

US EPA ARCHIVE DOCUMENT

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 hypothesized that differences in the toxicity of coarse PM ($PM_{10-2.5}$) samples are due to the source contributions of the particles

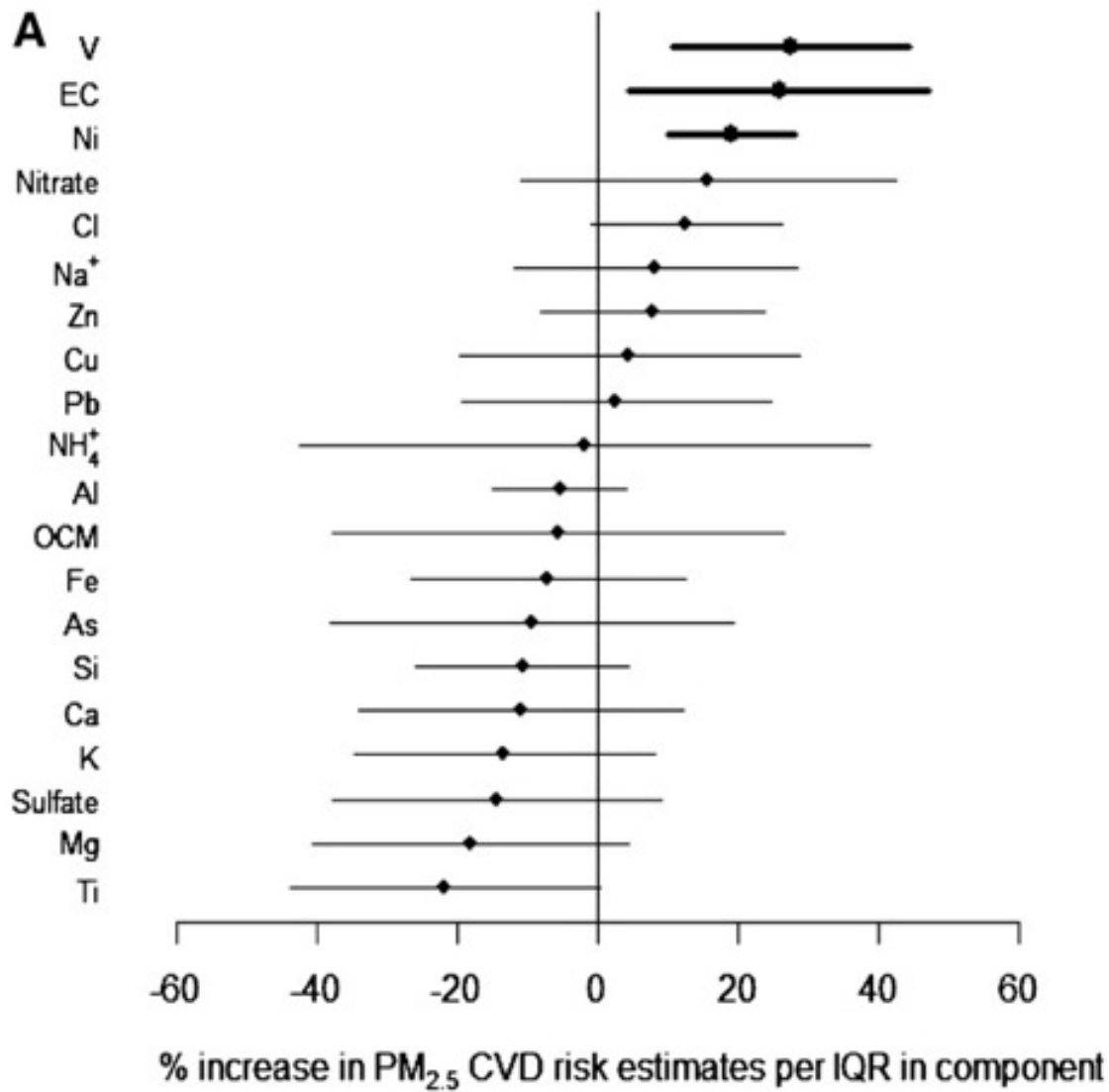
Experimental Design

- 1) To measure the differential toxicity of coarse particles both *in vitro* and *in vivo*;
- 2) To identify whether coarse particles from urban and rural sources differ in toxicity.

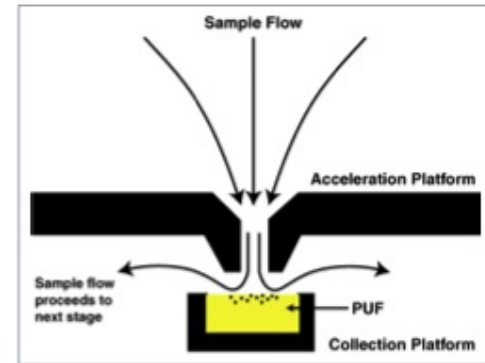
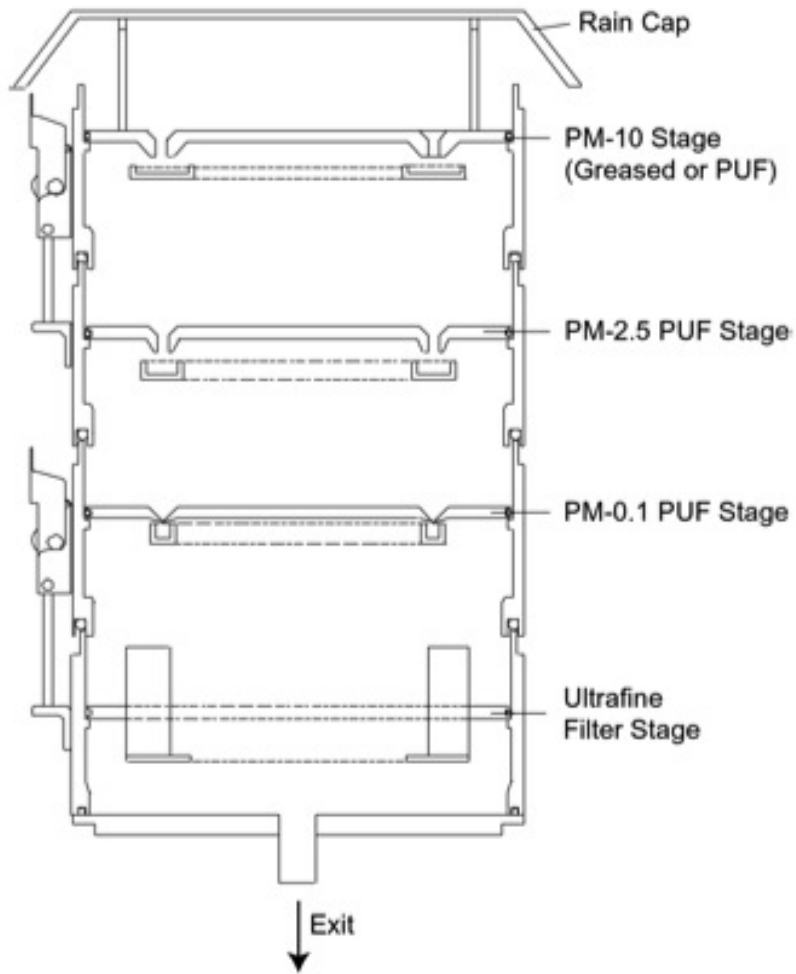
Study Design

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

Percent increase in health effects estimates for PM_{2.5} lag 0 and risk of cardiovascular hospitalizations per IQR increase in the fraction of PM_{2.5} total mass for each component



Collection Apparatus



Foam Impaction Stage

Study Design (cont...)

- Urban and rural sampling
 - NYC - winter and summer
 - San Joaquin Valley, CA - fall/winter
- 2 particle sizes (coarse and fine)
 - Co-located teflon and quartz filter samples at some locations
 - Supercoarse samples at some locations
- In vivo bioassay - mouse
- In vitro bioassay - 3 cell types
 - epithelial, vascular endothelial, cardiac myocytes

Human Cell Lines

- Airway epithelial/vascular endothelial cells
- 50 µg/ml (96 well plate)
- Cross-validate with primary cells
- Endpoints
 - Toxicity
 - ROS production (fluoroprobe)
 - Inflammatory mediators

Cardiac Myocytes

- 50 $\mu\text{g/ml}$
- Mouse embryonic stem cell system
- Endpoints
 - Beating frequency
 - mRNA

In Vivo Studies

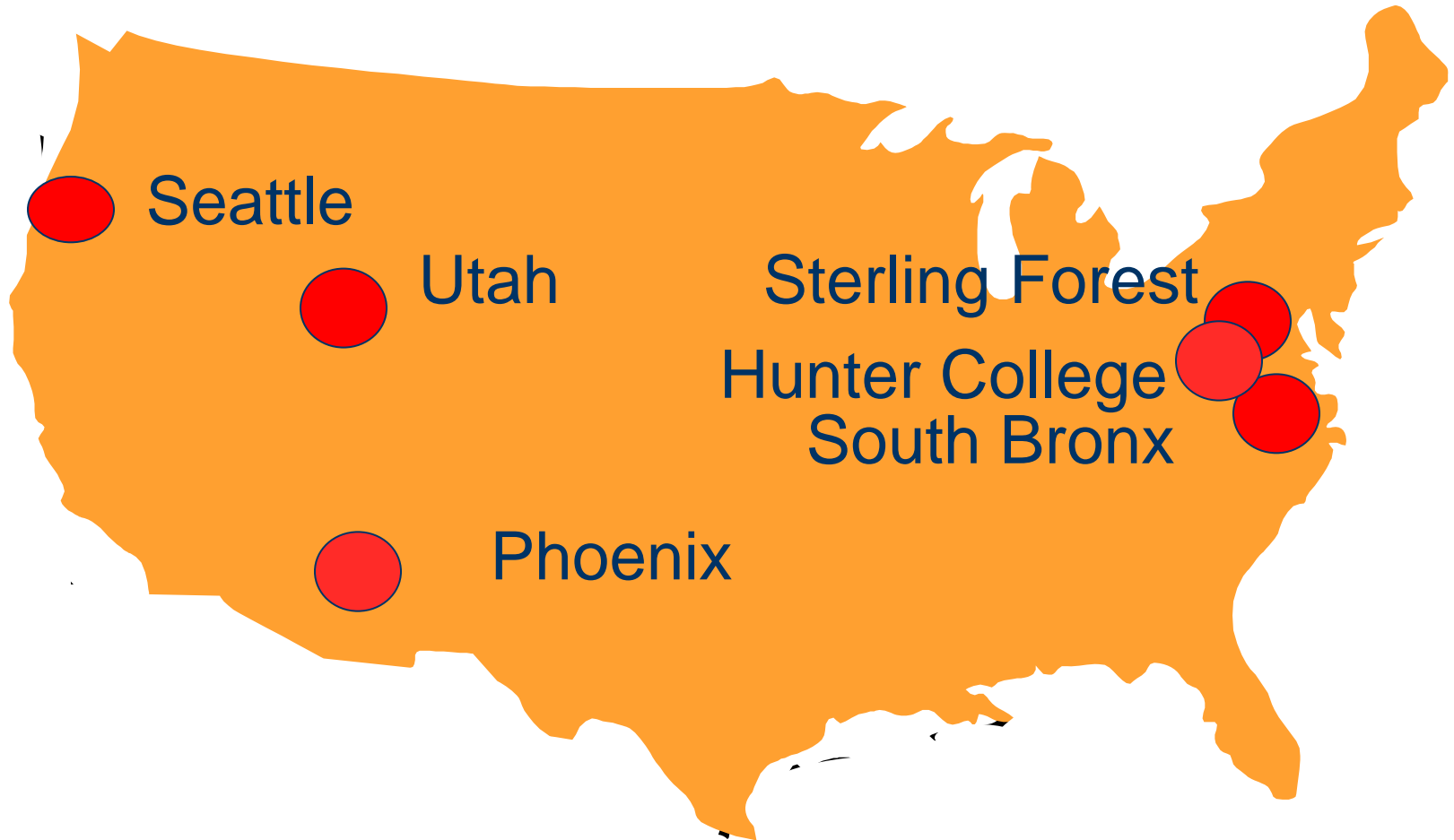
- FVB/N mice
- 50 µg/animal by oropharyngeal aspiration
- Pulmonary endpoints
 - Inflammation and injury
- Cardiovascular endpoints
 - Vascular changes in protein and mRNA for subset of factors studied *in vitro*

Source Apportionment

- Kaz Ito

Results

The Multi-City Ambient PM Study (MAPS)



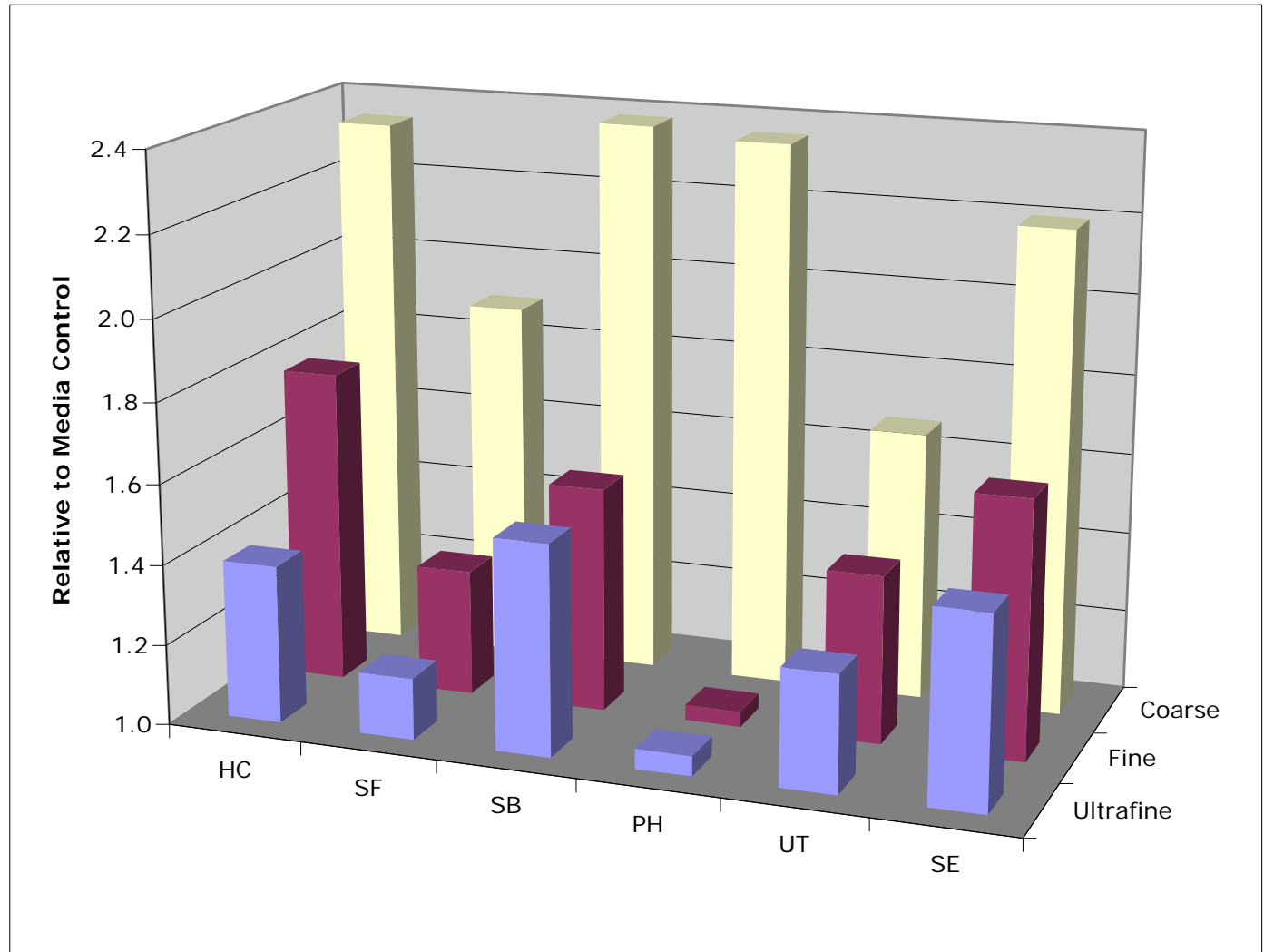
MAPS study suggests
size-dependent effects
of PM occurs both *in*
vitro and *in vivo*



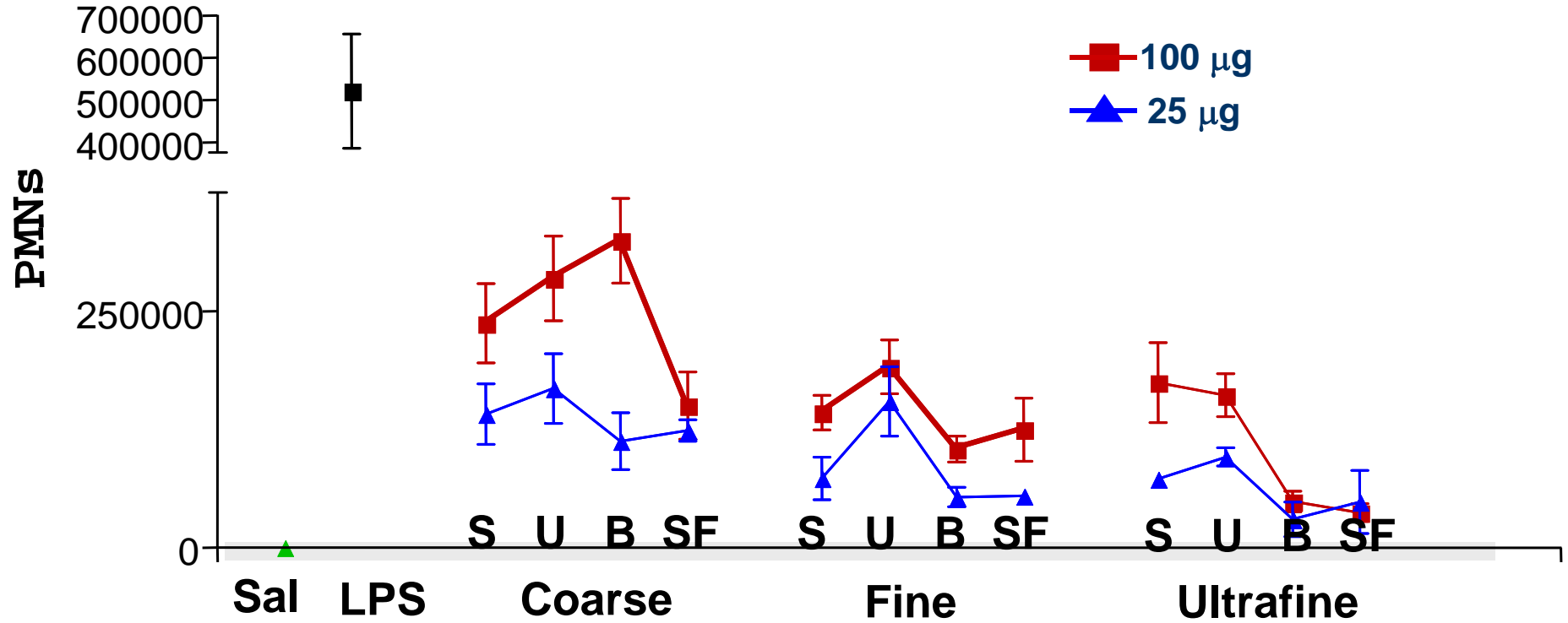
Effect of PM on Reactive Oxygen Species Production in Airway Epithelial Cells

Dose = 50 $\mu\text{g/ml}$

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

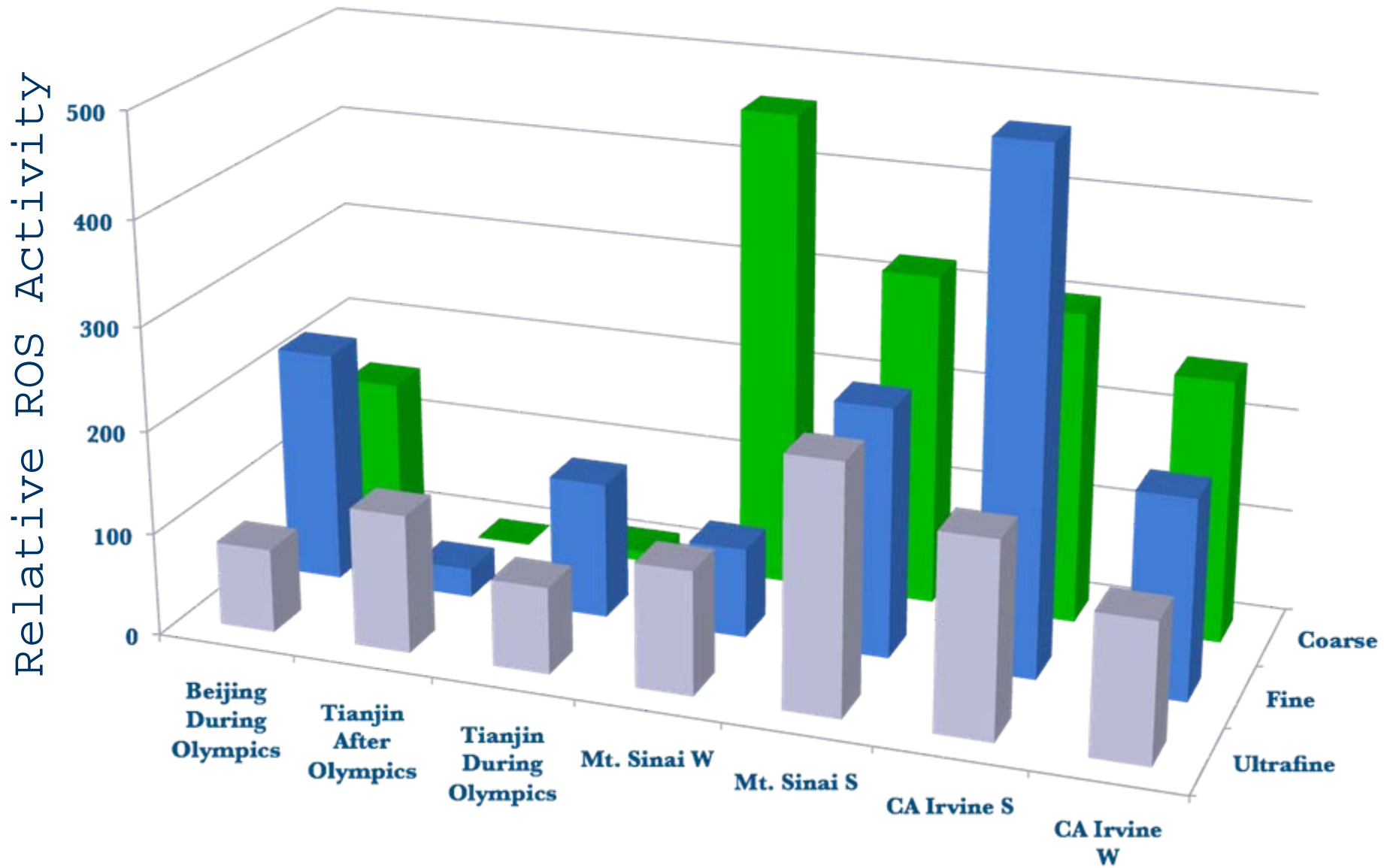
B = Bronx

SF = Sterling Forest

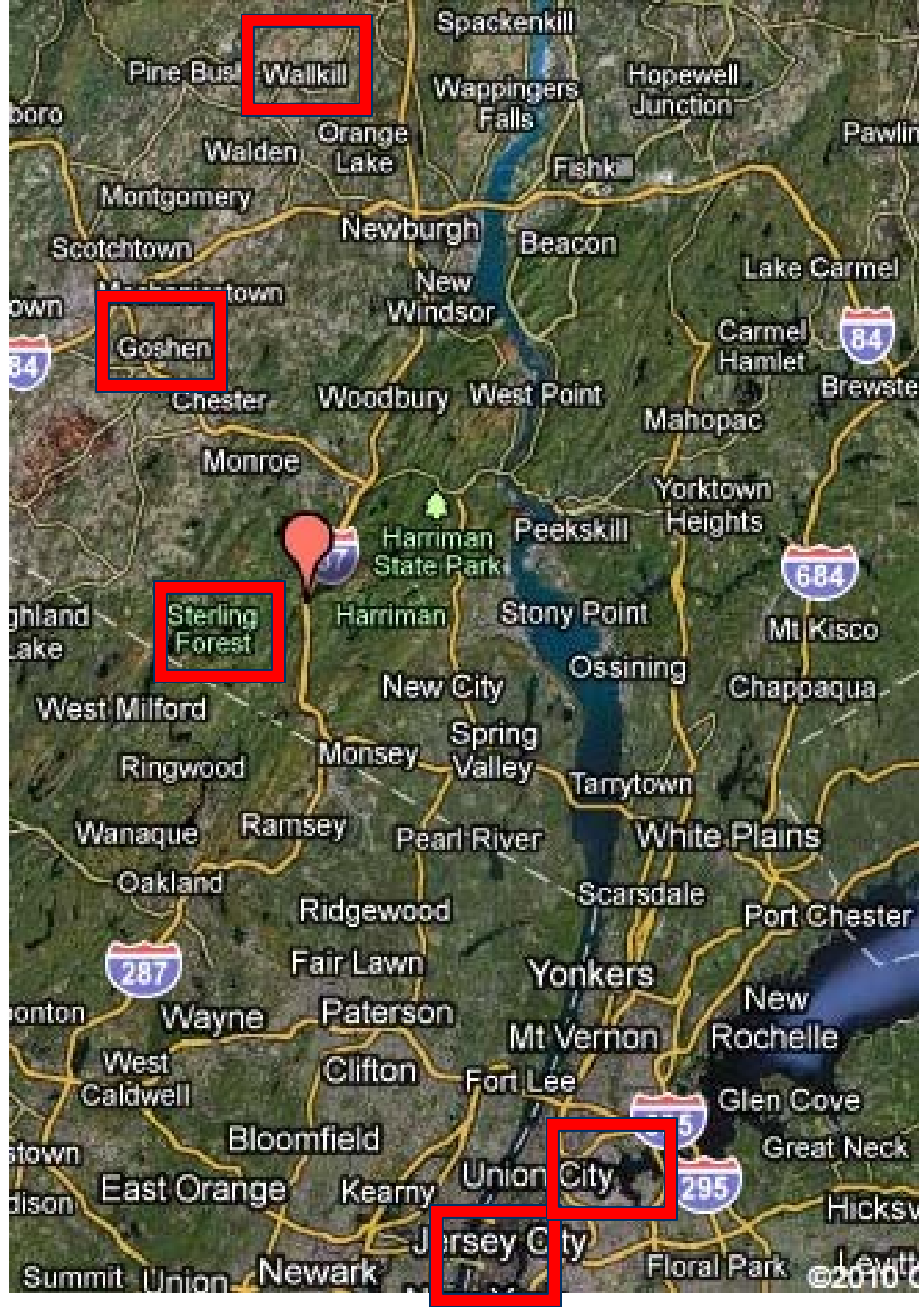
Country Differences?

- Would the observed size-dependent differences in *in vitro* ROS production occur in other countries?

PM - Samples from China vs. U.S.



NY
Urban
and
Rural
Site
s



Urban Enough?

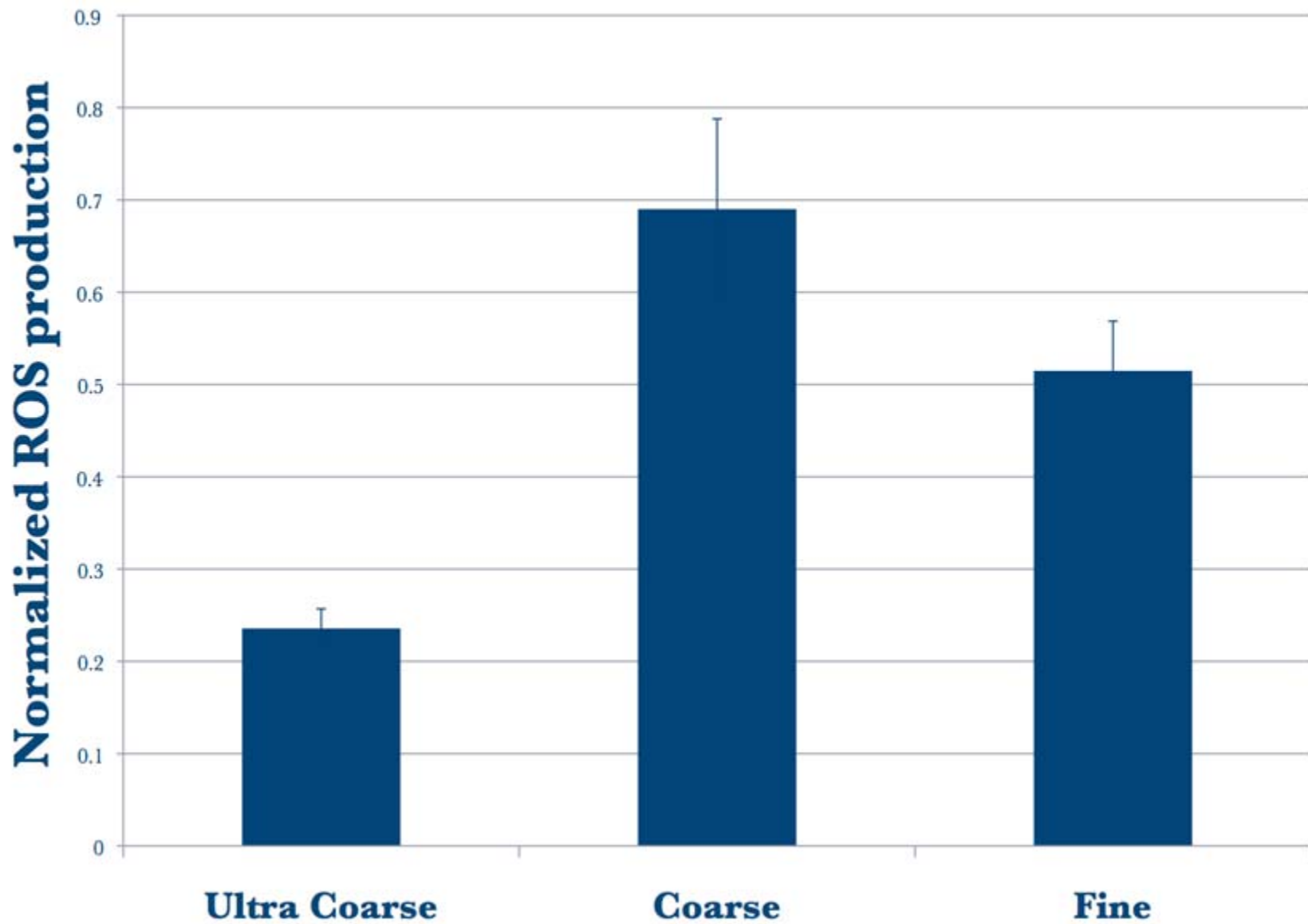


Rural Enough?

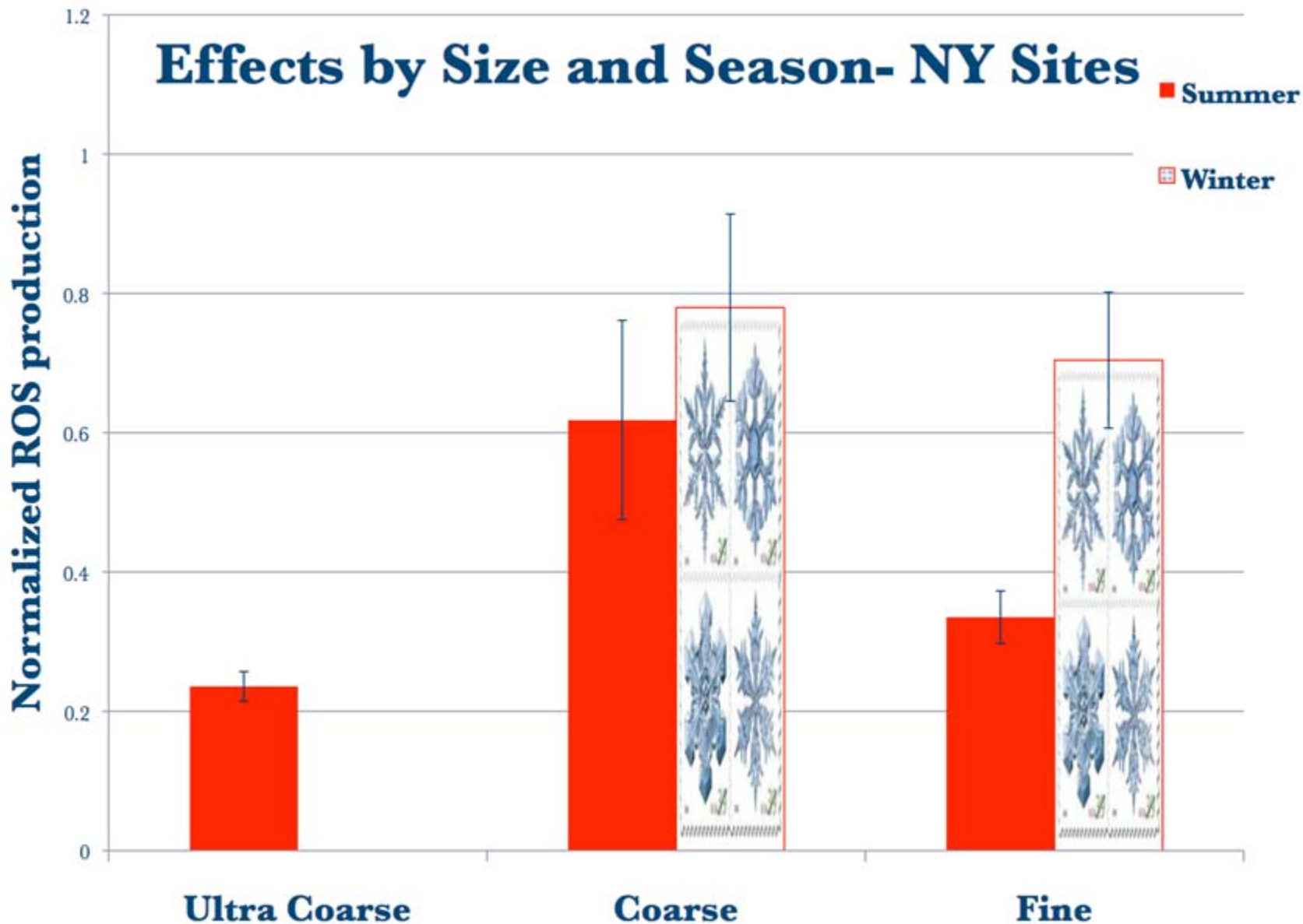


Red Boy

Effects by Size – NY Sites

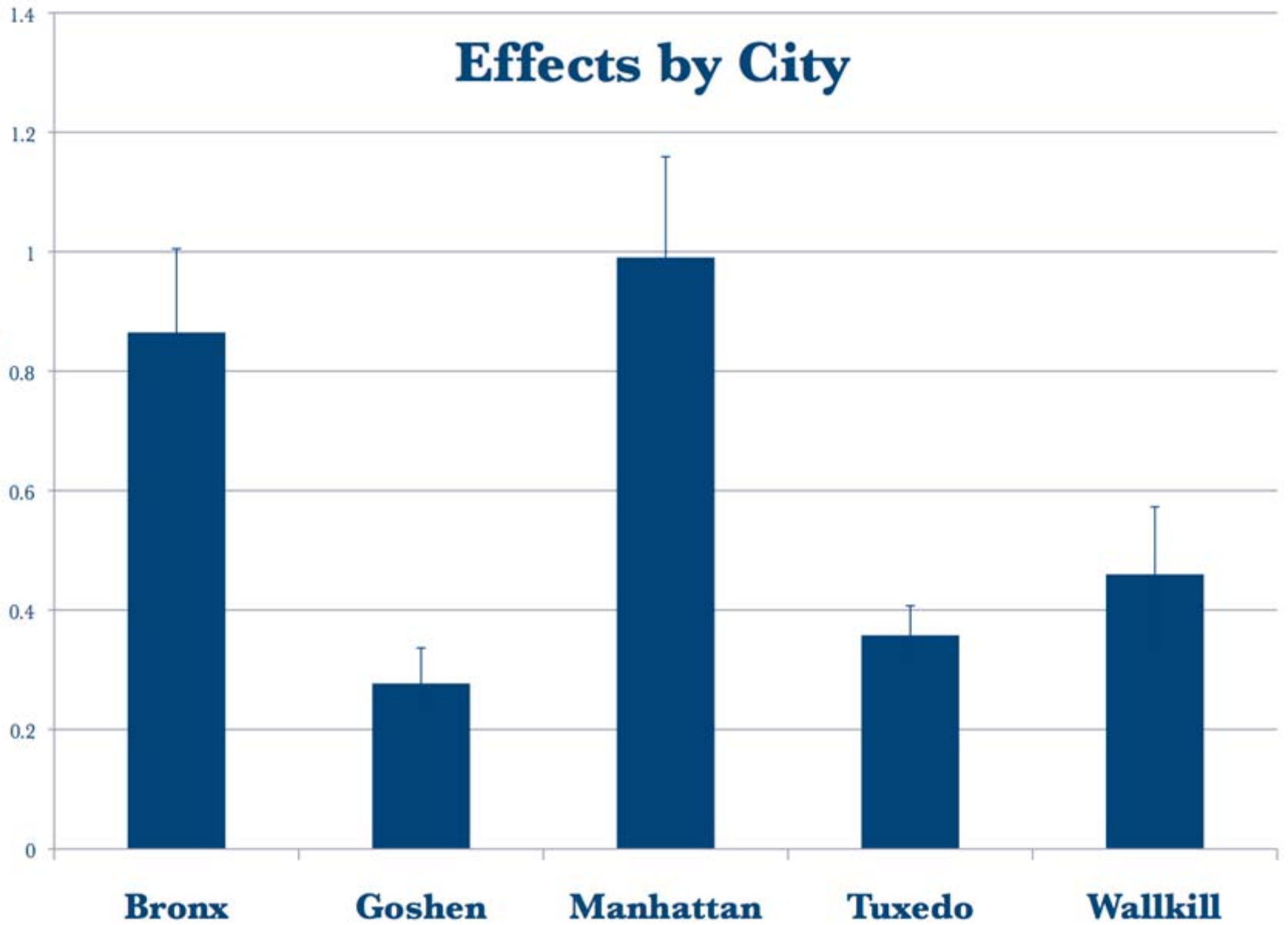


Effects by Size and Season- NY Sites

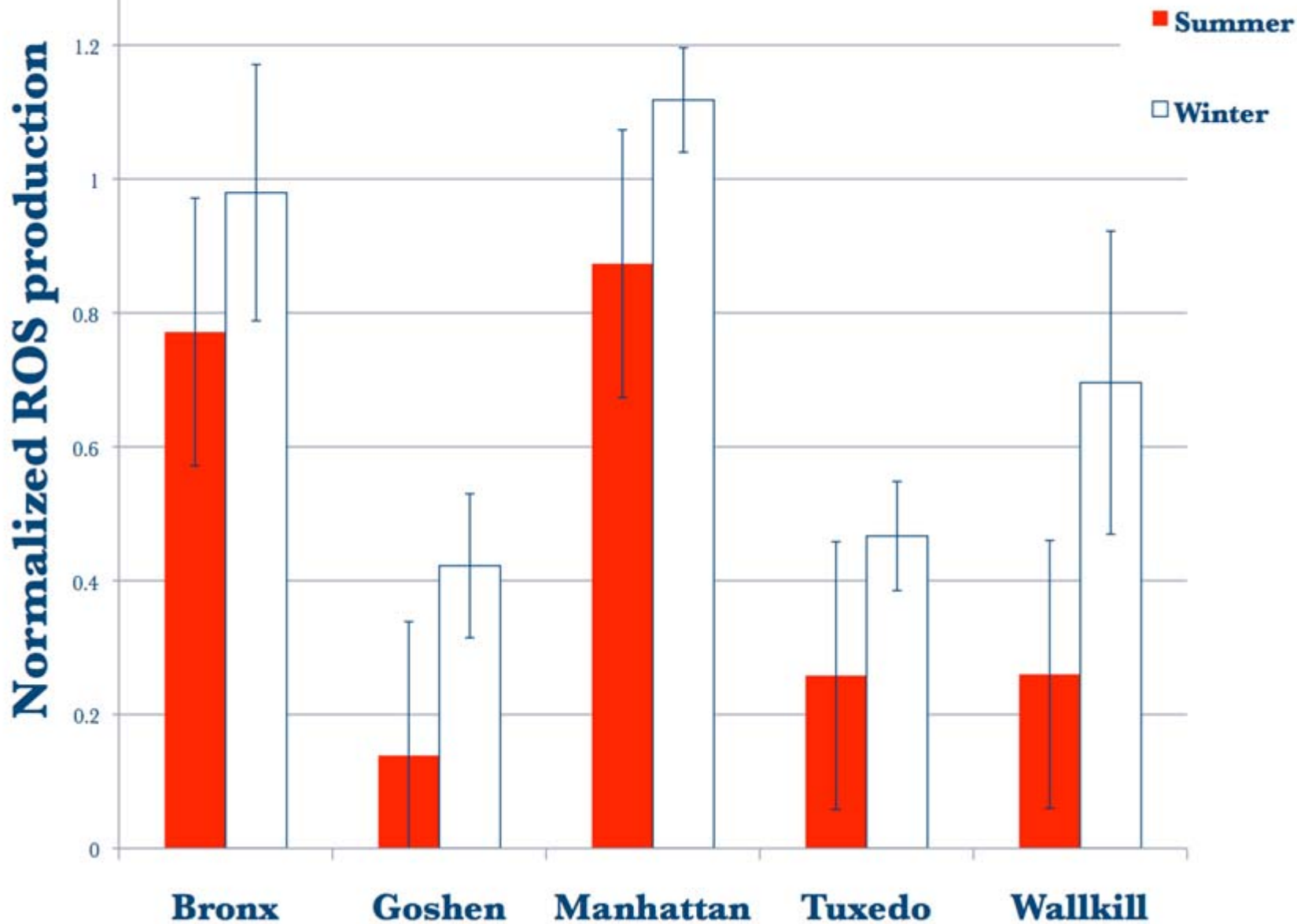


Effects by City

Normalized ROS production



Effect of Season and City



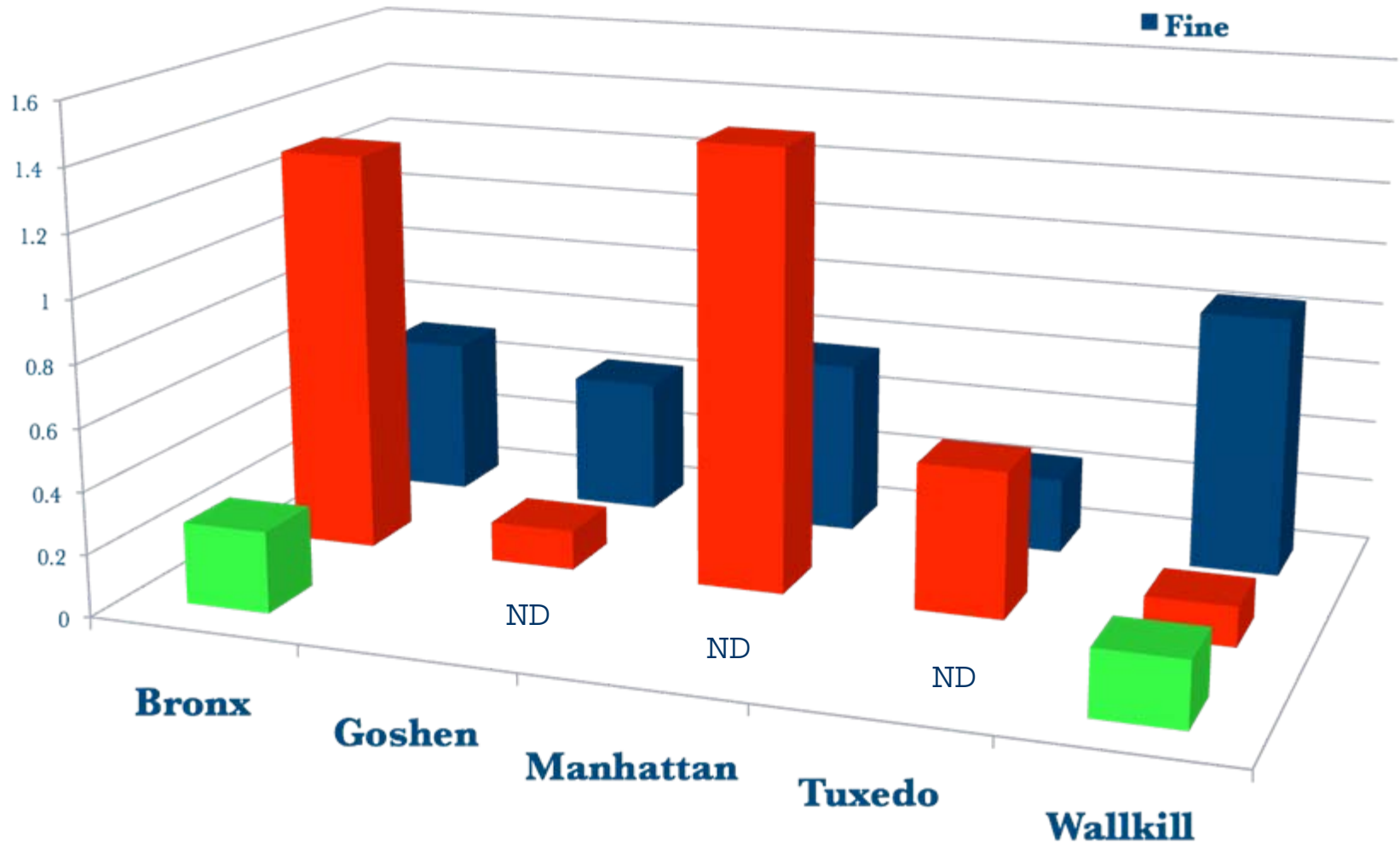
Individual Factors?

- Particle size matters
- Site matters
- Season matters

Effect of Size and City

Normalized ROS production

- Ultracoarse
- Coarse
- Fine



Conclusions (NY only)

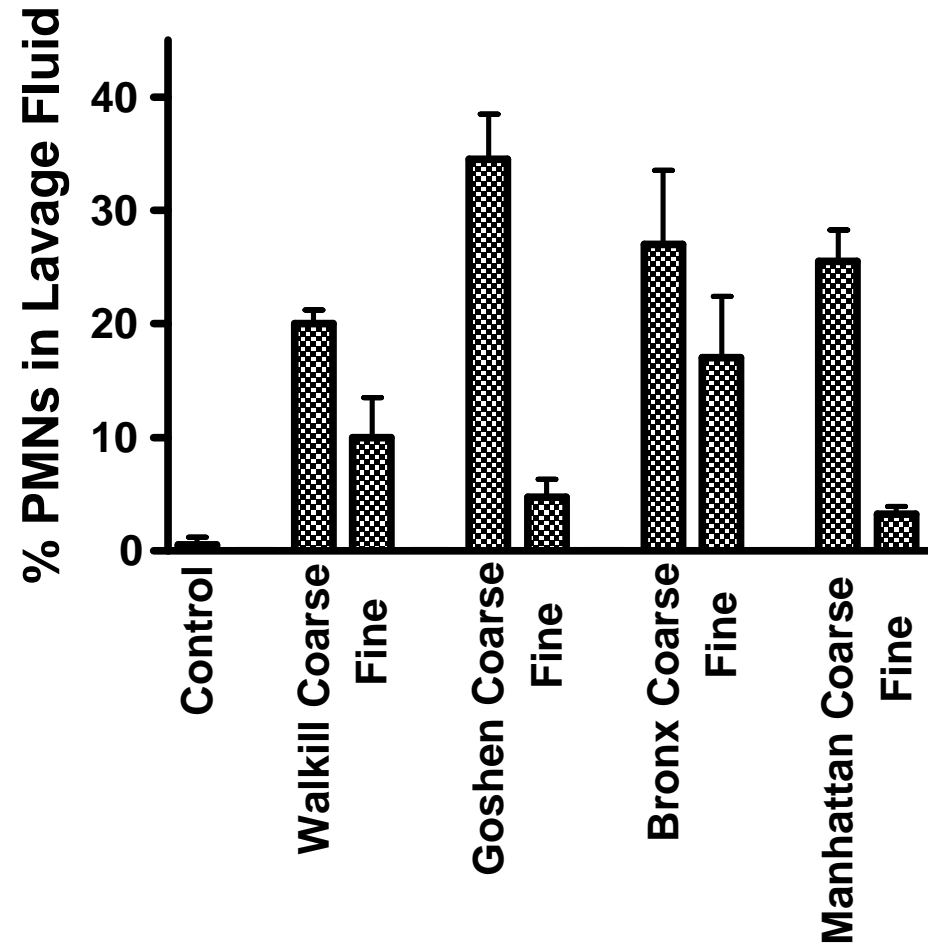
- Size, season, and site (urban vs. rural) were shown to be significant factors influencing ROS production *in vitro*.
- Generally, the coarse fraction elicited a greater ROS response than either fine or 'super coarse' PM.
- Generally, coarse PM collected in Winter elicited a greater ROS response than that collected in Summer.
- Generally, urban coarse samples (i.e., Bronx and Manhattan) produced greater effects than rural samples.
- Analysis of PM composition needs to be considered to gain a better understanding of these effects.

Does *in vitro* reflect *in vivo*?

- FVB/N mice
- 50 µg PM by aspiration
- Collect lavage fluid and serum at 24 hrs post treatment
- 2 urban vs. 2 rural (Winter)

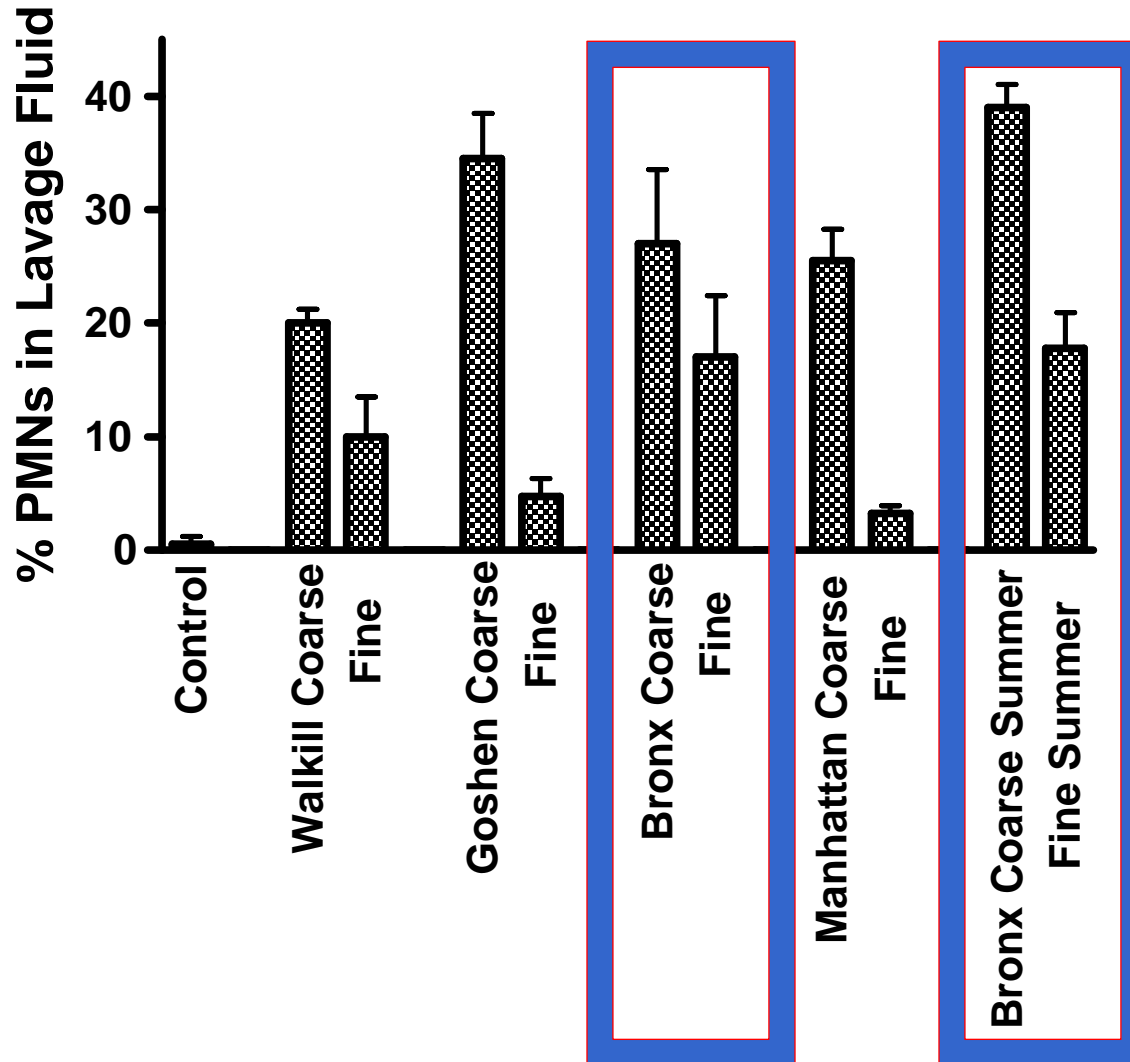
Pulmonary Inflammation - Winter

Coarse vs. Fine PM - Inflammation in Mice



Pulmonary Inflammation

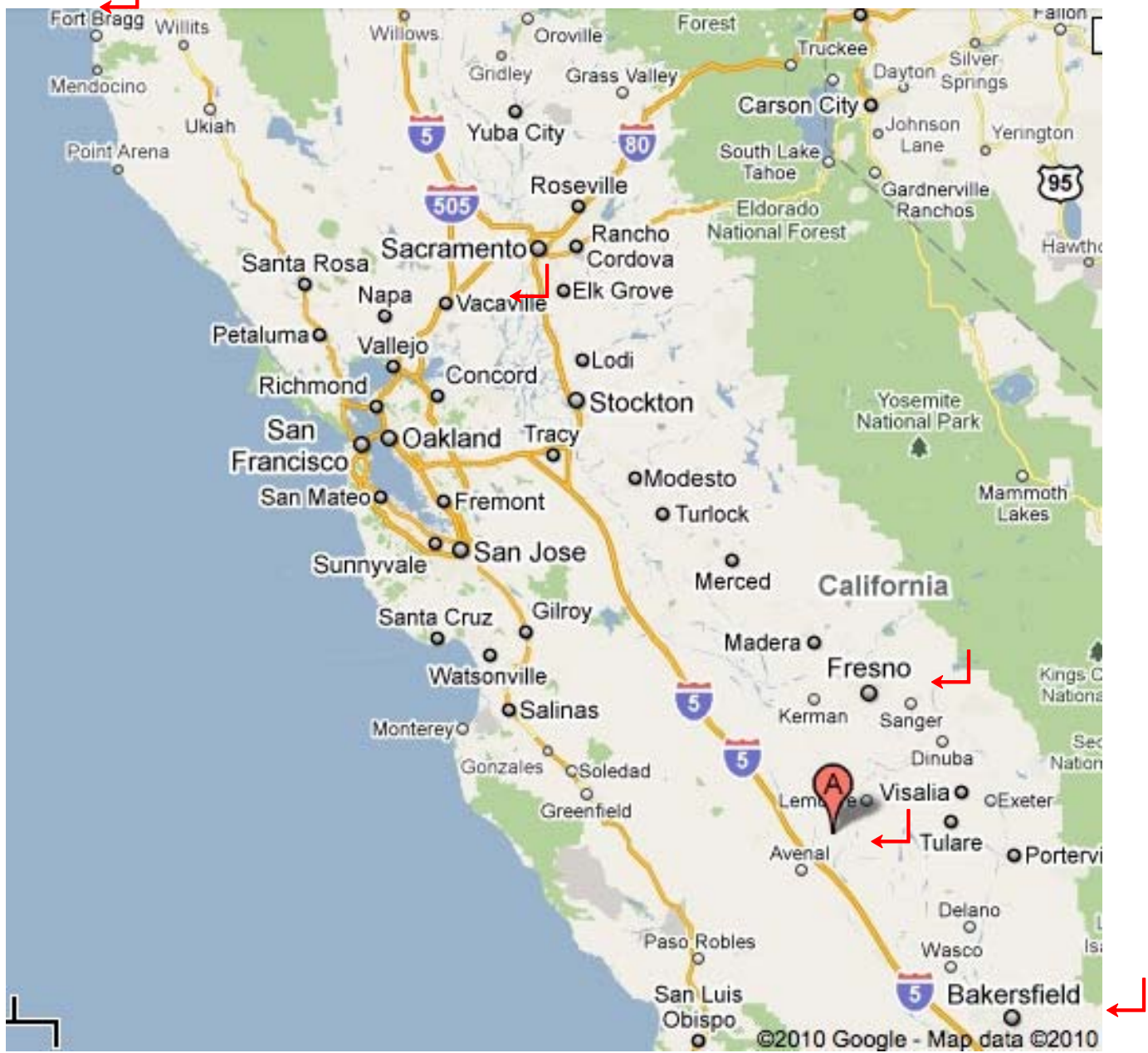
Coarse vs. Fine PM - Inflammation in Mice



Did *in vitro* predict *in vivo*?

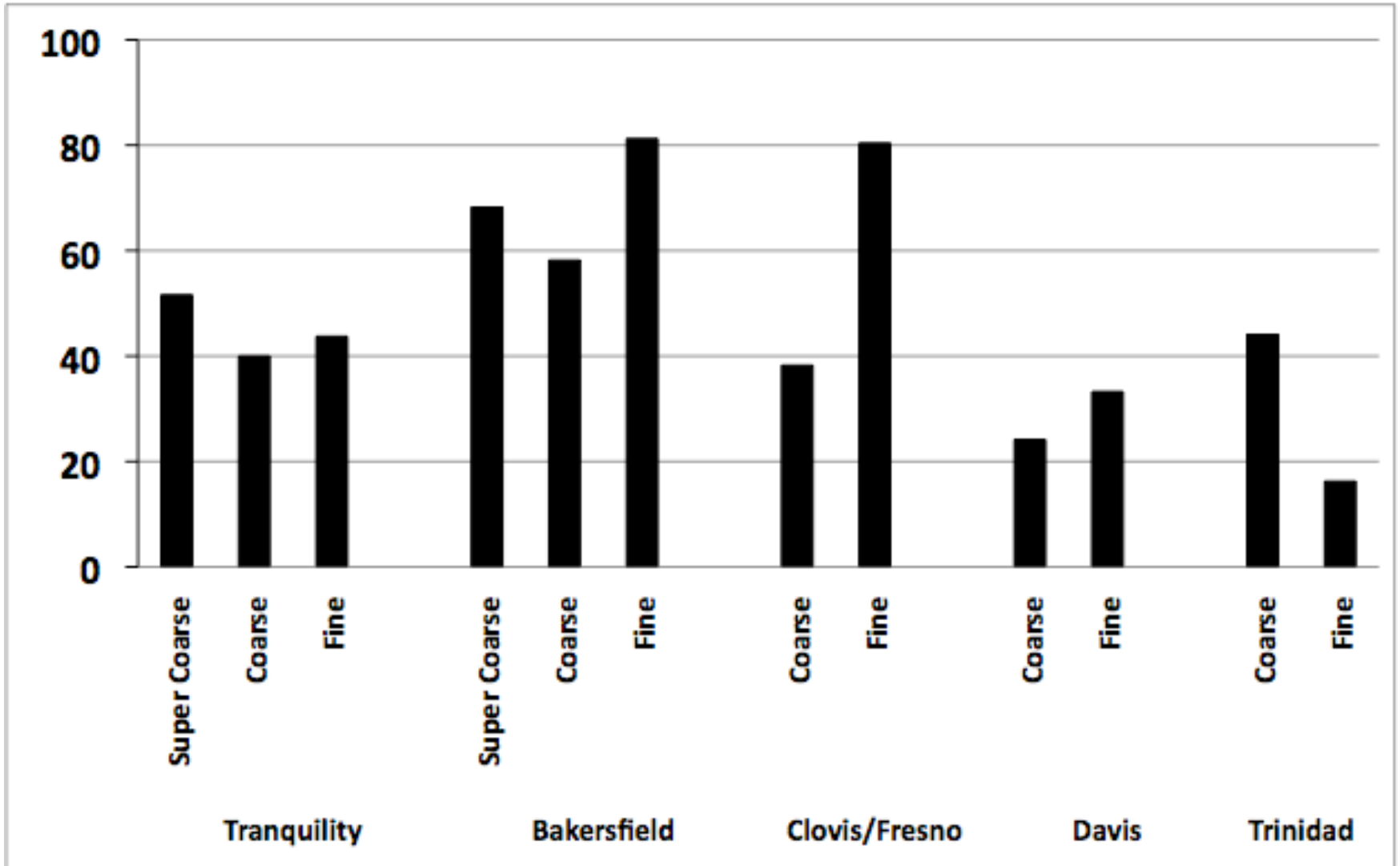
- Coarse particles produced a greater response in both bioassays.
- Despite clear differences *in vitro*, urban and rural PM samples didn't seem to produce different effects *in vivo*.
- Similar levels of inflammation with coarse and fine PM from 2 seasons.

California Sampling Sites



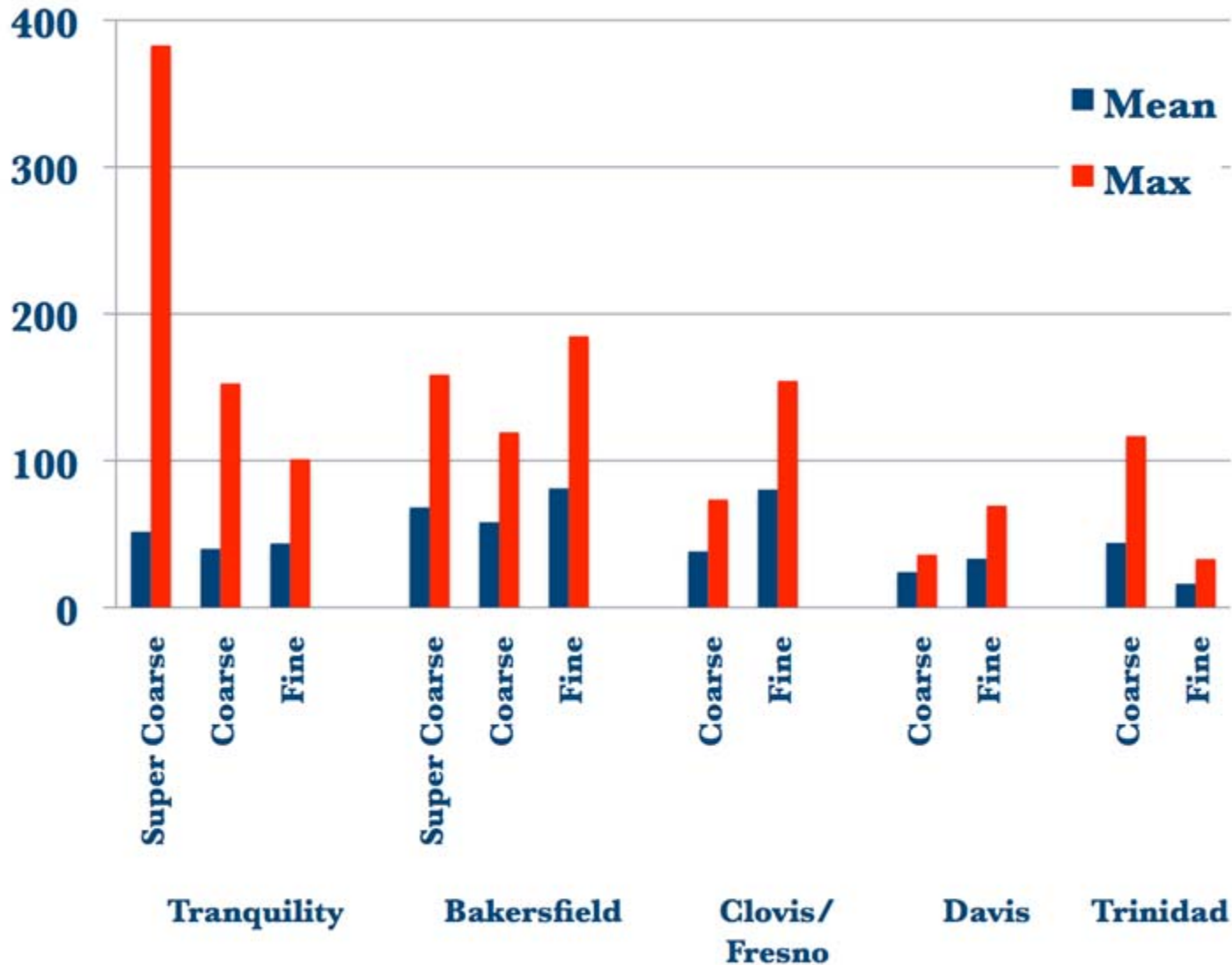
CALIFORNIA AIR SAMPLING

PM COLLECTED (mean per stage over 48 hrs)



CALIFORNIA

MAX PM COLLECTED (per stage over 48 hrs)



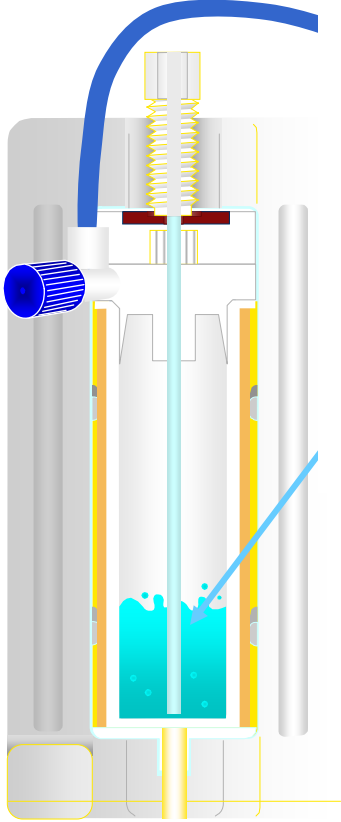
Work To Be Completed

- *In vitro* and *in vivo* bioassays on California samples
- Chemical analyses on NY and California samples
- Source apportionment
- Correlation of components and sources with *in vitro* and *in vivo* effects

Chemical analyses by ICP-MS

- Preparation of PM samples by microwave digestion
 - costly and timely
 - limited sample size

Microwave Digestion of PM Samples





- 48 samples/day
- As little as 50 μg PM
- No HF or perchloric acid
- Lose Si and Ti



Factor Loadings for 6 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

Collaborators

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