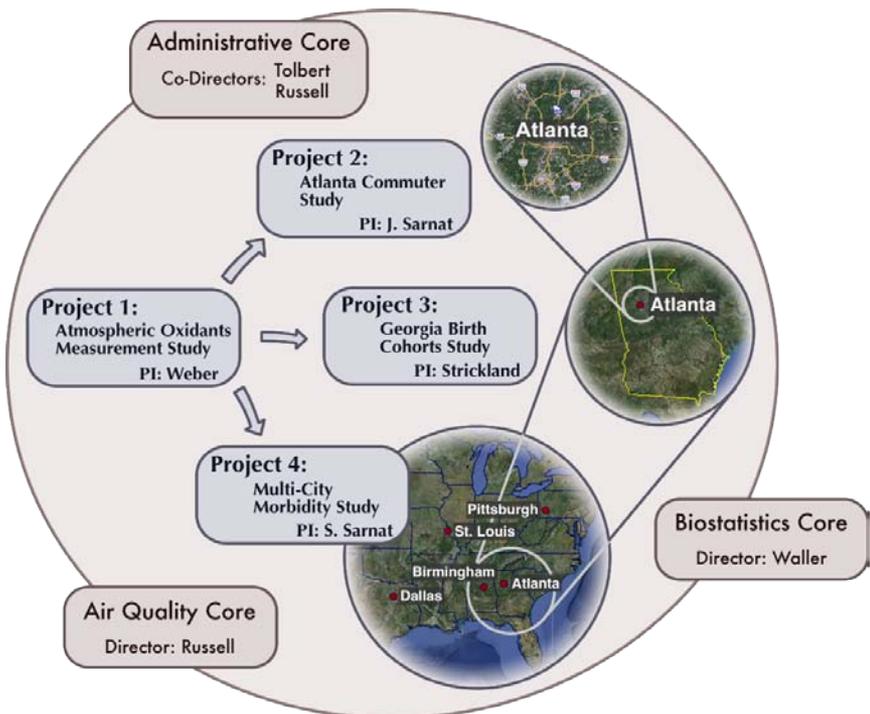


US EPA ARCHIVE DOCUMENT

Emory/Georgia Tech Clean Air Research Center



CLARCs Kick-Off Meeting

April 7-8, 2011

RTP, NC



Center Overview

- Objective
 - Using field measurements, modeling and epidemiologic approaches to improve our understanding of how air pollutant **mixtures** impact health
 - Advance beyond single pollutant approach (multispecies)
 - PM, ozone, metals, ...
 - Reactive oxygen species (ROS)
 - » Implicated in mechanistic studies
 - » Quinones, peroxides, some metals
 - Develop and apply methods to quantify source-air quality-health relationships

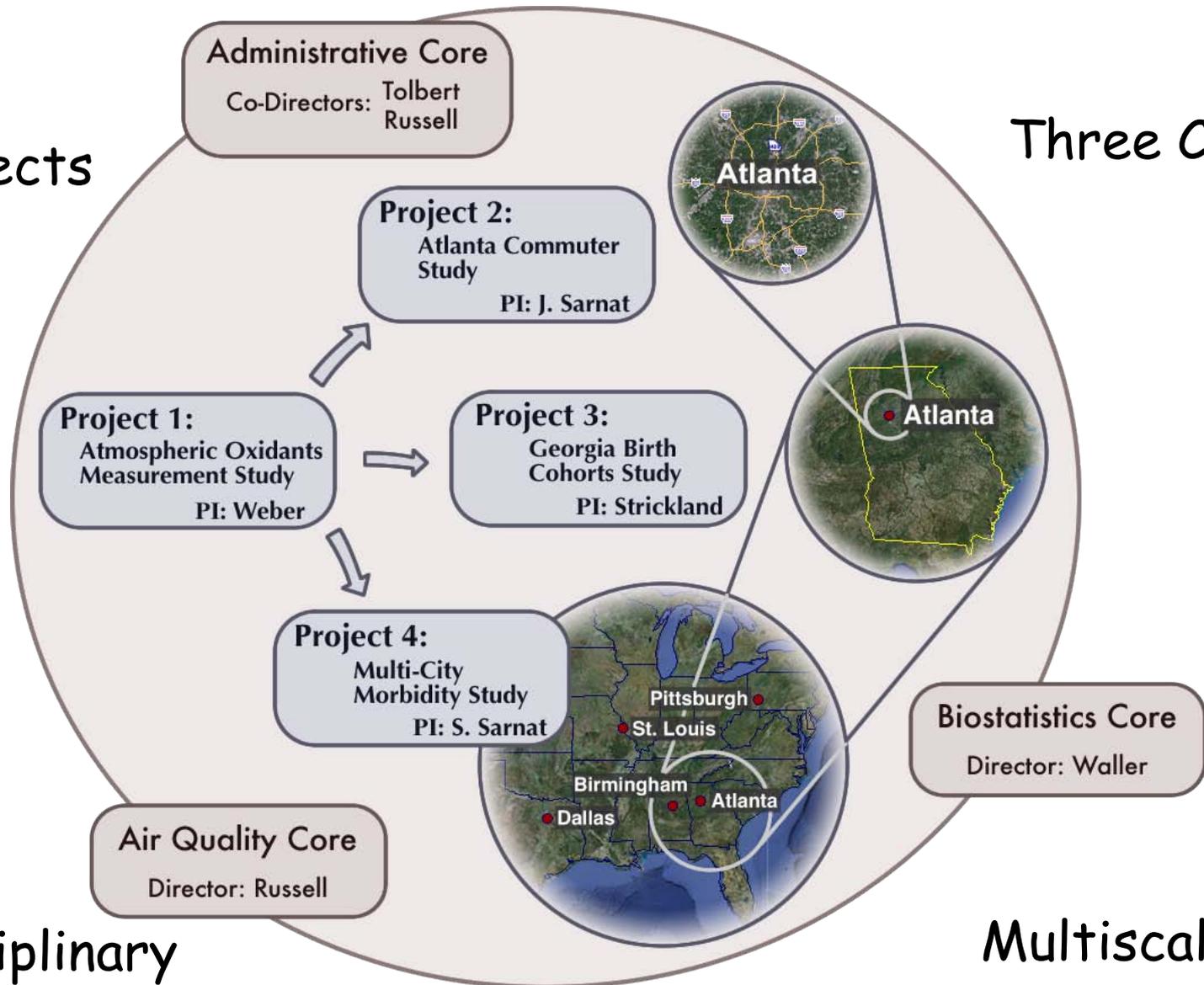
Center Themes

- **Characterize Mixtures from Multiple Perspectives**
 - *biologically-based perspective*
 - **assess the role of reactive oxygen species (ROS) and other oxidants as a group with potential biological activity relevant to oxidative stress-mediated responses**
 - *environmental management perspective*
 - **use state-of-the-art methods of source apportionment to better understand roles of groups of agents co-emitted from specific sources and their transformation products**
 - *evidence-based perspective*
 - **focus on vehicular emissions and near-roadway impacts, as accumulating evidence supports a major role for traffic**
 - *empirical perspective*
 - **apply data-based approaches to sort species and group them according to their associations with health endpoints of interest.**

Southeastern Center for Air Pollution and Epidemiology (SCAPE)

Four projects

Three Cores



Transdisciplinary

Multiscale

Air Quality Core

- Russell (Director), Hu, Odman, Mulholland
- Six support functions
 - Atmospheric data collection and management. Support of Projects 1-4.
 - Development of the Mixtures Characterization (MC) Toolkit
 - MC Toolkit includes processed and analyzed atmospheric data, analysis methods and air quality models
 - Use MC Toolkit for data analysis, model applications and interpretation of results. Support of Projects 2-4.
 - MC Toolkit provides
 - Analyzed species concentrations across scales
 - » Tools to estimate local concentration based on sparse observational network and air quality modeling tools
 - » Network limited in terms of spatial, temporal and species limitations
 - Source impacts
 - Apply CMAQ to characterize pollutant concentrations, sources and variations. Support of Projects 1- 4.
 - Integrate satellite remote sensing into health studies and air pollutant mixture characterization. Support of Project 3.
 - Assess exposure misclassification across scales and source regions. Support of Projects 3, 4.

Center Projects

Project 1: Development and Deployment of an Instrumentation Suite for Comprehensive Air Quality Characterization including Aerosol ROS

Investigators

Georgia Tech: Weber, Bergin, Mulholland, Nenes, Verma

Emory: J. Sarnat, S. Sarnat, Strickland

Project 1 Goals

Part A. Develop instrument for semi-continuous measurement of ROS.

Part B. Characterize multi-pollutant atmosphere with a suite of existing and new methods with focus on near-real-time chemical data to better characterize sources, evolution and associations between components of a multipollutant atmosphere.

Project 1: Atmospheric Oxidants Measurements Study

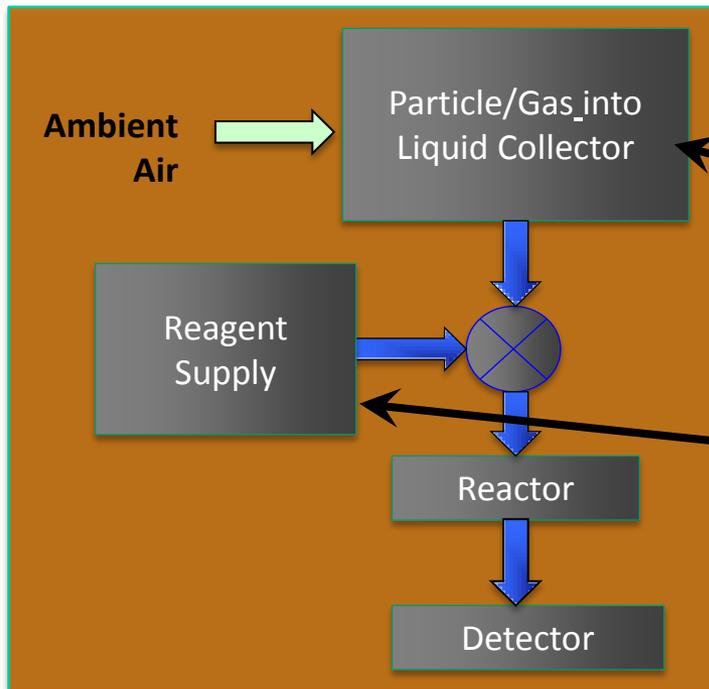
Part A: Online ROS Method

- Why online vs offline:
 - Reduce artifacts (ROS: volatile, reactive, short lifetime ?)
 - Investigate links to other species/sources and ROS evolution
 - Instrument for in vehicle studies (Project 2)
- GOAL: develop a simple robust system for extensive field deployments adaptable to different ROS chemical probes

Project 1: Atmospheric Oxidants Measurements Study

Part A: Online ROS Method

General Approach



ROS Method Development

Develop/Test systems for collection of $PM_{2.5}$ ROS and Gas-phase ROS

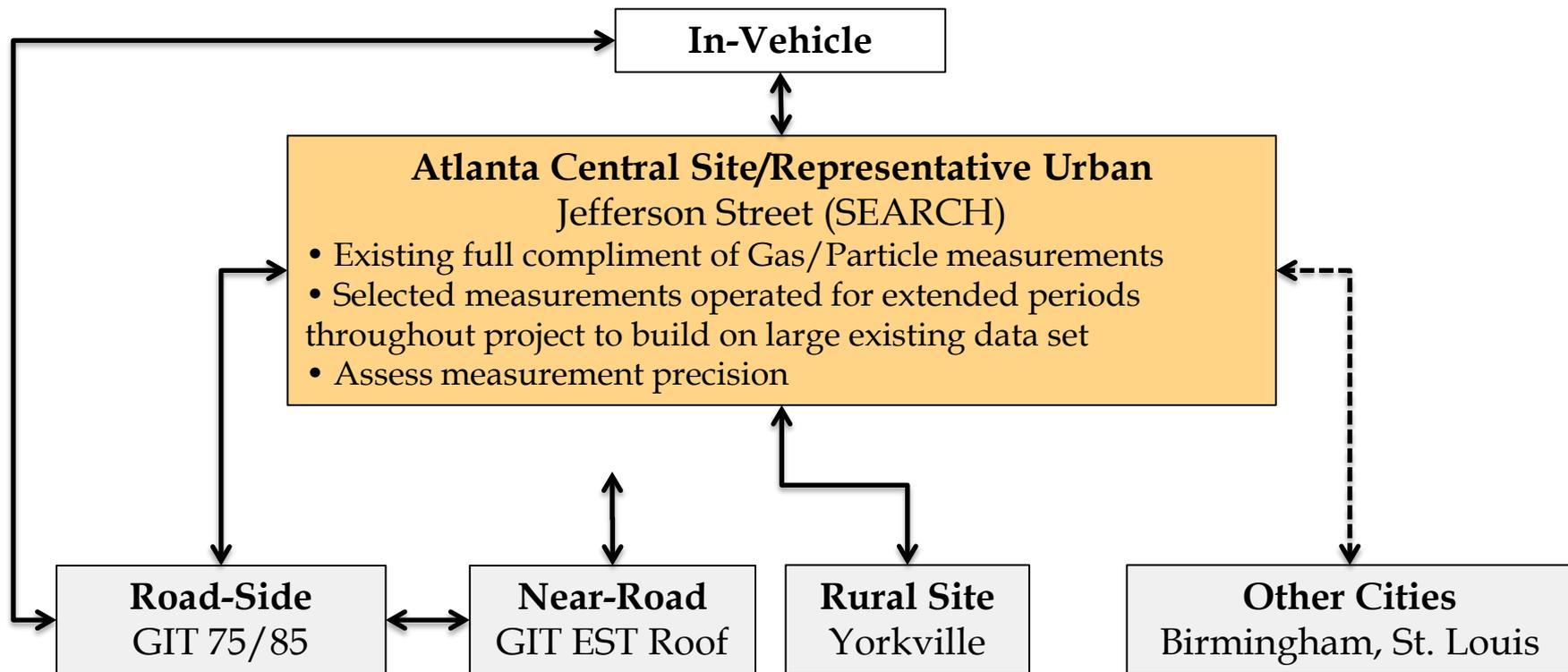
- PILS, Mist Chamber, Scrubbing Coil

Develop/Test Various Chemical Probes

- Chemically comprehensive vs specific

Project 1: Atmospheric Oxidants Measurements Study

Part B: Ambient Measurements



When: 3-4 weeks per pair, repeated during different seasons

Project 1: Atmospheric Oxidants Measurements Study

Part B: Ambient Measurements

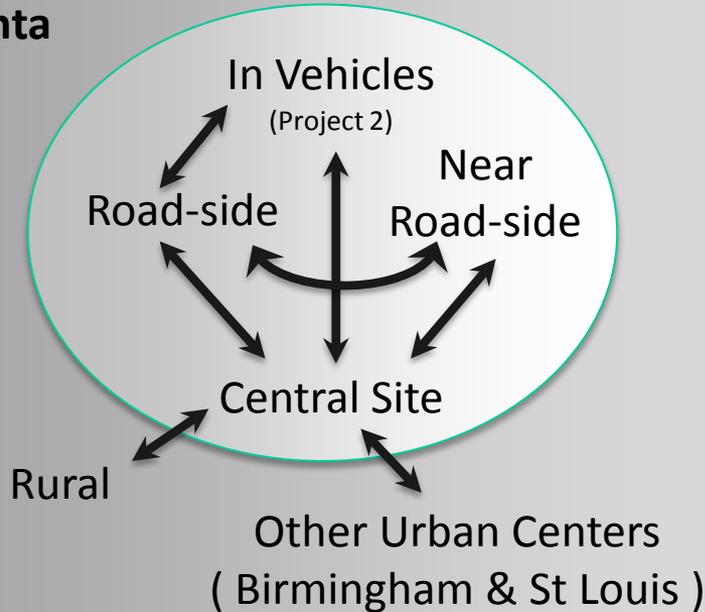
Online ($\leq 1\text{hr}$) **Offline**

Where: "Main" Site	Where: "Secondary" Site * Project 2: In vehicle
<p>Met Mass TEOM PM2.5, PM10 (Vol to Mass) compact OPC BC compact Aeth. OC EC WSOC, WIOC PM1.0 Inorganic Ions, OM, OOA, HOA, Mass: AMS ROS Surface PAHs (EcoChem) Ultrafine N dist'n 0.01-0.5 um WS_Fe(II)</p> <p>Filter: Ions/Metals/OCEC HiVol Filter: OA speciation (GC-MS)</p> <p>VOCs/CO2/CO Whole air cans (Irvine) NOx, O3</p>	<p>Met Mass TEOM PM2.5, PM10 (Vol to Mass) compact OPC * BC compact Aeth. *</p> <p>WSOC, WIOC</p> <p>ROS * Surface PAHs (EcoChem)* Ultrafine N dist'n 0.01-0.5 um</p> <p>Filter: Ions/Metals/OCEC/WSOC* HiVol Filter: OA speciation (GC-MS)</p> <p>VOCs/CO2/CO Whole air cans (Irvine)* NOx</p>

Project 1 Summary

Characterize Multipollutant Mixtures with State-of-the-Art Air Quality Instruments

Atlanta



Research Objectives:

1. ROS characterization:
temporal, spatial, relationships with other pollutants
2. Multipollutant atmosphere characterization:
relationships amongst pollutants as a function of site location, time of day/season

Overall Research Question

How do air pollutant mixtures vary by location and what chemical and physical processes influence these differences?

Project 2: Atlanta Commuter Study

Investigators

Emory: J. Sarnat, Brown, Fitzpatrick, Flanders,
Greenwald, Winqvist, Wongtrakool

Georgia Tech: Bergin, Guensler

Project 2 Overview

- Outgrowth of Atlanta Commuters Exposure (ACE) Study (CDC)
- Examine the associations between pollutant mixtures during automobile commuting and corresponding oxidative stress-mediated pathways of cardiorespiratory injury
- Panel study with 30 healthy and 30 asthmatic adults
 - Characterize in-vehicle pollutant levels
 - Measure biomarkers (e.g., glutathione) in subjects
 - Before, during & after prescribed commutes
- Improved understanding of mechanisms of toxicity, microenvironmental (μ E) exposures, mixtures associated with oxidative stress
 - Assess how underlying health status modifies risk

Project 2 Biomarkers



↓ LUNG FUNCTION

SPIROMETRY

↑ ENDOGENOUS ROS

↑ GRANULOCYTE INFILTRATION

eNO

↑ CYTOKINES/PROTEINS

CRP , IL-6 (BLOOD)



PROCESS

BIOMARKER

OXIDANT INSULT
O₃, NO₂, PAHS, METALS,
EXOGENOUS ROS

⇒ ENDOGENOUS ROS

↑ ANTIOXIDANT

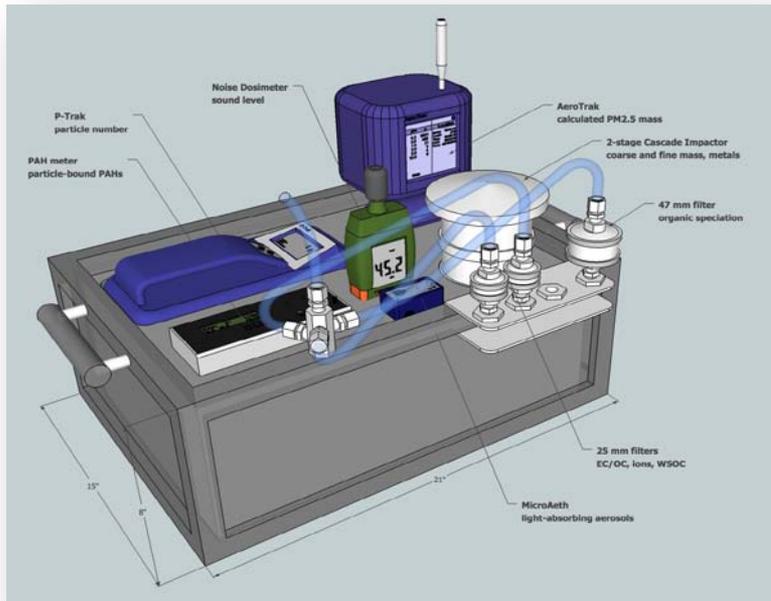
GSH/GSSG (EBC)

↑ LIPID PEROXIDATION

Malondialdehyde, 8-Isoprostane (EBC)



Project 2 In-Vehicle Measurements



Pollutant	Temporal resolution	Instrument	Analytical Method
Coarse and fine mass	2 hr.	CCI ^a	Gravimetric
Trace elements	2 hr.	CCI	ICP-MS ^b
Organic speciation	2 hr.	47 mm quartz filter	TD-GC/MS ^c
EC/OC ^d	2 hr.	25 mm quartz filter	TOT ^e
WSOC ^f	2 hr.	25 mm quartz filter	TOC ^g
Ionic species	2 hr.	25 mm quartz filter	Ion Chromatography
ROS ^h (integrated)	2 hr.	25 mm quartz filter	Fluorescence
ROS (continuous)	5 min.	PILS-ROS ^j	Fluorescence
PM _{2.5} mass	1 min.	TSI AeroTrak	OPC ^k
Light-absorbing aerosols	1 min.	Magee MicroAeth	Filter transmittance
Number Concentration	1 min.	TSI P-Trak	CPC ^l
Particle-bound PAHs ⁱ	10 sec.	EcoChem PAS 2000CE	Photoionization
Noise	1 sec.	Extech HD600	Noise dosimeter

Project 2 Sampling Design

Day 1

Day 2

7:00 PM	7:00 ^a AM	9:00* AM	10:00* AM	11:00* AM	12:00* PM	7:00 ^a PM	7:00 ^a AM	9:00* AM	10:00* AM	11:00* AM	12:00* PM	7:00 ^a PM
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Location: Subject home Subject home Clinic (Emory) Subject work/home Clinic (Emory) Subject work/home

Activity: Sampler set-up **Scripted Commute or Clinic visit** Hourly health measurements Regular activities **Scripted Commute or Clinic visit** Hourly health measurements Regular activities

Schematic of two-day sampling period for each subject.

- ^a Indicates collection of invasive (i.e., venipuncture) and non-invasive health measurements.
- * Indicates collection of non-invasive health measurements only.

Project 2 Summary

Characterize in-vehicle exposure

Direct measurements (e.g., ROS)

Source apportionment



Characterize response

Examine links between mixtures and biomarkers of acute oxidative stress during 2 hour commute

PROCESS

BIOMARKER

OXIDANT INSULT
O₃, NO₂, PAHS, METALS,
EXOGENOUS ROS

⇒ ENDOGENOUS ROS

↑ ANTIOXIDANT

GSH/GSSG (EBC)

↑ LIPID PEROXIDATION

8-ISOPROSTANE (EBC)

↑ ENDOGENOUS ROS

↑ GRANULOCYTE INFILTRATION

ENO

↑ CYTOKINES/PROTEINS

CRP (BLOOD)

↓ LUNG FUNCTION

SPIROMETRY

Panel study

Healthy adults

Asthmatic adults

How do measured in-vehicle pollutant mixtures relate to cardiorespiratory markers in commuting drivers?

Project 3: Novel Estimates of Pollutant Mixtures and Pediatric Health in Two Birth Cohorts

Investigators

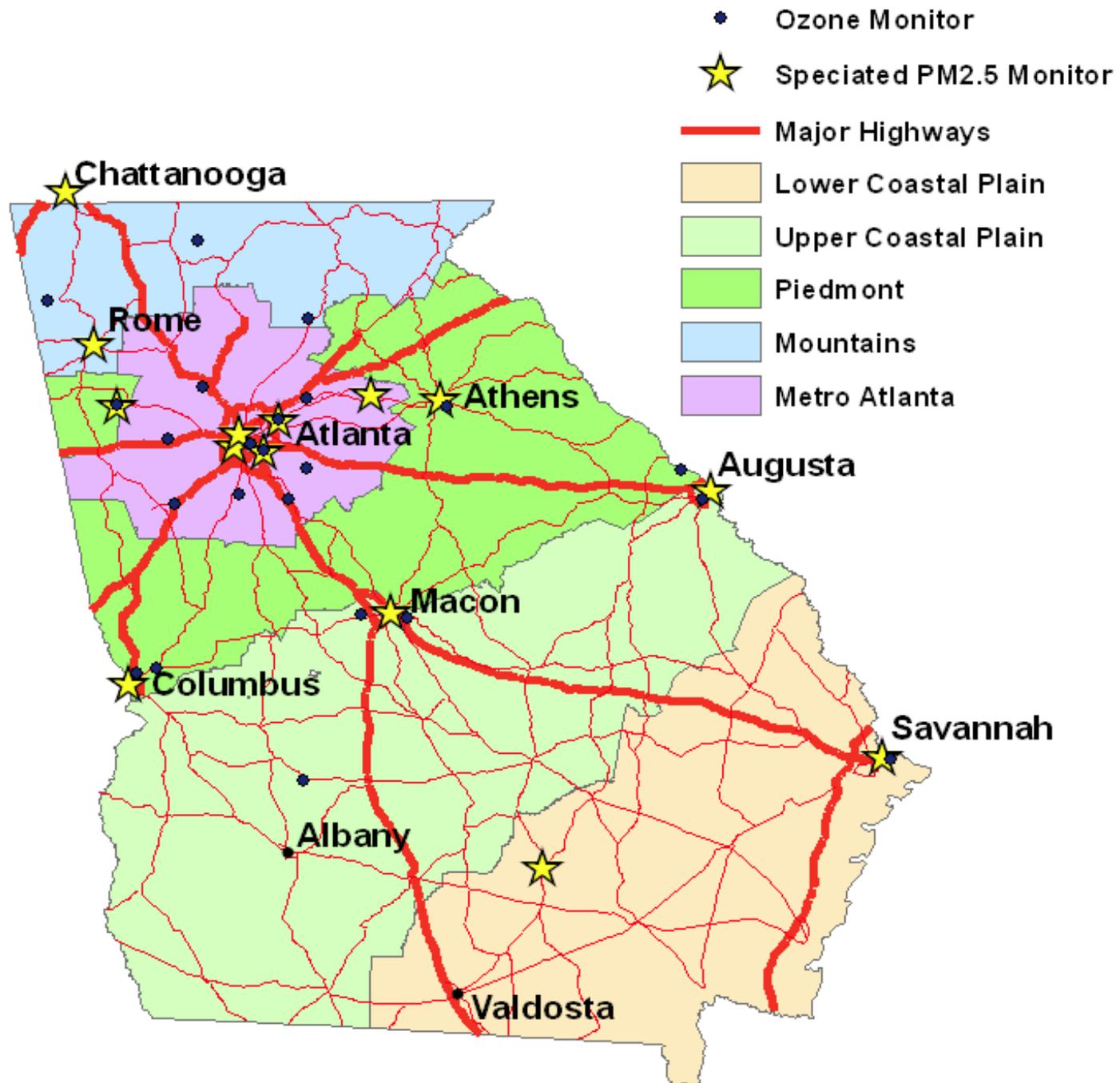
Emory: Strickland, Darrow, Klein, Liu, Waller

Georgia Tech: Guensler, Mulholland, Russell

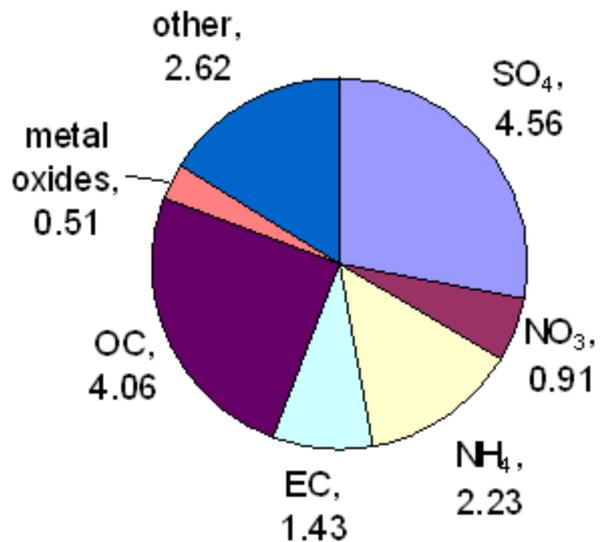
Kaiser Permanente: Davis

Project 3 Overview

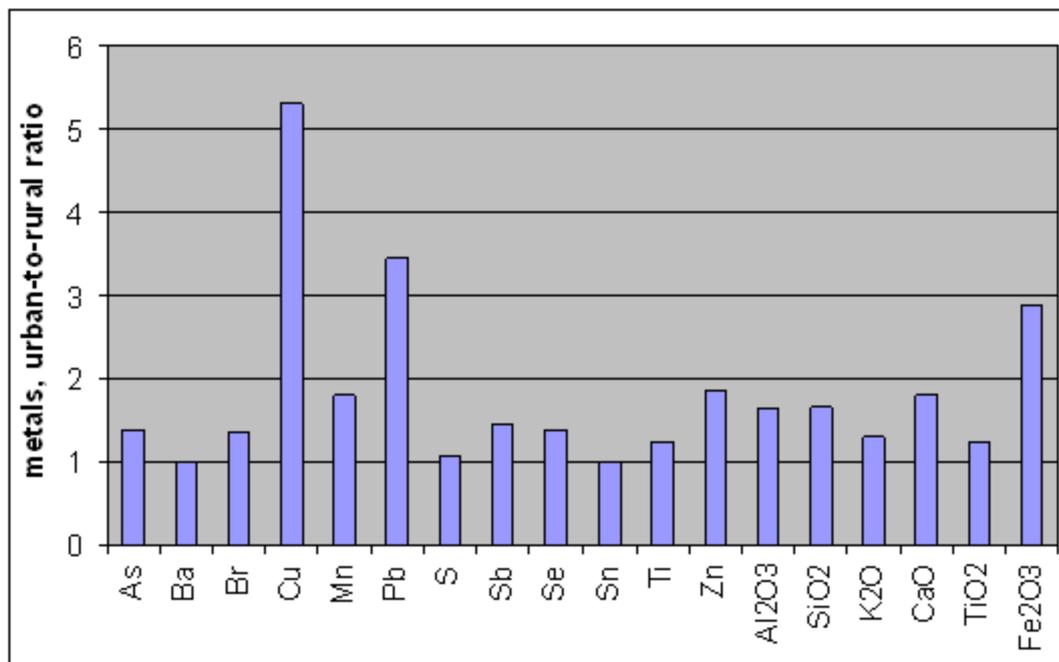
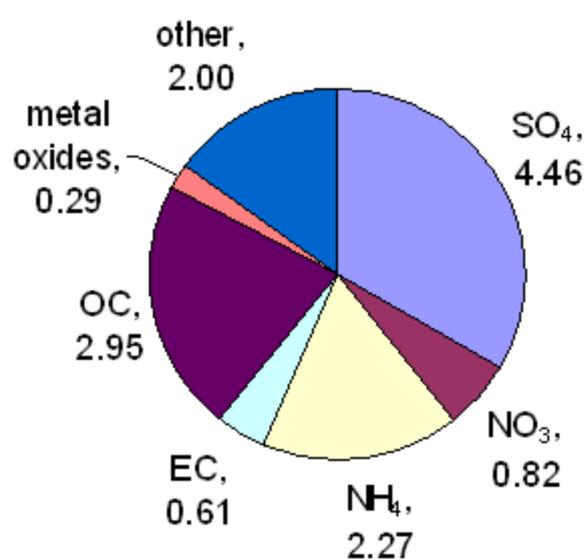
- Health data from two different cohorts:
 1. Birth records linked with emergency department visits in Georgia
 2. Newborns covered by Kaiser Permanente insurance in Atlanta
- Utilize characterizations of the multi-pollutant atmosphere developed through the Air Quality Core and Study 1
 1. CMAQ-receptor data assimilation for spatial interpolation
 2. PM_{2.5} source apportionment
 3. CMAQ-MOBILE MATRIX/CALINE for near-roadway gradients
 4. Satellite remote sensing for regional air quality information and characterization of biomass burning events
 5. Measurement & modeling of reactive oxygen species (ROS)



Atlanta (urban) PM_{2.5}, 16.3 μg/m³



Yorkville (rural) PM_{2.5}, 13.4 μg/m³



Georgia Birth Cohort

- Statewide birth records (1994-2010)
 - Maintained by Georgia Department of Community Health
 - ~ 2.3 million births (1/8 preterm)
- Statewide emergency department visits (2002-2010)
 - Maintained by Georgia Hospital Association
 - ~ 8.8 million pediatric emergency department visits
(175,000 asthma visits; 206,000 otitis media)

Linked by the Georgia Department of Community Health



Georgia Birth Cohort Objectives

1. Investigate relationships between ambient air pollutant mixtures during pregnancy and risk of preterm delivery and reduced birth weight.

2. Investigate short-term relationships between ambient air pollutant mixtures and pediatric emergency department visits for:

- Bronchiolitis and wheeze in infants and toddlers
- Otitis media (ear infections) in infants and toddlers
- Asthma in children age 5 years and older

and investigate whether these relationships are modified by gestational age or birth weight.

Kaiser Permanente Birth Cohort

Kaiser Permanente Georgia

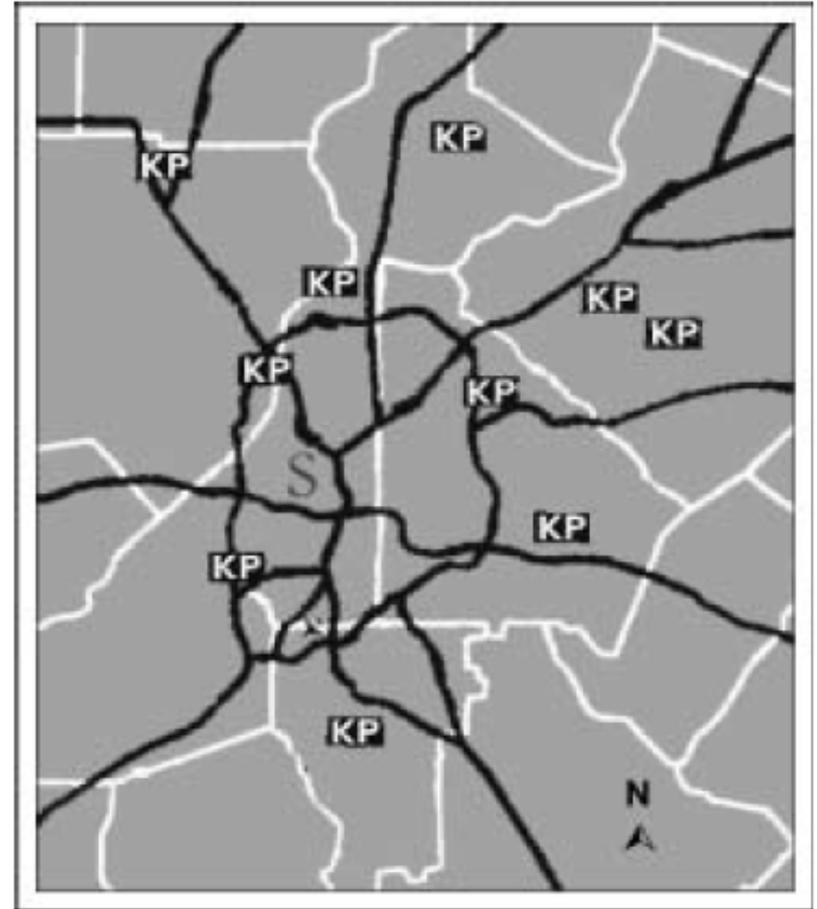
~ 250,000 members at any time

- 54% White
- 35% Black
- 3% Hispanic
- 11% Other

~ 3,000 births per year

2000-2006 birth cohort

- 21,326 births
- 52% enrolled through age 3
- 44% enrolled through age 5
 - 12% asthma diagnosis



J. Air & Waste Manage. Assoc. 54:1212-1218

Center will use the 2000-2008 birth cohort

Kaiser Permanente Birth Cohort Objective

Investigate longer-term relationships between ambient air pollutant mixtures during the first year of life and incident asthma in childhood.

Project 3 Summary

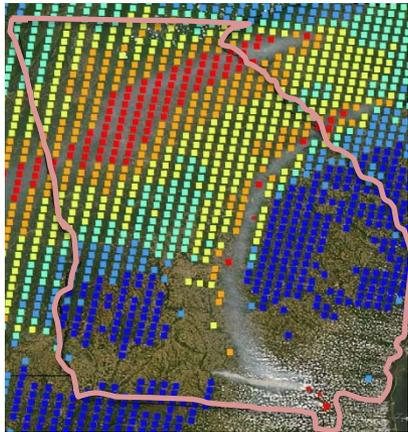
Characterize pollutant mixture

Direct measurements

Satellite remote sensing

Atmospheric modeling
(e.g., ROS)

Source apportionment



During pregnancy

Preterm delivery,
low birth weight

**Acute and
Longer-term**

Asthma,
bronchiolitis,
otitis media

Create two birth cohorts

Georgia Cohort:
Birth records linked with
ED visits

Kaiser-Permanente Cohort:
Children covered by the
HMO from birth through
early childhood



What is impact of *in utero* and early childhood air pollution on children's health?

Project 4: A Multi-City Time-Series Study of Pollutant Mixtures and Acute Morbidity

Investigators

Emory: S. Sarnat, Darrow, Winquist, Klein, Tolbert

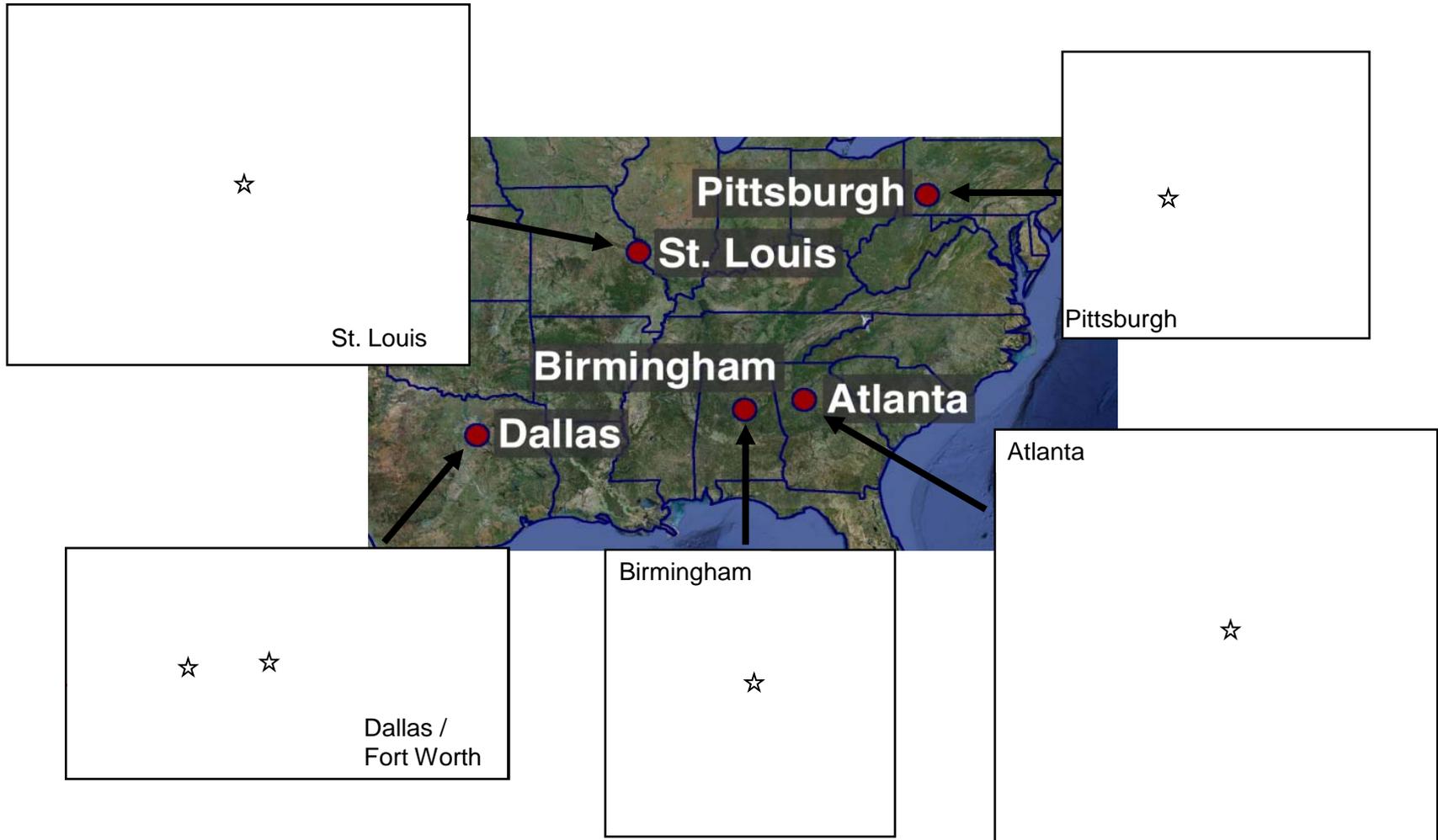
Georgia Tech: Mulholland, Russell

Project 4 Overview

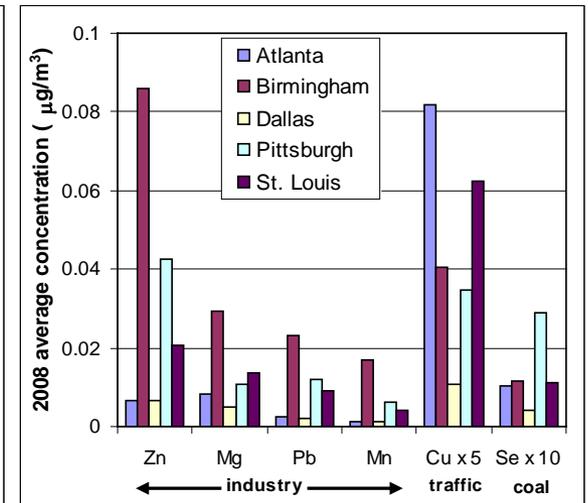
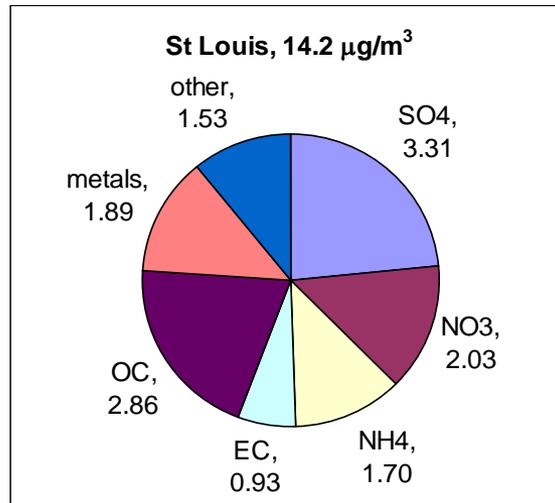
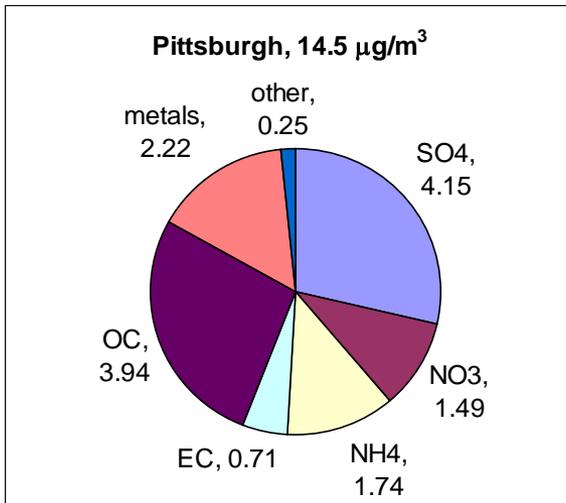
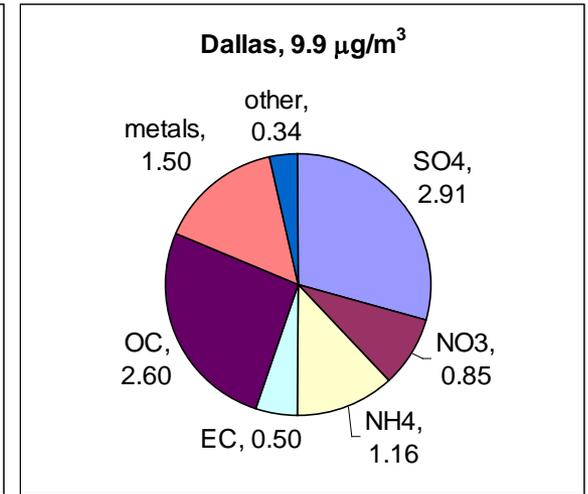
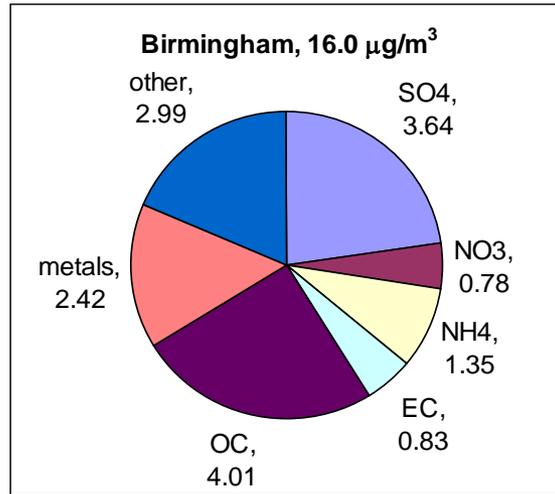
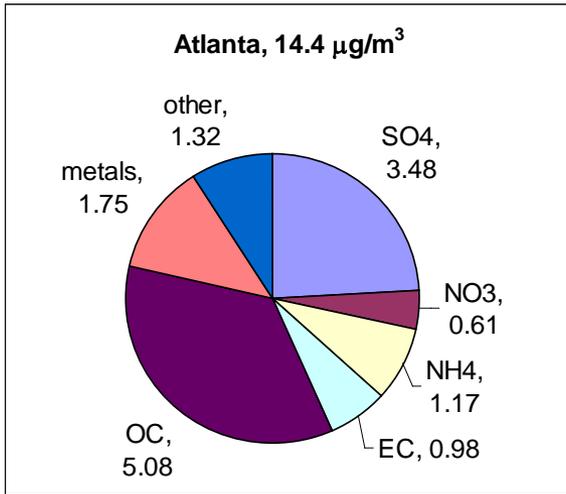
- A multi-city time-series study to clarify the impacts of air quality on acute cardiorespiratory severe morbidity in five US cities
 - Using data on emergency department (ED) visits and hospital admissions (HAs)
- To assess generalizability of Atlanta results to other locations
- Examine and explain heterogeneity of associations across cities

Project 4 Cities

- Extensive and well-characterized air quality and health outcome databases
- Relatively high PM levels and heterogeneity in source strengths



Average 2008 STN PM_{2.5} data



Project 4 Mixture Characterization Metrics

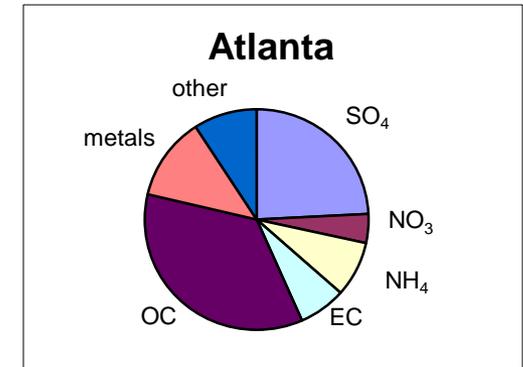
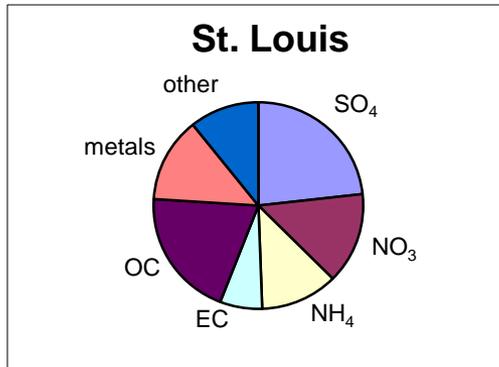
- 1) Population-weighted averages and spatially-resolved concentrations
- 2) Single-species source tracer data
- 3) PM_{2.5} source apportionment outputs using CMB approaches
- 4) Factor analysis outputs using PMF and UNMIX
- 5) Modeled ROS/oxidant levels developed in Project 1
 - Build ROS prediction model for Atlanta
 - Apply and validate model in Birmingham and St. Louis
 - Apply model in Dallas and Pittsburgh

Project 4 Analysis Objectives

Examine and explain heterogeneity of associations across cities:

- Apply multi-pollutant air pollution mixture models
- Examine season and temperature specific effects
- Assess and compare concentration-response functions
- Assess and compare impacts of exposure measurement error
- Assess and compare associations in susceptible/vulnerable populations

Project 4 Summary



Characterize daily pollutant mixtures

Direct measurements

Atmospheric modeling (e.g., ROS)

Source apportionment

Conduct multi-city epidemiologic analysis

Examine impacts of air pollution mixtures on acute severe morbidity

Examine and explain heterogeneity of associations across cities

Characterize populations and health outcomes

ED visits

Hospital admissions

Sociodemographic and housing factors

How and why do associations between air pollution mixtures and acute morbidity vary across cities?

Biostatistics Core

- Waller (Co-Director), Flanders (Co-Director), Klein
- Methodological development
 - Develop methods for identification of model misspecification
 - Develop methods to assess measurement error
 - Empirical mixtures approaches:
 - Adapt methods for analyses of time series:
 - » Regression: Multiple interaction terms (shrinkage techniques such as LASSO used for model stabilization)
 - » Classification and regression tree (CART) analysis used to identify levels of air pollution that best characterize high risk days
 - Adapt principal component methods for identifying mixtures that associate with health outcomes
 - » After detrending, which pollutant residuals load with outcome residuals?

