Comparative toxicity of coarse particles

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Objective

- To determine the contribution of coarse particles to the adverse effects associated with exposure to ambient PM.
  - We hypothesize that differences in the toxicity of coarse PM ($PM_{10-2.5}$) samples are due to the source contributions of the particles

Experimental Design

We will:

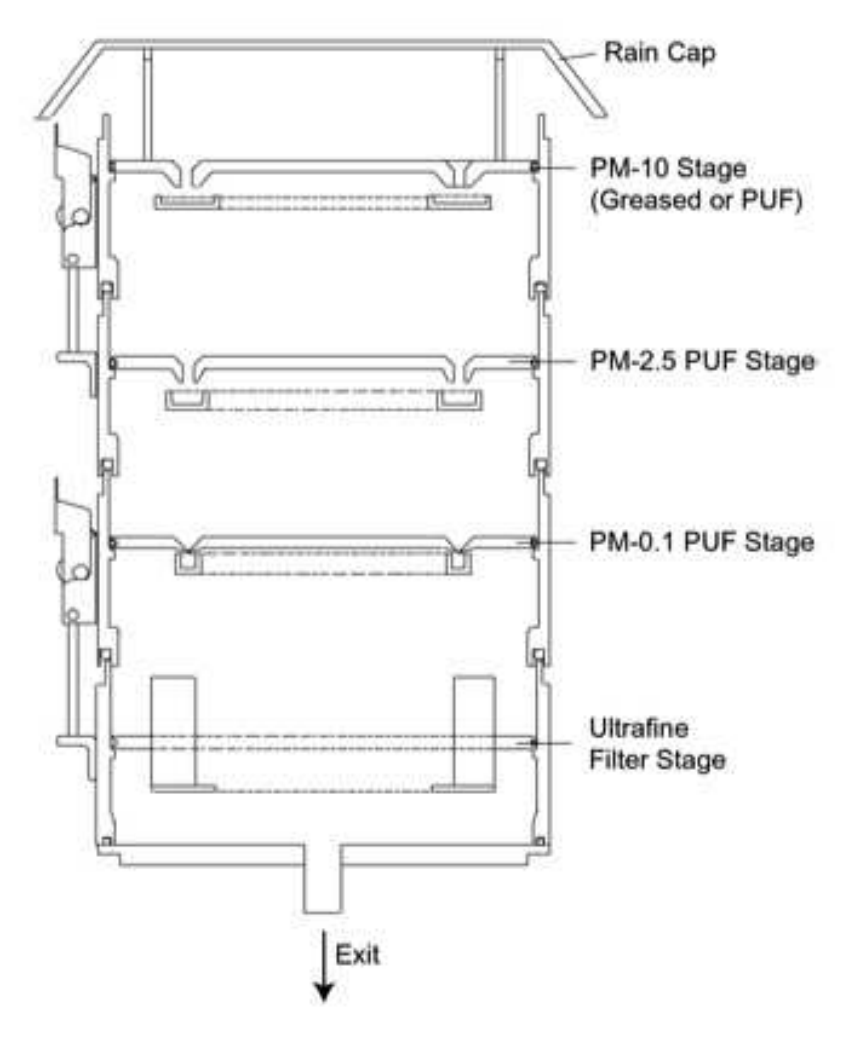
1) measure the differential toxicity of coarse particles both *in vitro* and *in vivo*;

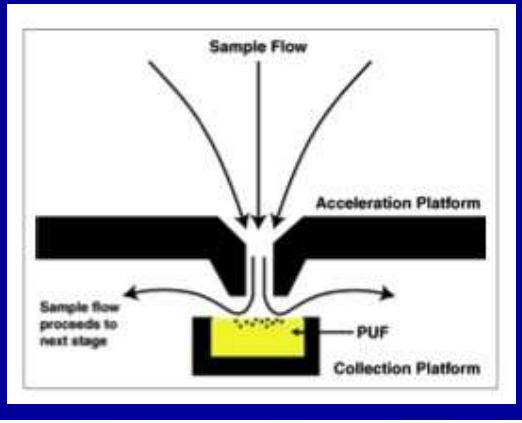
2) identify whether coarse particles from urban and rural sources differ in toxicity.

Study Design

- Design was copied from European scientists (Netherlands/Germany)

Collection Apparatus





Foam Impaction Stage

Study Design (cont….)

- several sites - winter and summer
- 2 particle sizes (coarse and fine/UF)
  - Co-located teflon and quartz filter samples
- In vivo bioassay - mouse
- In vitro bioassay - 3 cell types

Airway Epithelial Cells

- 10 and 50 µg/ml in 96 well plates
- BEAS-2B cell line (cross-validate with primary cells)
- Endpoints
  - Toxicity
  - Cytokine production - Luminex system
  - ROS production (fluoroprobe and NFK-B reporter)

Vascular Endothelial Cells

- 10 and 50 µg/ml in 96 well plates
- Primary human pulmonary vascular cells
- Endpoints
  - Toxicity
  - ROS production
  - C-reactive protein (risk marker for cardiovascular events)
  - tissue factor (a transmembrane procoagulant glycoprotein
  - von Willebrand factor and thrombin (coagulation factors)
  - iNOS and eNOS (inducible and endothelial forms of nitric oxide

Vascular Endothelial (cont….)

- Endpoints
  - VEGF, required for vascular development
  - tissue plasminogen activator (tPA, plays a role in fibrinolysis and tissue remodeling)
  - IL-1, IL-6, and IL-8 (inflammatory cytokines)
  - VCAM-1 and ICAM-1 (adhesion molecules)
  - endothelin-1 (potent physiological vasoconstrictor).

Cardiac Myocytes

- 50 µg/ml
- Primary rat neonatal cardiac cells
- Endpoints
  - Beating frequency
  - mRNA

Cardiac Myocytes

Genes to be measured in cardiac myocytes

Gene	Function
Cx40	Connexin 40, gap junction
Cx43	Connexin 43, gap junction
Kv1	Potassium channel
Kv4.2	Potassium channel
KvLQT1	Potassium channel
L-type Ca channel	calcium channel
IL-6	Inflammatory cytokine
IL1	Inflammatory cytokine
HSP 70	Heat shock protein
GAPDH	House keeping

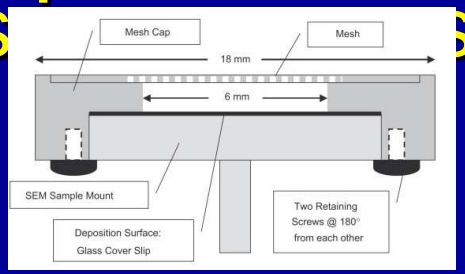
In Vivo Studies

- BALB/c mice
- 50 µg/animal by oropharyngeal aspiration
- Pulmonary endpoints
  - Inflammation and injury
- Cardiovascular endpoints
  - Vascular changes in protein and mRNA for subset of factors studied *in vitro*

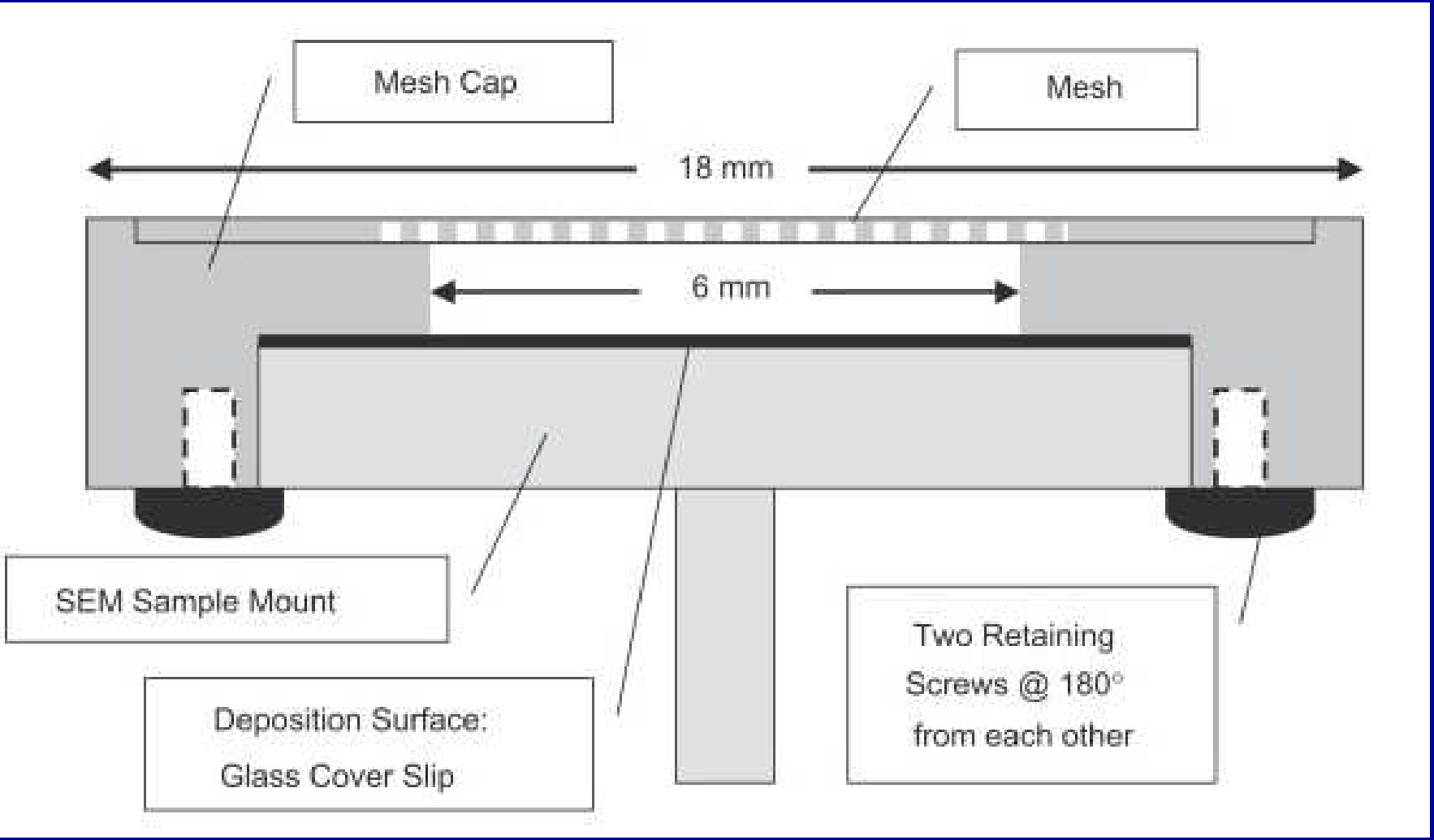
Other Sampling

- Co-located Sioutas personal impactors
  - Teflon (XRF measurement o elements)
  - Quartz (OC/EC measurement

- Pass se monitor



Passive Sampler



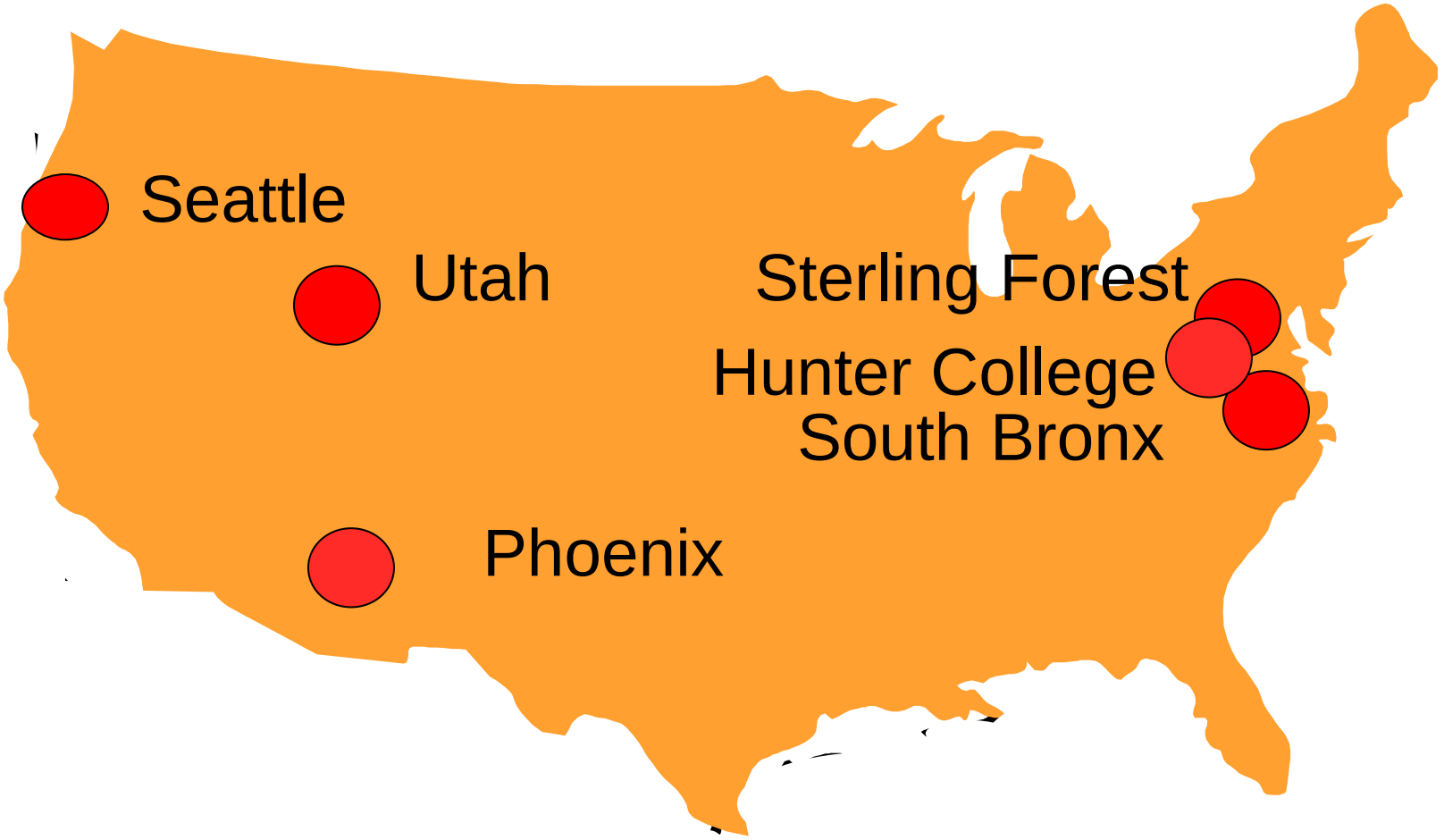
Source Apportionment

- Kaz Ito

Expected Results

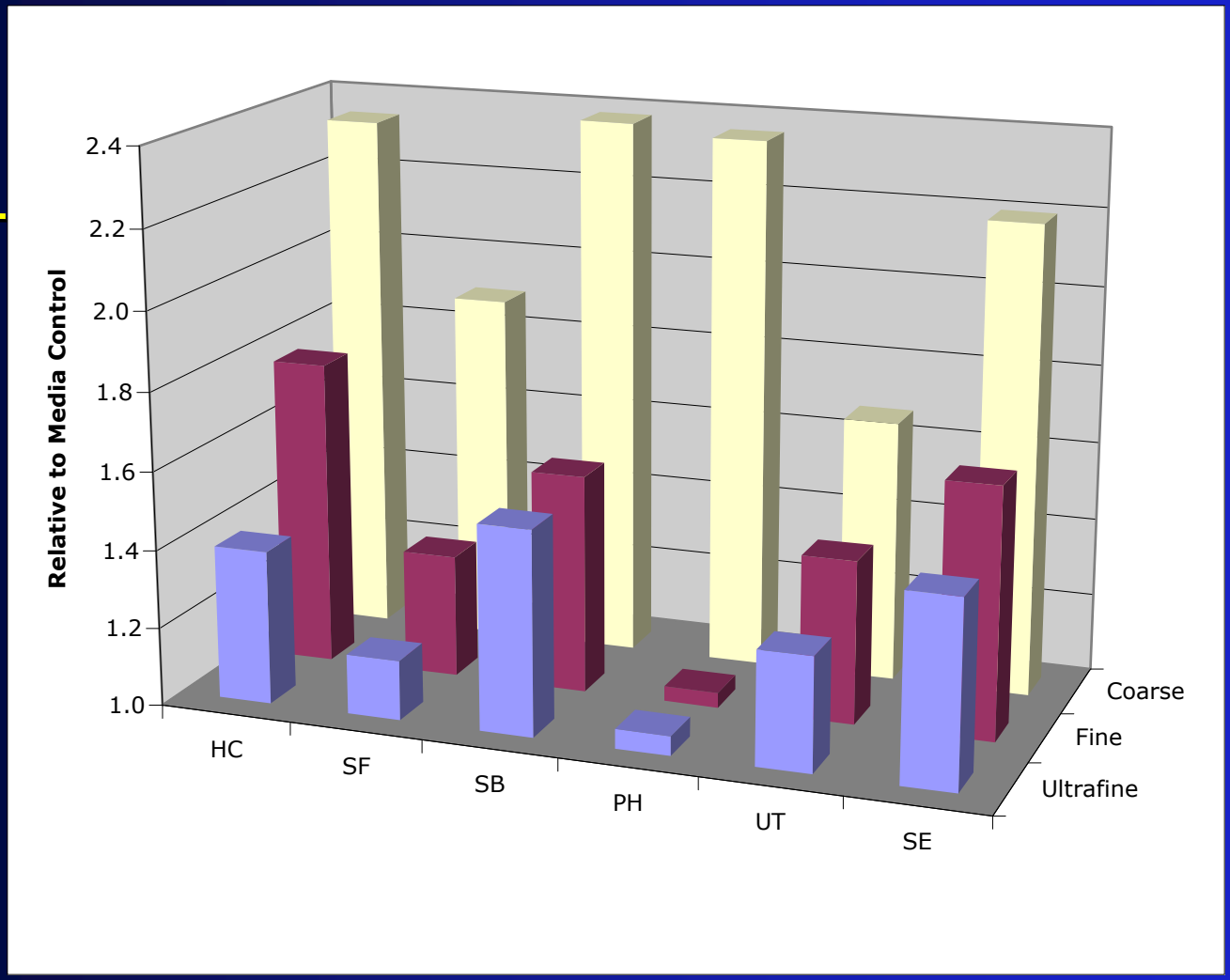
- Previous study on coarse, fine, and UF PM done in collaboration with EPA PM Centers

The Multi-City Ambient PM Study (MAPS)



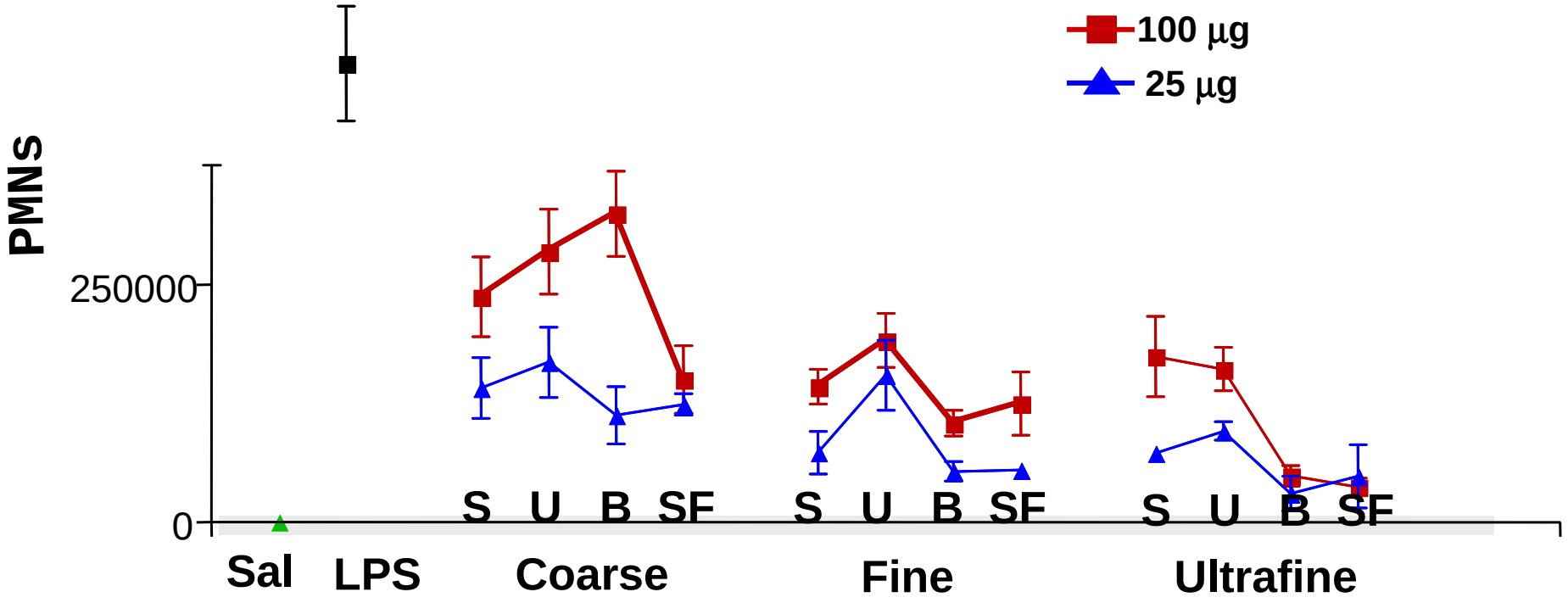
ROI Summary

Dose =
50 µg/ml



HC: Hunter College
SF: Sterling Forest
SB: South Bronx
PH: Phoenix
UT: Utah
SE: Seattle

Effect of Aspirated PM in Mice



S = Seattle
U = Utah
B = Bronx
SF = Sterling Forest

Gilmour

Factor Loadings for 5 Sites

Using ChemVol Samplers

CITY	SIZE	SOIL	TRAFFIC	OIL
UTAH	Coarse	**1.82**	-0.79	-0.31
SEATTLE	Coarse	**2.54**	-0.72	-0.14
STERLING FOREST	Coarse	0.43	0.31	-0.21
SOUTH BRONX	Coarse	-0.06	**3.78**	0.14
PHOENIX	Coarse	**1.09**	0.65	-0.43
MANHATTAN	Coarse	0.42	**1.55**	0.62

Lall and Thurston

Project Time Table

Month	Task
0 - 12	To collect coarse PM at urban and rural sites during Winter and Summer for 2-weeks/site.
12 - 24	To analyze 2-week samples and test *in vitro* and *in vivo*. Continue sampling at multiple urban and rural sites in the LA and NYC metropolitan areas.
21 - 27	To collect daily coarse PM samples for 6 months at 2 sites. Begin source apportionment analyses with results of 2-week samples
27 – 34	To analyze 6-month samples and test *in vitro* and *in vivo*.