Harvard/EPA PM Center

Novel Exposure Scenarios to Define the Health Effects of Particle Sources

Harvard University
University of Toronto
University of Michigan
Brigham & Women's Hospital
Veteran's Administration

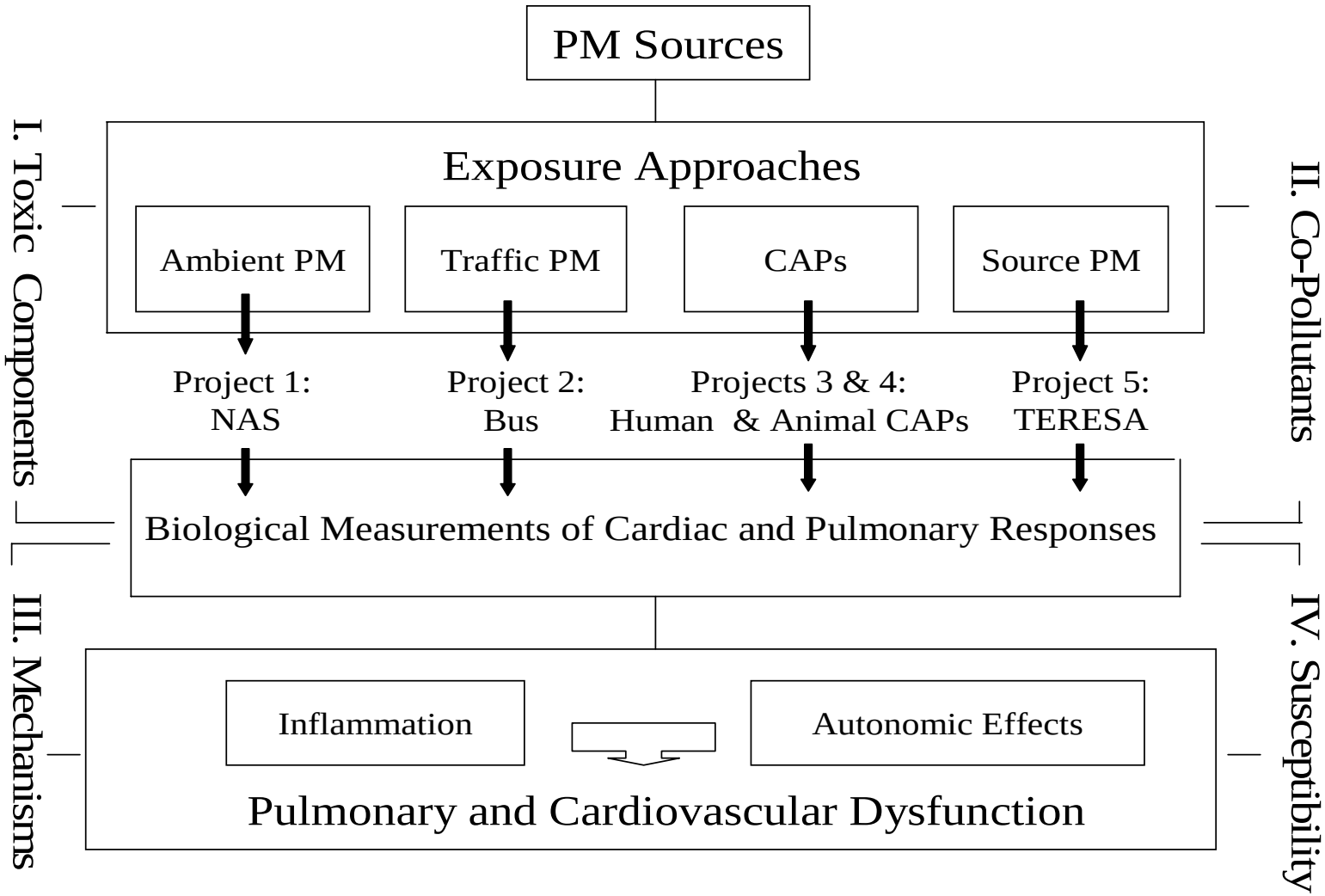
Investigators

Petros Koutrakis (PI), Robert Brook
Jeff Brook, Brent Coull,
Phil Demokritou, Douglas Dockery,
John Godleski, Diane Gold,
Beatriz Gonzalez-Flecha,
Joel Schwartz, Frances Silverman,
Frank Speizer, Peter Stone,
Helen Suh, Pantel Vokonas
Bruce Urch

IMPORTANT QUESTIONS

- Do PM exposure-response relationships depend on particle composition, size, formation processes and origin **(toxic components)**?
- What are the effects of gaseous **co-pollutants** on the observed PM exposure-response relationships?
- What are the **biological mechanisms** whereby PM exposures can induce inflammation and autonomic responses that lead to pulmonary and/or cardiac dysfunction?
- Are certain individuals more **susceptible** to PM due to their health condition, age, genetic characteristics and/or nutritional factors?

Linking inflammation, autonomic effects and vascular dysfunction to PM sources



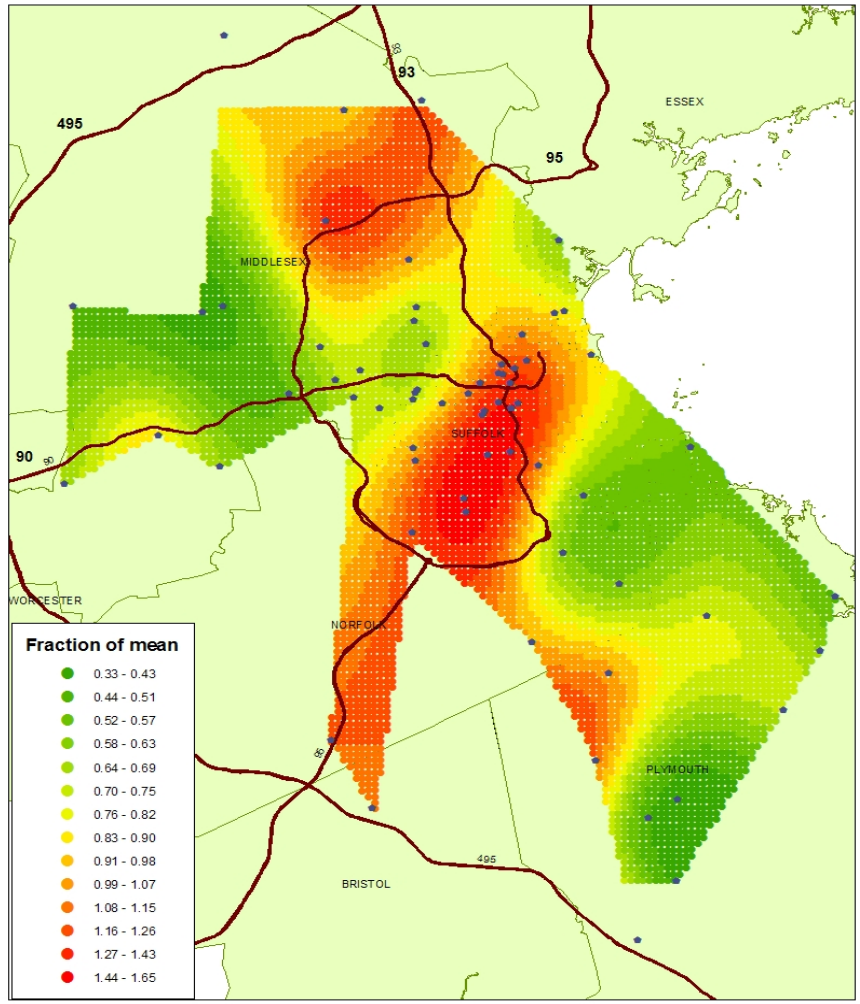
Project 1

Cardiovascular Responses in the Normative Aging Study: Exploring the Pathways of Particle Toxicity

PI: Joel Schwartz

Normative Aging Study (NAS)

- A large prospective cohort of 700 participants living in Eastern Massachusetts
- Health monitoring by VA Hospital
- PM2.5/BC associations with decrements in HRV
- BC associations with increased CRP and fibrinogen levels



Study Objectives

- Investigate associations between exposures and:
  - **Acute inflammation and/or endothelial dysfunction** (CRP, sICAM-1 and sVCAM-1)
  - **Autonomic dysfunction** (HRV)
  - **General cardiovascular responses** (BP and ECG)
- Examine the role PM composition on the observed cardiovascular

Study Objectives

- Examine if PM effects will be modified by subject characteristics (genetic, dietary, or pharmacological) that influence susceptibility to:
  - **Oxidative stress, endothelial dysfunction, and/or acute inflammation** (GSTM1 null or HO-1 genotypes; statin, beta blocker, or calcium channel blocker use, Vitamin C or Ω-3 fatty acids use)
  - **Autonomic dysfunction** (beta blocker, calcium channel blocker or Ω-3 fatty acids)
  - **General cardiovascular disease** (hypertension)
  - **Reactive airways disease** *(*methacholine reactivity)

Study Design

- Individual health data will be collected
  - ECG
  - Blood inflammatory markers
  - Medication use
  - Genes
  - Food frequency
- Individual-specific exposures will be measured inside each participant's home for one-week
- Ambient air pollution will be measured at our stationary ambient monitoring site

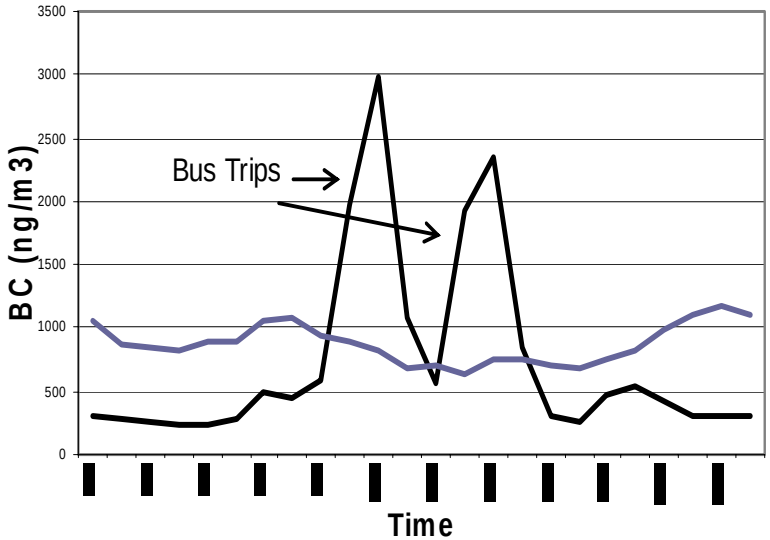
Project 2

Cardiovascular Effects of Mobile Source Exposures: Effects of Particles and Gaseous Co-pollutants

PI: Helen Suh

St. Louis Study Results

- Associations between
  - BC and eNO
  - PM2.5/BC and blood inflammatory markers
  - PM2.5 and HRV



Study Objectives

- Examine whether PM and/or gaseous traffic pollutants are associated with autonomic dysfunction and pulmonary and systemic inflammation

Boston Bus Study Design

- A crossover study of 36 older adults (likely with coronary artery disease)
- 3 sessions of 12 individuals will be exposed to
  - PM plus gaseous motor vehicle pollution or
  - only gaseous motor vehicle pollution (Bus with filters)
  - a month latter the individuals will switch buses

Study Design

- Before, during, and after each trip, participants will be monitored for
  - HRV (autonomic function)
  - eNO (pulmonary inflammation)
  - Blood markers (systemic inflammation)
- Personal group-level measures BC, PC, PM, O3, NOx and CO will be measured before, during and after each trip

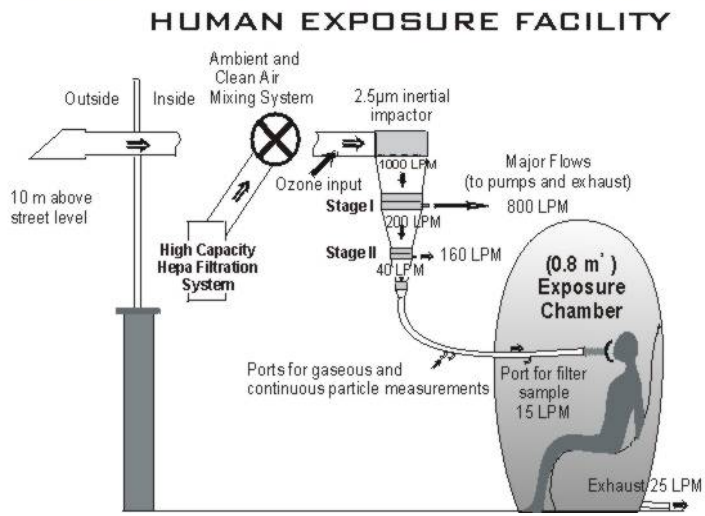
Project 3

Cardiovascular Toxicity of Concentrated Ambient Fine, Ultrafine and Coarse Particles in Controlled Human Exposures

PI: Frances Silverman

Previous Findings

- Healthy adults were exposed to fine CAPs + O3
  - Acute conduit artery vasoconstriction
  - Increased diastolic blood pressure



Study Objectives

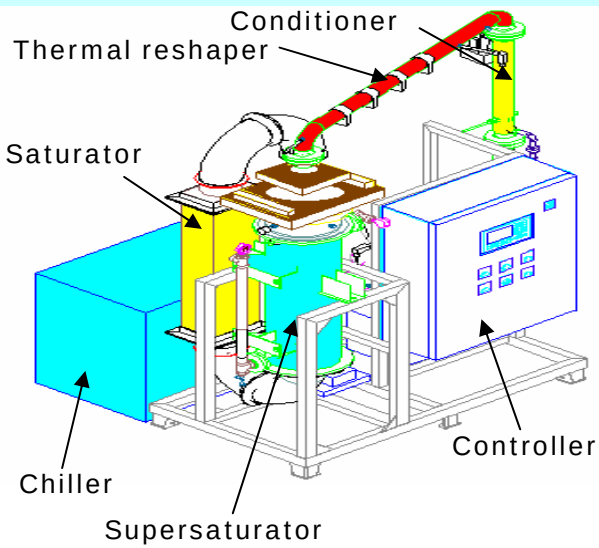
- Investigate the cardiac effects of Ultrafine, Fine and Coarse CAPs
- Investigate the effects of particle composition

Study Design

- 50 healthy adults will be exposed to UF, F and C CAPs and filtered air in a random sequence
- UF and C particle concentrators will be built and installed at the University of Toronto

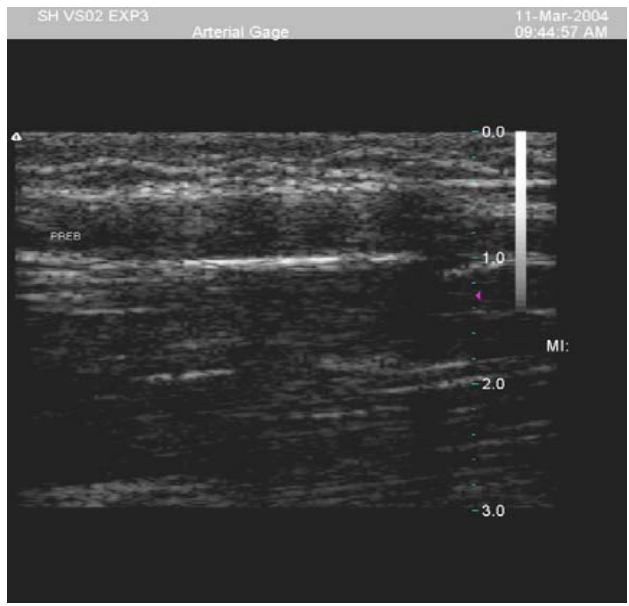
Harvard Ultrafine Particle Concentrator (HUCAPS)

Condensational Growth → **Concentration** → **Size restoration**



Study Design

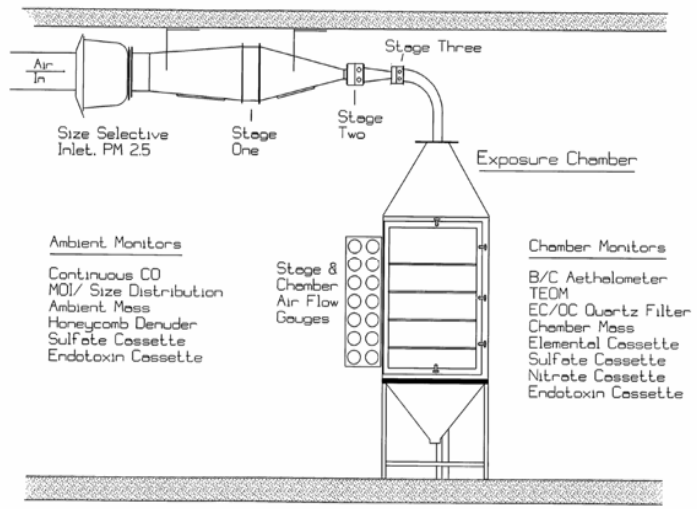
- Biological outcomes will include:
  - Vascular narrowing (brachial artery diameter)
  - Autonomic dysfunction (HRV)
  - Inflammation (IL-6, CRP)
  - Endothelial activation (endothelins)



Project 4

Assessing Toxicity of Local and Transported Particles Using Animal Models Exposed to CAPs

PI: John Godleski



Previous CAP Studies (since mid 90s)

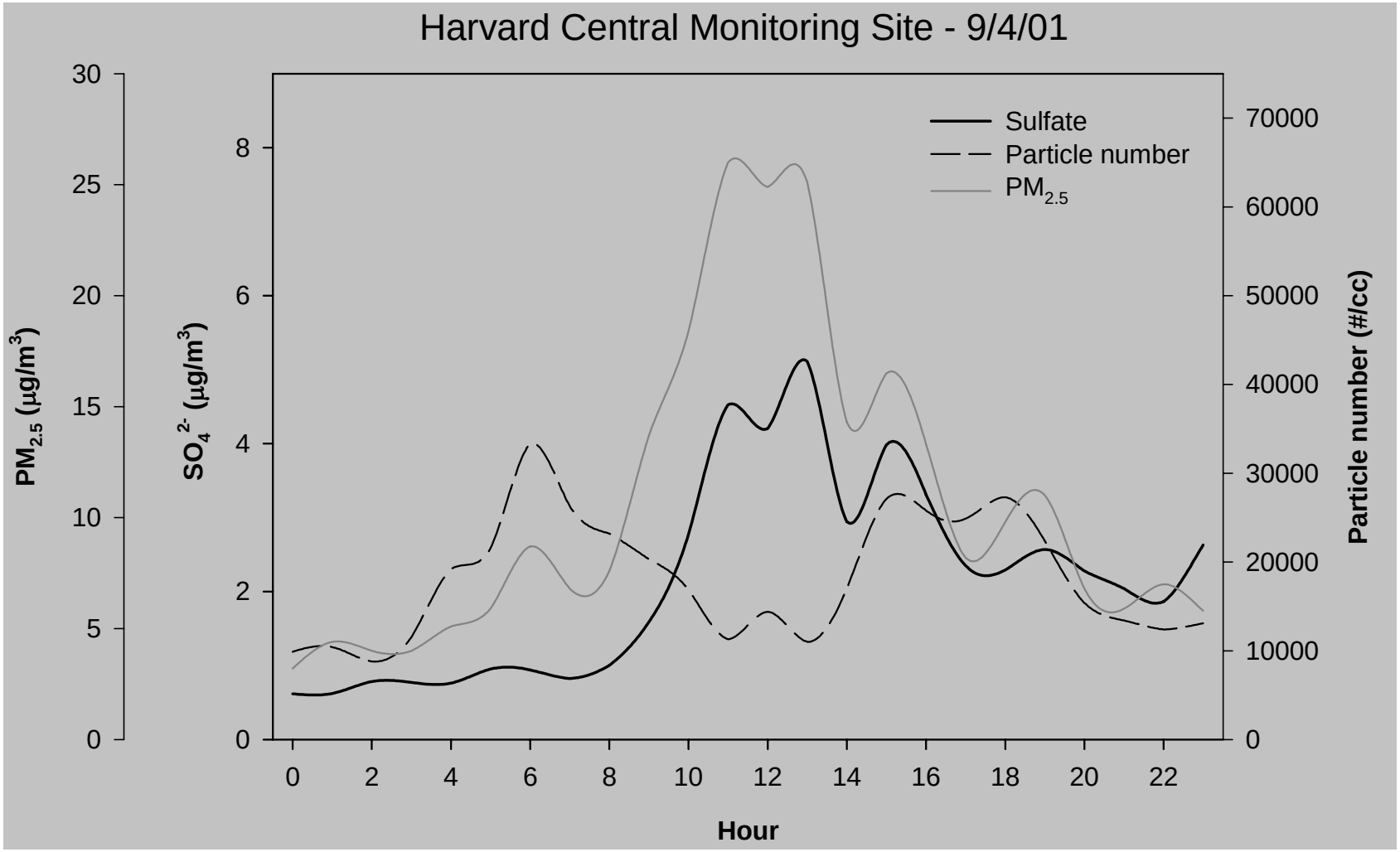
Normal and compromised animal exposures to CAPs in Boston have produced consistent and reproducible findings of biologic importance including:

- Morphometric evidence of vasoconstriction
- Increases in reactive oxygen species in the heart and lungs
- Increases in severity of myocardial ischemia during acute coronary artery occlusion

Study Objectives

- Differentiate the cardiovascular effects of locally emitted particles from those of transported particles using normal animals
- Determine whether spontaneously hypertensive rats have enhanced vascular responses to PM exposures as compared to normal animals

Diurnal Concentration Profiles



Biological Outcomes

- Pulmonary, systemic, and cardiovascular effects using *in vivo* organ chemiluminescence, histopathology, bronchoalveolar lavage, blood cytology
- Continuous measurements of cardiac and pulmonary function

Project 5

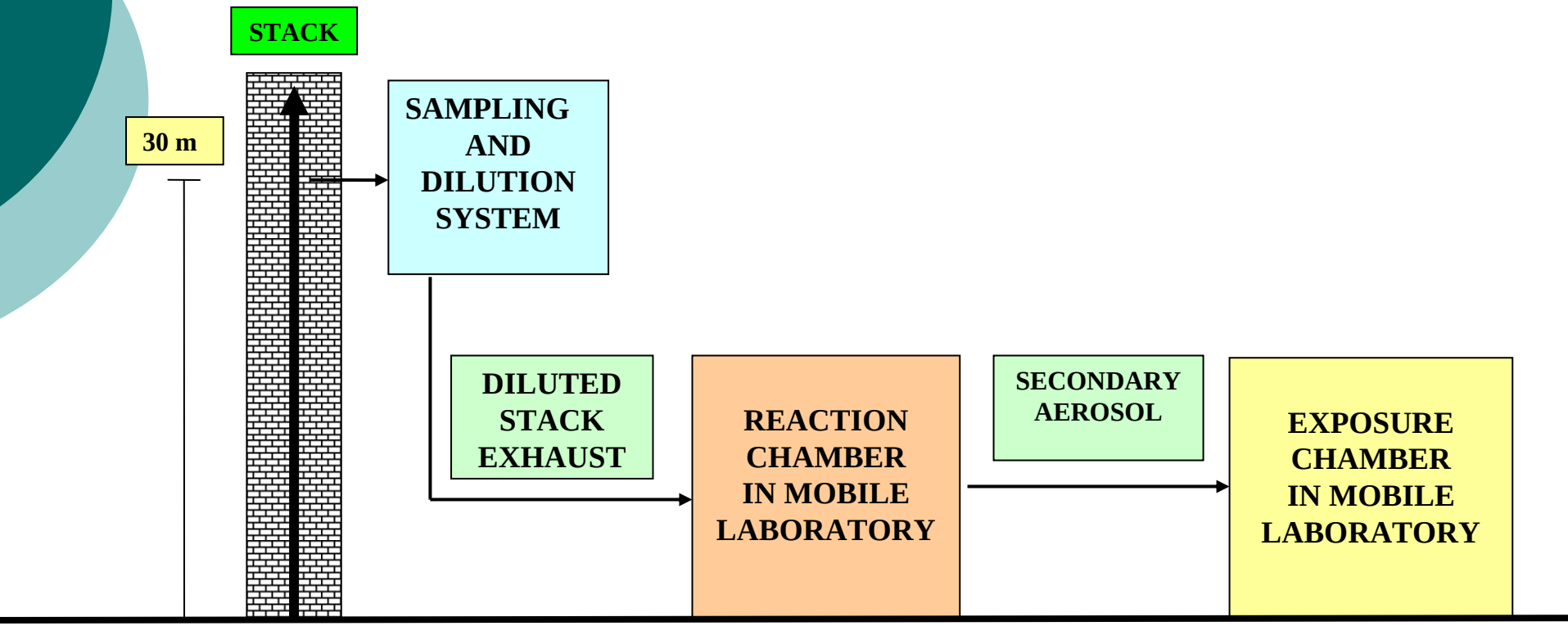
Toxicological Evaluation of Realistic Emission Source Aerosol (TERESA): Investigation of Vehicular Emissions

PI: Petros Koutrakis

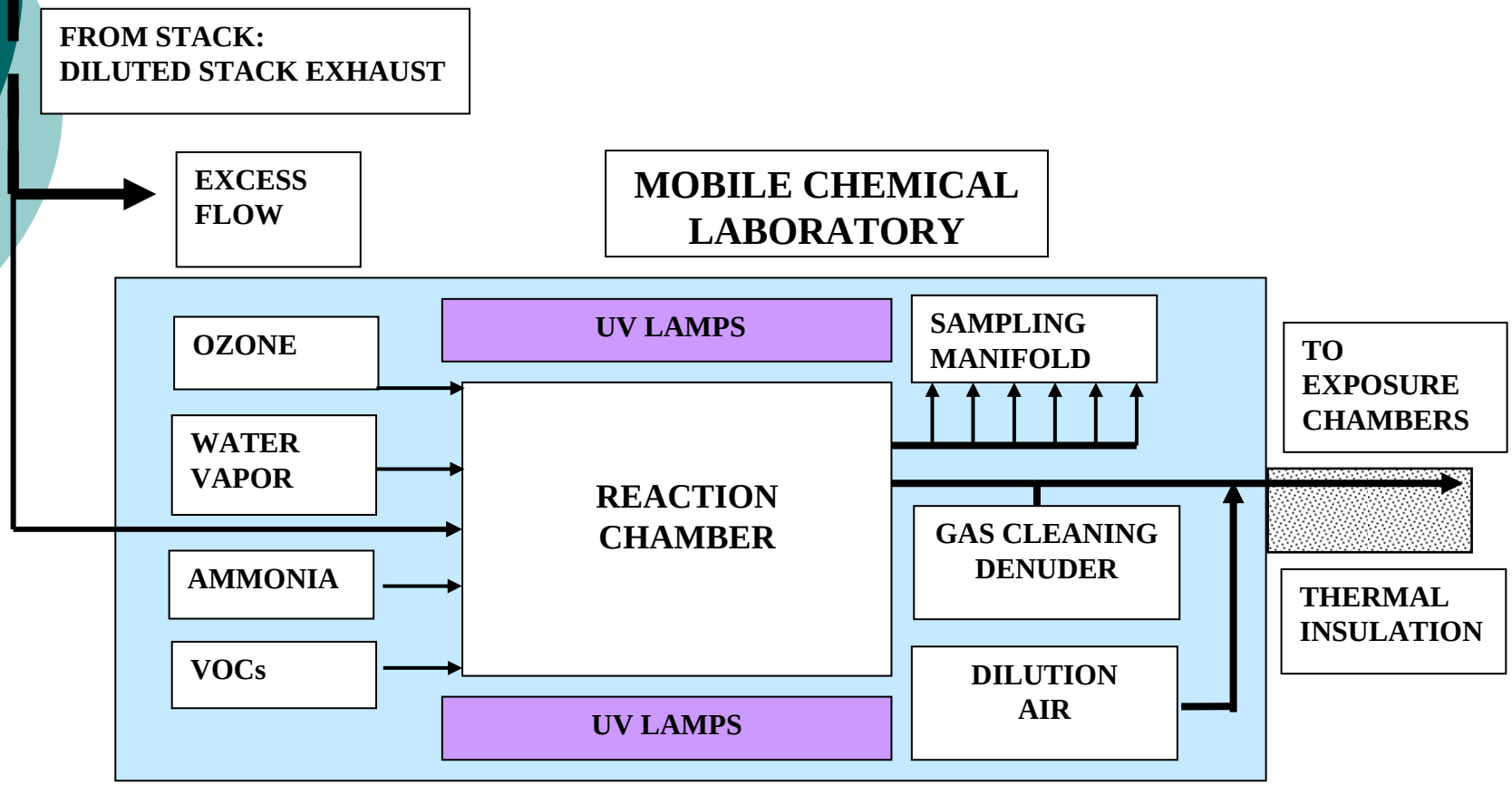
Previous TERESA Studies

- Investigate the importance of atmospheric processes by comparing the toxicity of
  - Primary pollutants
  - Secondary pollutants
- Innovative approach already applied to coal power plants
  - Have developed technologies

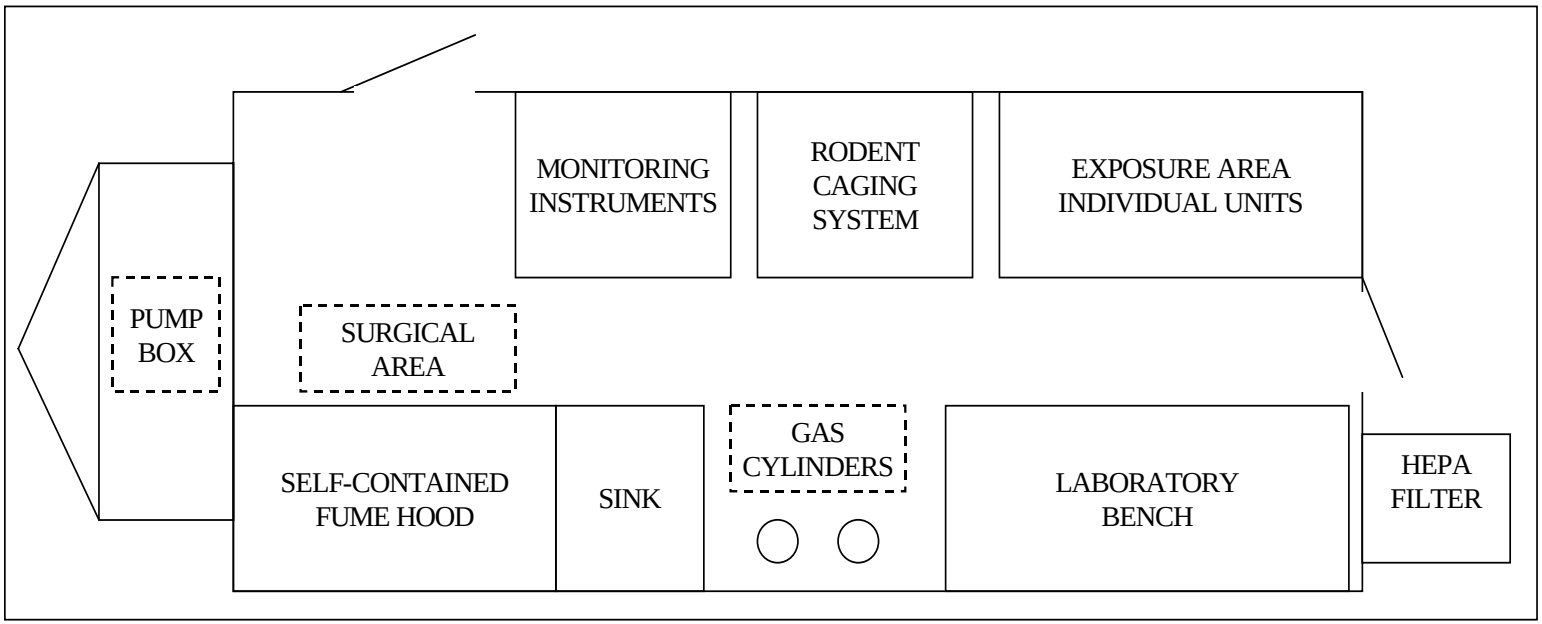
Field Layout



Reaction Chamber



Mobile Exposure Laboratory



Study Objectives

- Investigate the cardiovascular effects of fresh and photochemically aged traffic emissions in normal and spontaneously hypertensive

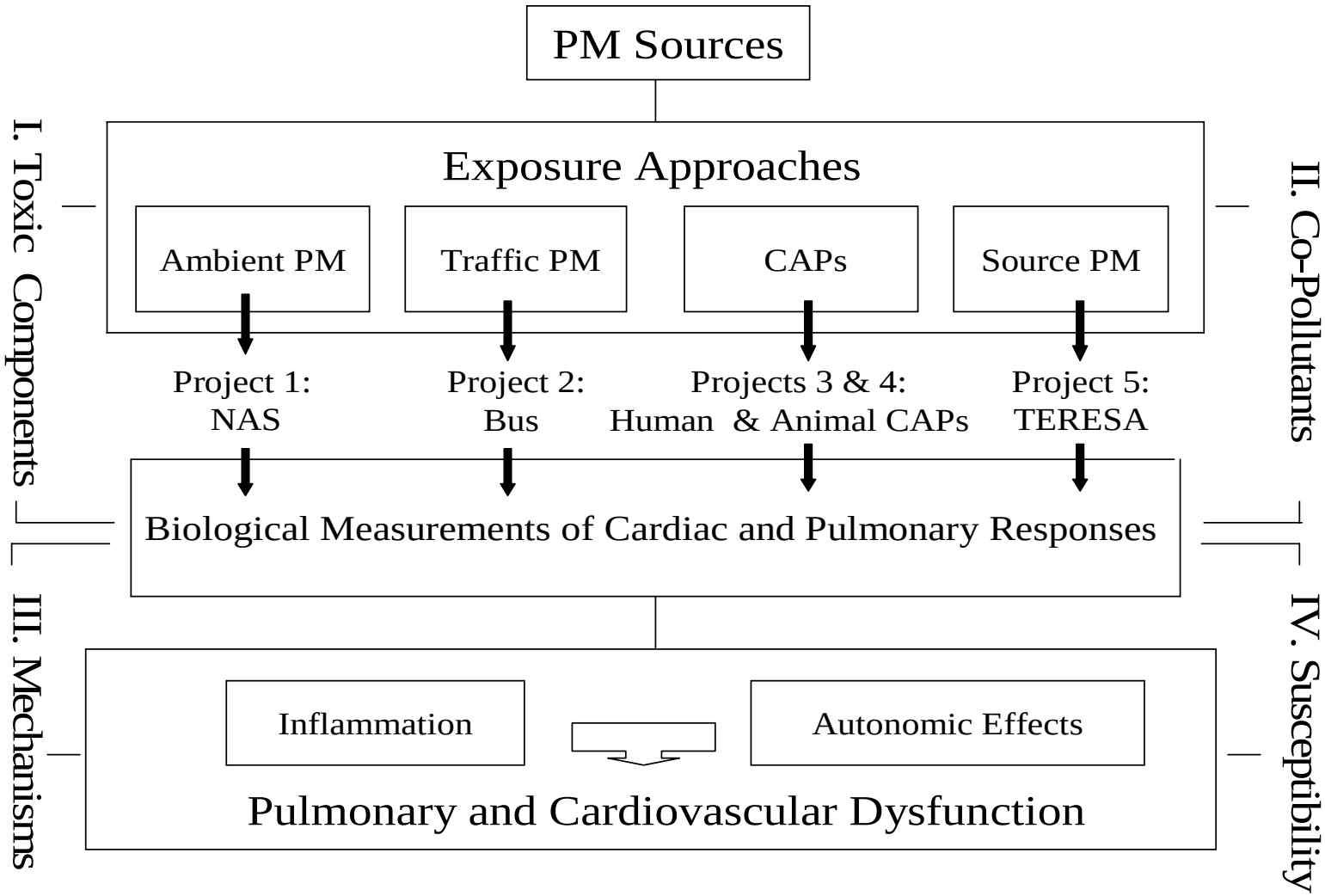
Study Design

- A large tunnel within the metropolitan area of Boston will be used as the source of primary emissions
- The mixture of primary particles and gases will undergo photochemical oxidation to form secondary PM
- Five different exposure scenarios will be used:
  - Filtered air
  - Primary gas and particle emissions
  - Primary plus secondary particles
  - Primary plus neutralized secondary particles
  - Secondary particles formed in the absence of primary particles

Biological Outcomes

- Normal animals will be exposed to each of the five scenarios. Biological measurements will include
  - pulmonary, systemic, and cardiovascular effects using *in vivo* organ chemiluminescence, histopathology, bronchoalveolar lavage, blood cytology
  - continuous measurements of cardiac and pulmonary function
- The most and least toxic scenarios will be further investigated using spontaneously hypertensive rats

Linking inflammation, autonomic effects and vascular dysfunction to PM sources



THANK YOU