA with spatial prediction and by propagating uncertainty into health analysis with measurement error correction
- We will extend our methods to mobile monitoring data and MESA Air once we have made sense of the mobile data *and* developed multi-pollutant methods for the somewhat simpler spatial setting

# Cross-center collaborations

Other EPA Clean Air Research Centers (CLARCs)

- Emory/Georgia Tech (“SCAPE”)
- Harvard (“Harvard”)
- Michigan State/Michigan (“GLACIER”)

Collaboration specifics

- $50,000 per center per year
- Involves 2 or more CLARCs

Planning

- Discussed at the first CLARC annual meeting in May

# UW CLARC collaborations

- Mobile sampling in Atlanta (with Emory)
- Toxicology (with Harvard and Michigan State)
- Exposure measurement error correction (with Harvard and Emory)
- Satellite (remote sensing) data for $PM_{2.5}$ (with Emory and Harvard)

# Exposure measurement error correction

- With Harvard and Emory

- Georgia birth cohort endpoints and $PM_{2.5}$

- Common $PM_{2.5}$ exposure predictions based on LUR +/- satellite

- 3 statistical approaches (1/CLARC) for measurement error correction:
    - parameter bootstrap
    - simulation extrapolation
    - Bayesian

# Satellite $PM_{2.5}$ estimation

- With Emory and Harvard
- Standard set of data for North Carolina, 2006-08
- 6 candidate models for $PM_{2.5}$ prediction
  - Harvard x 2
  - Emory x 3 (incl CMAQ)
  - UW x 1 (spatio-temporal model)
    - assess added value of satellite data
- commons metrics for model evaluation

# Mobile sampling in Atlanta

- With Emory (SCAPE), following the Project 1 mobile monitoring in Winston-Salem – summer 2013

- J Sarnat doing a scripted commute health study with detailed in-vehicle monitoring

- Aims:
  1. compare instrumentation measures
  2. vehicle infiltration fractions
  3. complete another near roadway campaign

# Animal toxicology

- Michigan State (GLACIER) rat (mouse?) model of cardiometabolic syndrome
  - high fructose diet
  - Campen ex vivo endothelial cell assays

- Transfer animal model to Lovelace and Harvard
  - McDonald CCAR exposures and endpoints (incl. telemetry)
  - Godleski using Boston Tunnel exposure