

***Cardiopulmonary Health Effects of Semi-Volatile
and Non-Volatile Components of PM***

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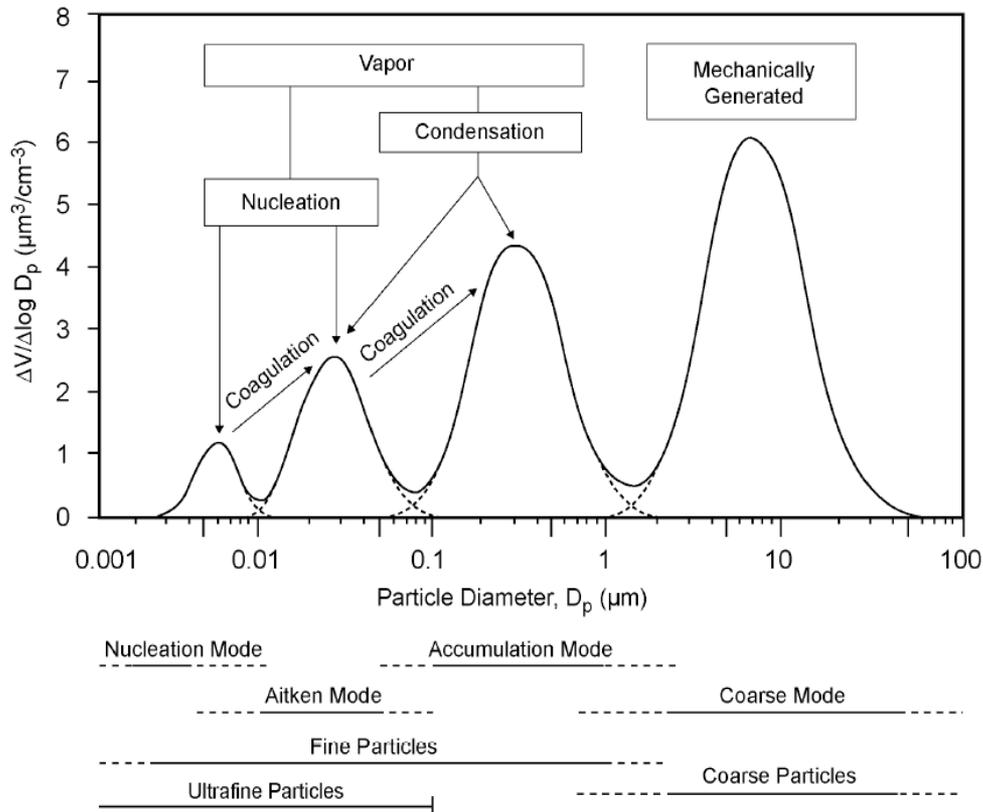
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Outline

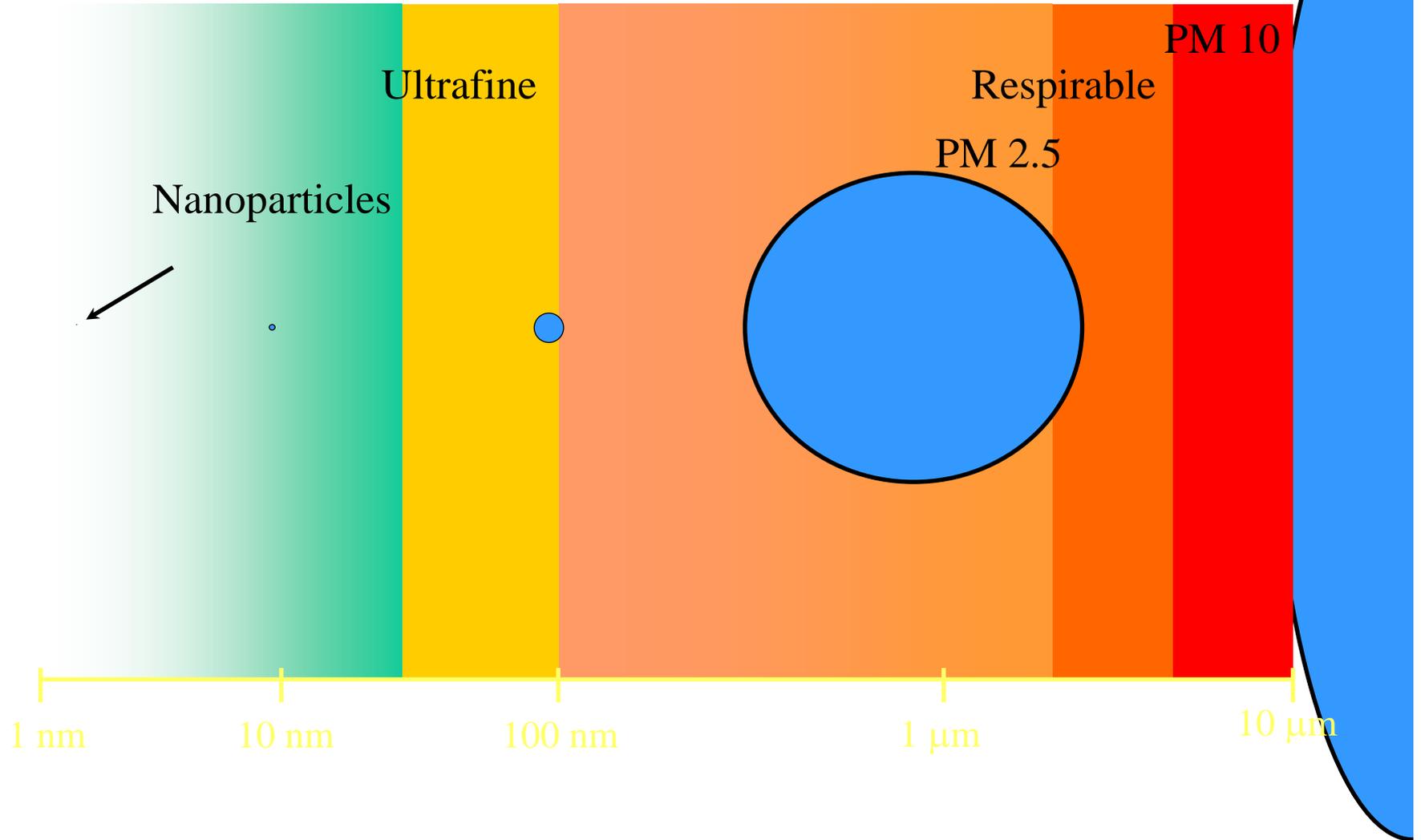
- Brief Overview of Origin of Volatile and Non-Volatile Ambient Fine and Ultrafine Particles.
- Exposure Routes, Retention and Deposition Patterns
- Characteristics and Sources of Black and Brown Carbon
- Possible Mechanisms of Effect
- Cardiovascular Health Effect Study
 - Methods
 - Results
 - Conclusions and Discussion
- Acknowledgements

Much of our thinking about nanoparticles stems from our knowledge of traffic-related particulate matter (EPA, 2004)



- The four polydisperse modes of traffic-related ambient particulate matter span approximately 4 orders of magnitude from below 1 nm to above 10 μm .
- Nucleation and Aitken mode particles are defined as ultrafine particles ($< \sim 100$ nm).
- Source-dependent chemical composition is not well controlled and varies considerably.
- In contrast engineered nanoparticles (1-100 nm) have well controlled chemistry and are generally monodispersed.
- The particles < 10 nm have surface properties that are quantum dominated and may represent a separate class of materials.

Particle Scale

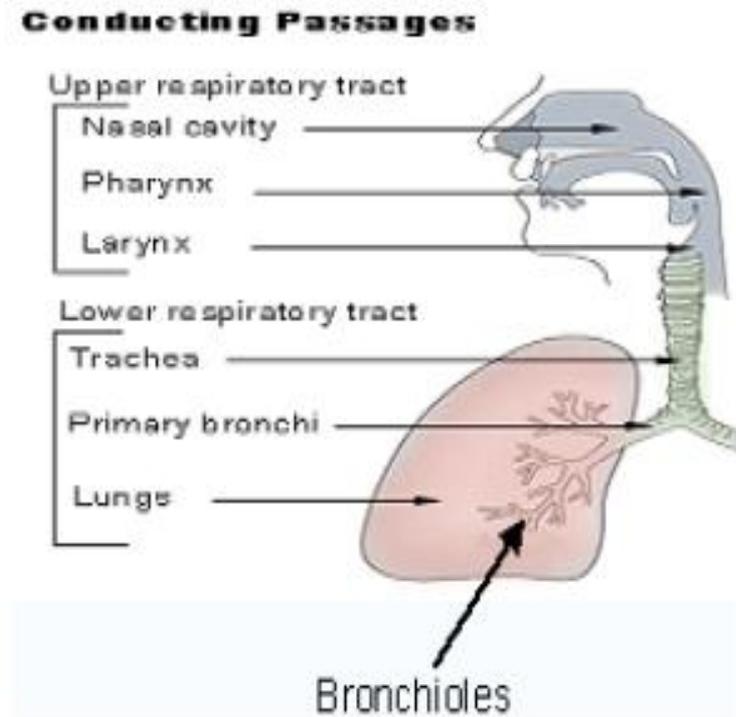


Black and Brown Carbon Aerosols are Important Constituents of PM_{2.5} and UFP

- Black carbon (BC) is the most strongly light-absorbing component of particulate matter (PM), and is formed by the incomplete combustion of fossil fuels, biofuels, and biomass.
- BC is emitted directly into the atmosphere in the form of fine particles (PM_{2.5}) and ultrafine particles (PM_{0.1}). These are also considered nanoparticles.
- BC is the most effective form of PM, by mass, at absorbing solar energy: per unit of mass in the atmosphere, BC can absorb a million times more energy than carbon dioxide (CO₂).
- BC is a major component of “soot”, a complex light-absorbing mixture that comprised of a mixture of Elemental Carbon (EC) and Particulate Organic Carbon (OC).
- Organic carbon aerosols are a significant absorber of solar radiation. The absorbing part of organic aerosols is referred to as “brown” carbon (BrC).

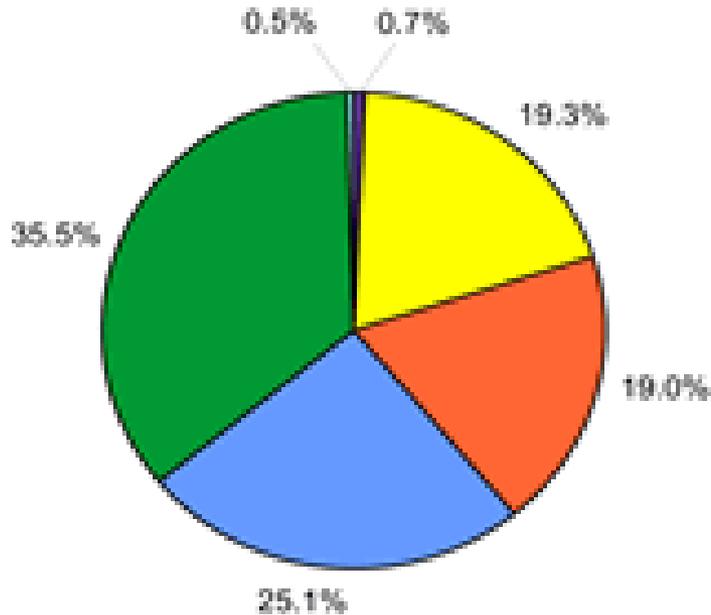
Understanding How Inhaled Particles can Affect Health Begins With Understanding the Respiratory System

- Particles can deposit in the head and the chest.
- The human lung is a complex, branching structure.
- The structure is also complex at the cellular level .
- This complexity means that different parts of the lung have different sensitivities to particles.

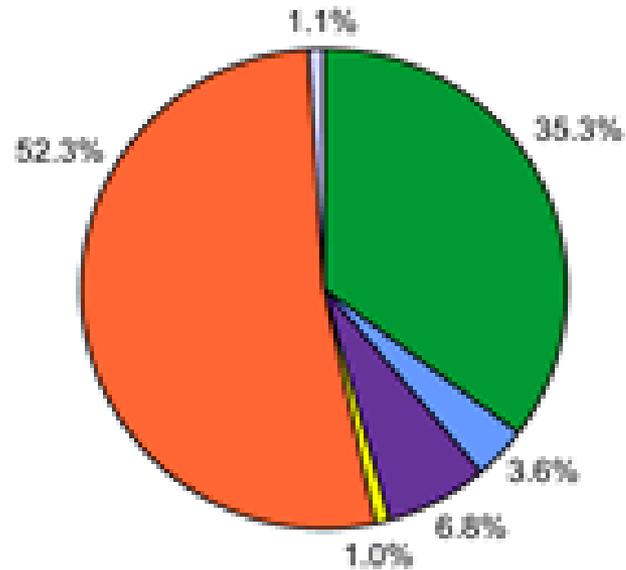


From Where Does Black Carbon Come?

Global BC Emissions, 2000 (7,600 Gg)



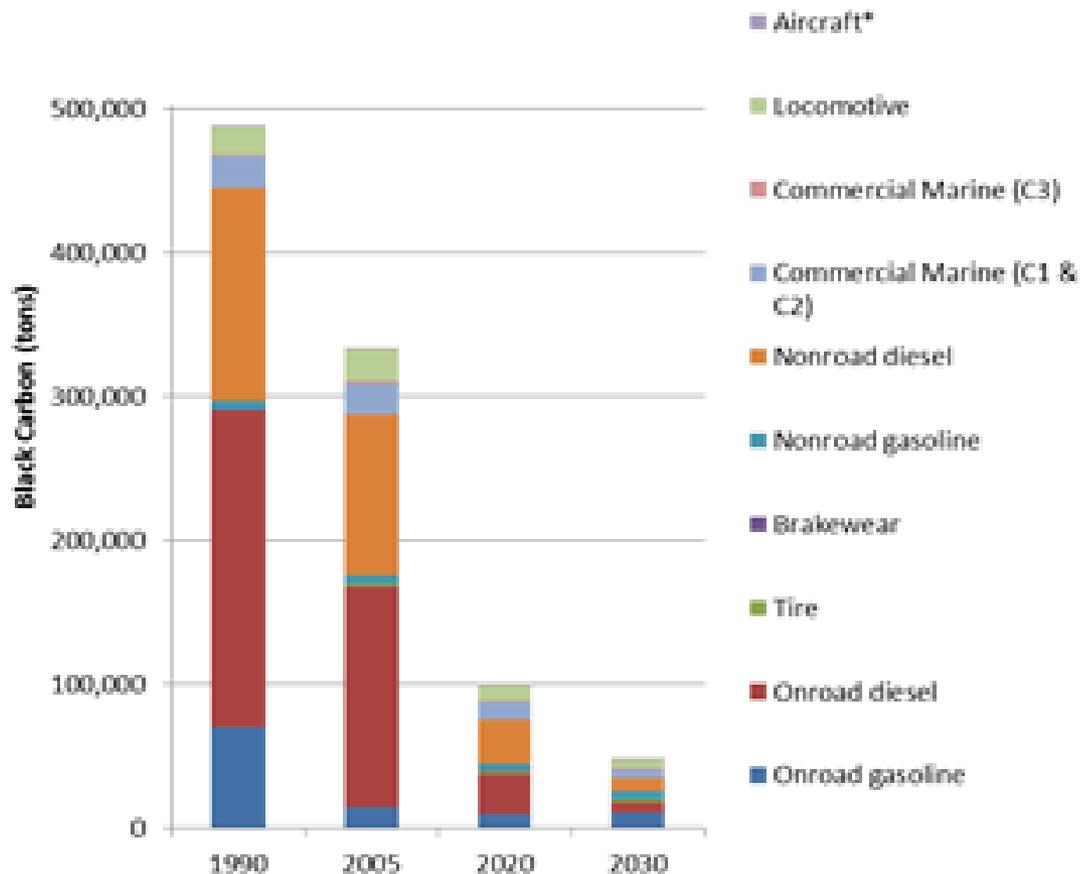
U.S. BC Emissions in 2005 (0.64 Million Tons)



- Open Biomass Burning (Includes Wildfires)
- Transport
- Energy/Power
- Domestic/Residential
- Industry
- Other

BC Emissions Have Been Trending Down!

U.S. Mobile Source Emissions Trends, 1990-2030



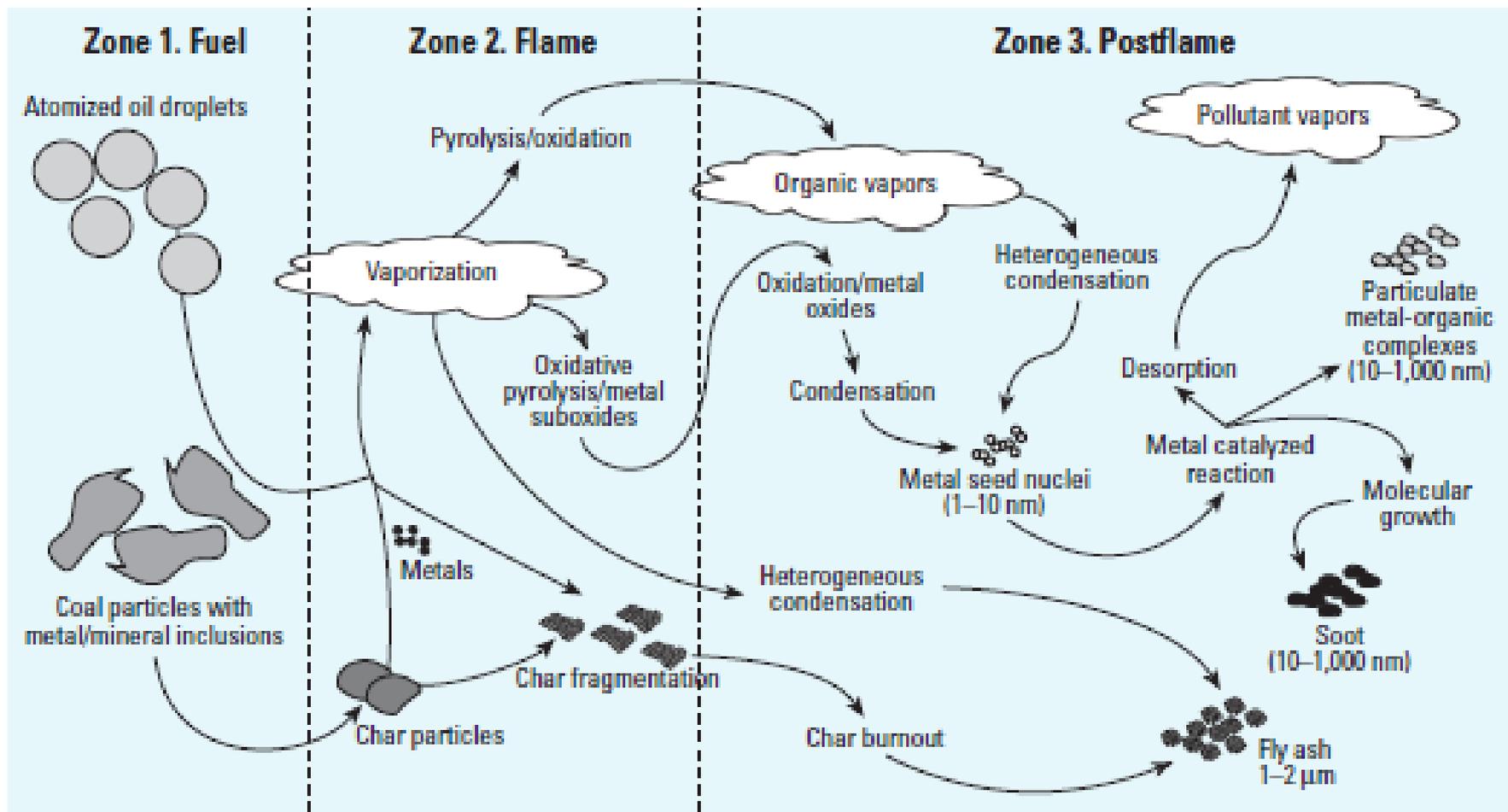


Figure 2. Nanoparticle formation/growth and mediation of pollutant-forming reactions in combustion systems. The combustor reaction zones described in Figure 1 effect particle formation as well as gas-phase pollutant formation. Metals and other refractory compounds are vaporized in the flame zone. They can recondense as cluster or seed nuclei in the postflame zone, where they catalyze further particle growth and pollutant formation in the cool zones.

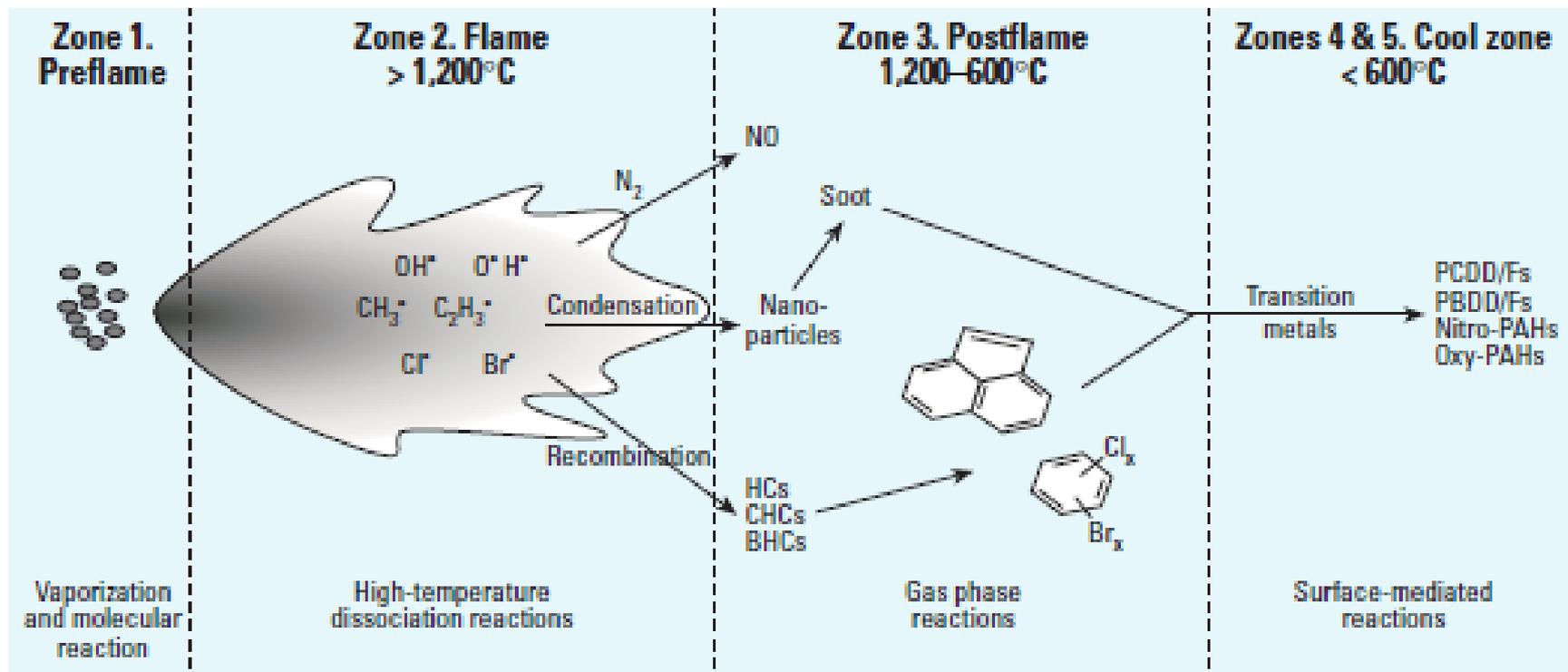


Figure 1. Combustor reaction zones. Zone 1, preflame, fuel zone; zone 2, high-temperature, flame zone; zone 3, postflame, thermal zone; zone 4, gas-quench, cool zone; zone 5, surface-catalysis, cool zone. PBDD/Fs, polybrominated dibenzo-*p*-dioxins and dibenzofurans. Reaction products from upstream zones pass through downstream zones and undergo chemical modifications, resulting in formation of new pollutants. Zone 2 controls formation of many “traditional” pollutants (e.g., carbon monoxide, sulfur oxides, and nitrogen oxides). Zones 3 and 4 control formation of gas-phase organic pollutants. Zone 5 is a major source of PCDD/Fs and is increasingly recognized as a source of other pollutants previously thought to originate in zones 1–4.

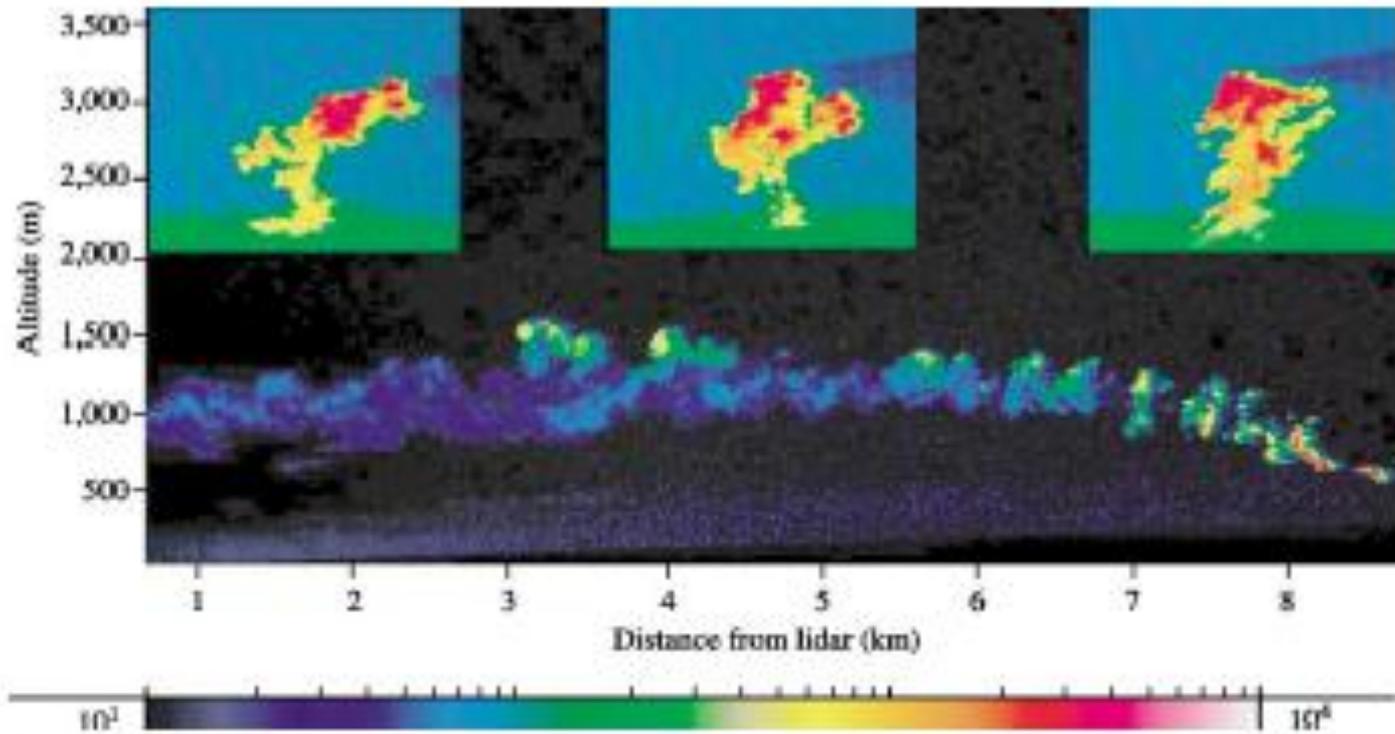


Figure 20 Lidar images of an aerosol-rich plume emitted from a power plant. The plume, viewed lengthwise from the ground, is above the PBL at an altitude of ~ 0.3 km. The inserts are enlarged cross-sections of a similar plume, taken at 1 min intervals. The shapes of such sections change continuously with both position along the length of the plume and with time. Nanticoke power plant, Ontario, Canada. The lengthwise and cross-section images were taken on January 22 and 19, 2000, respectively at 1,064 nm, with scan speeds adjusted depending on distance from source and proximity of mobile lab to produce a full-scan image in less than 1 min. The images were obtained by and are courtesy of K. Strawbridge, Meteorological Service of Canada.

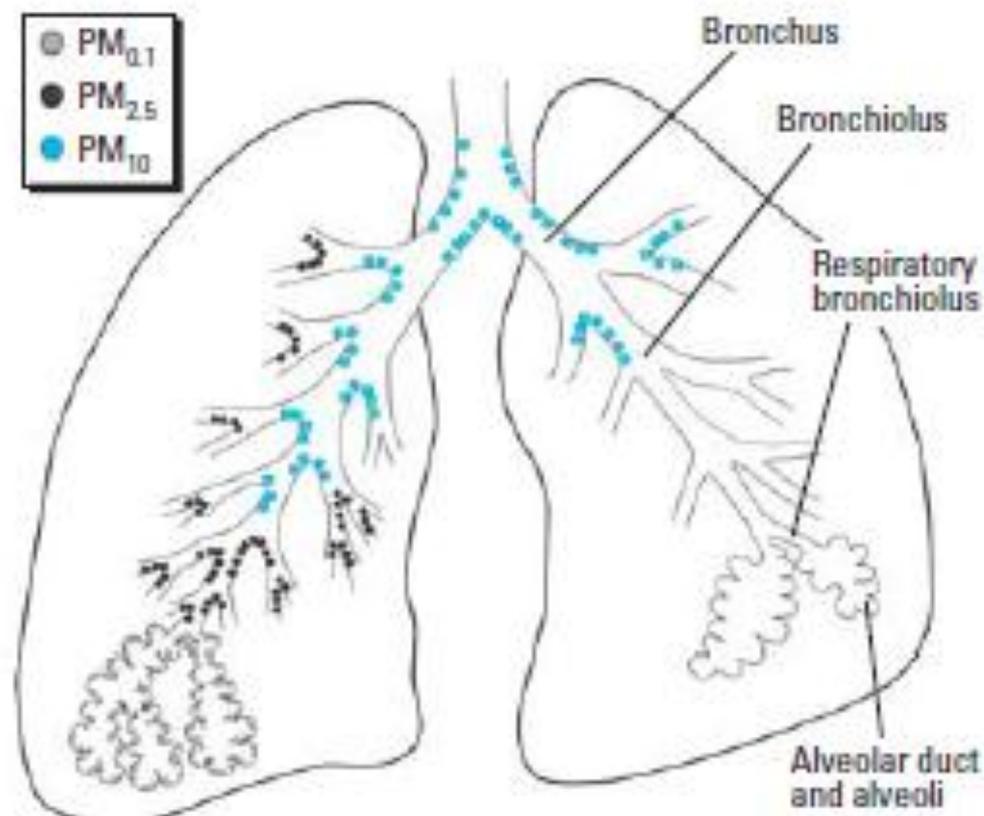
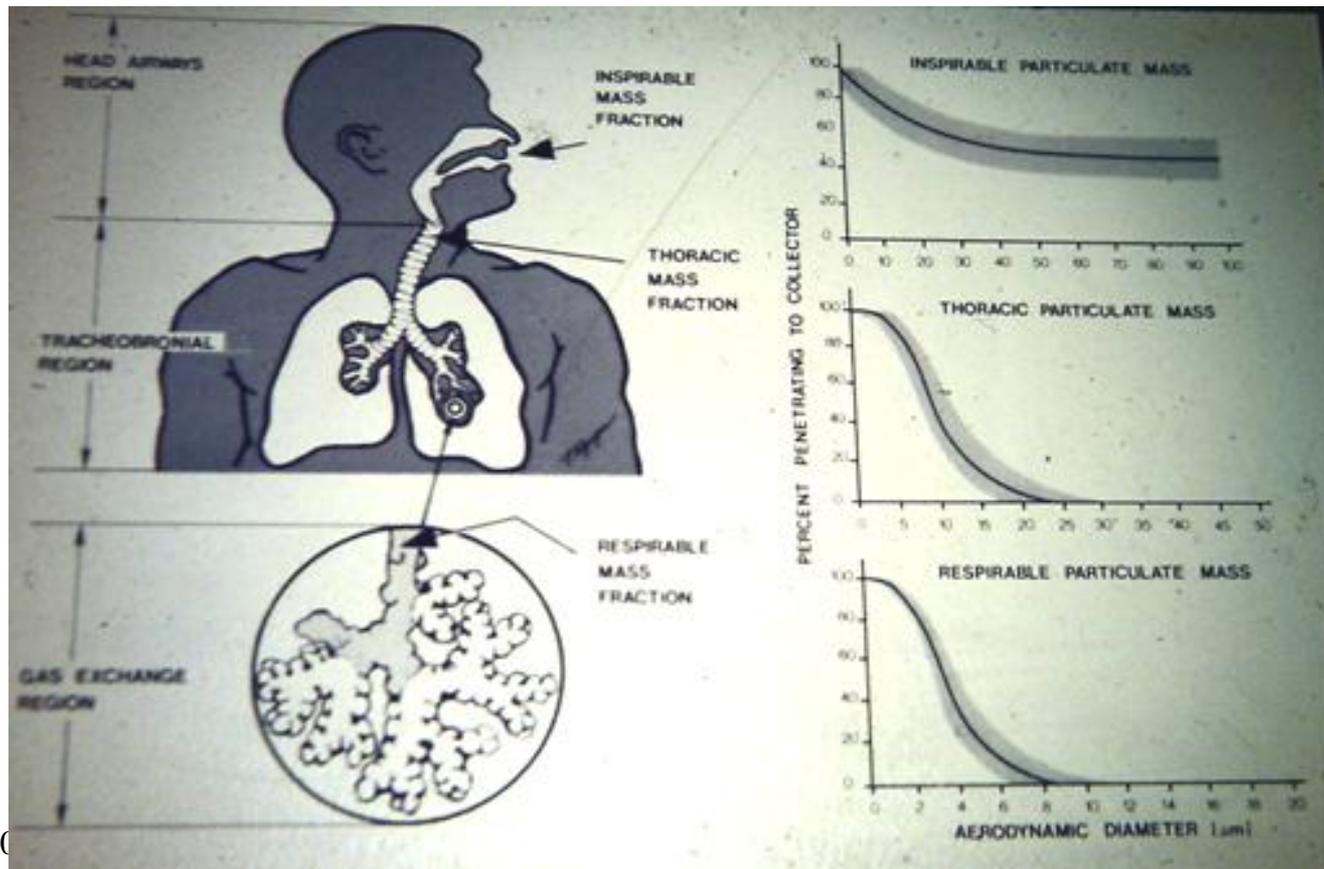
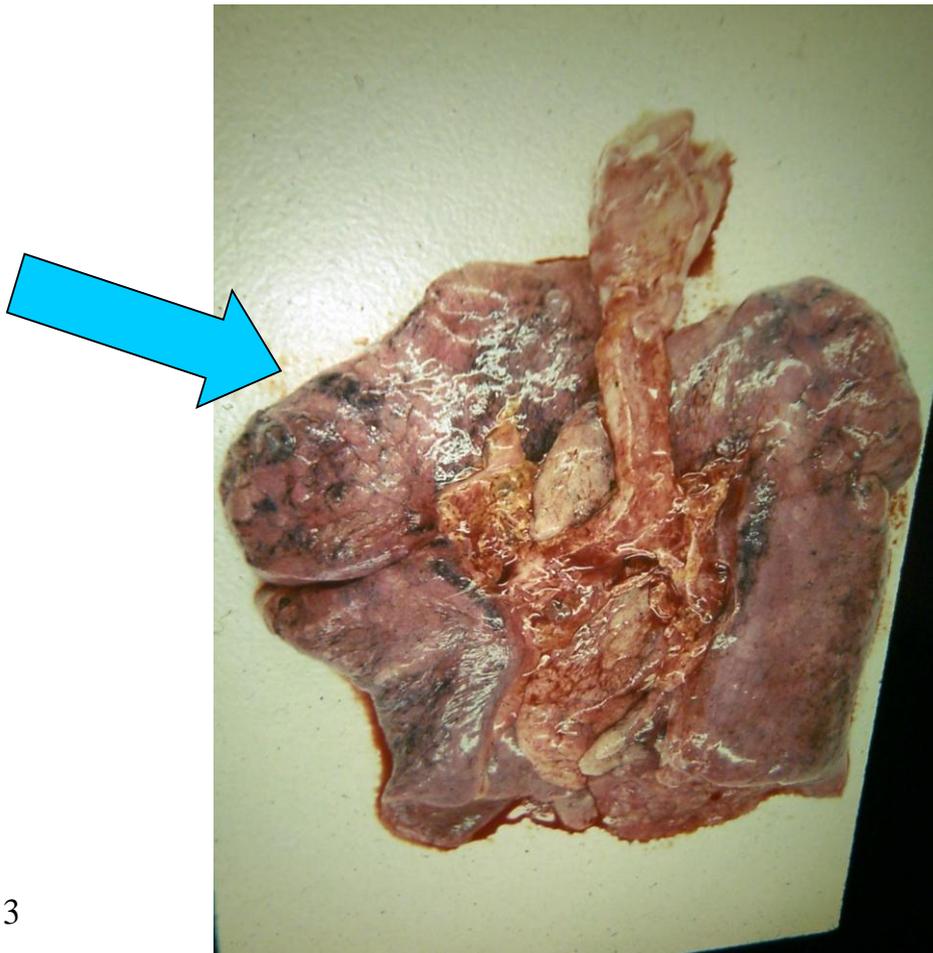


Figure 3. Distribution of PM in the airways. PM ≥ 10 μ m in diameter enter the nose and mouth. The thoracic fraction, PM_{10} , passes the larynx and penetrates the trachea and bronchial regions of the lung, distributing mainly at pulmonary bifurcations. The respirable fraction, $PM_{2.5}$, and ultrafine PM, $PM_{0.1}$, enter the nonciliated alveolar regions and deposit deep within the lungs.

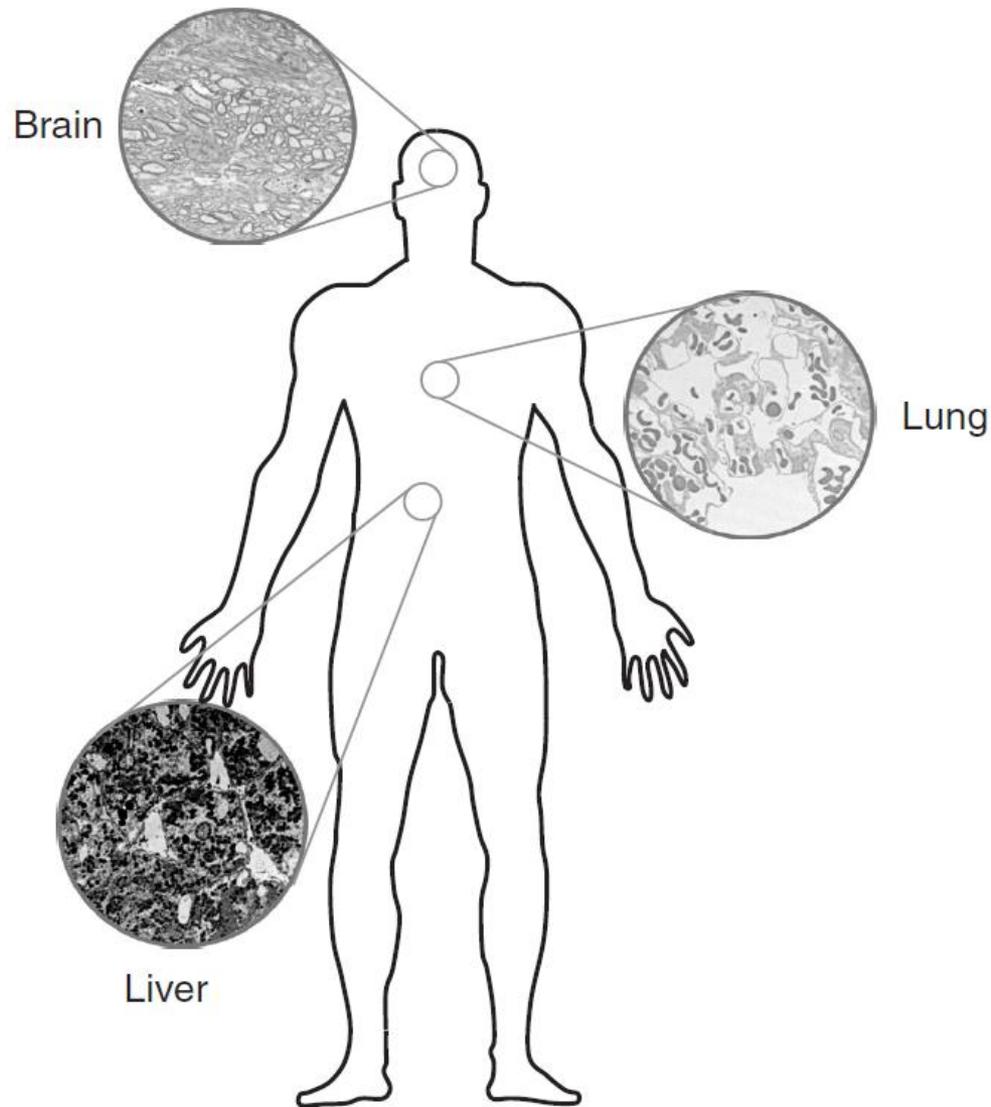
Particles of Different Size Deposit in Different Places in the Respiratory System . Size Influences Target Sites in the Lung



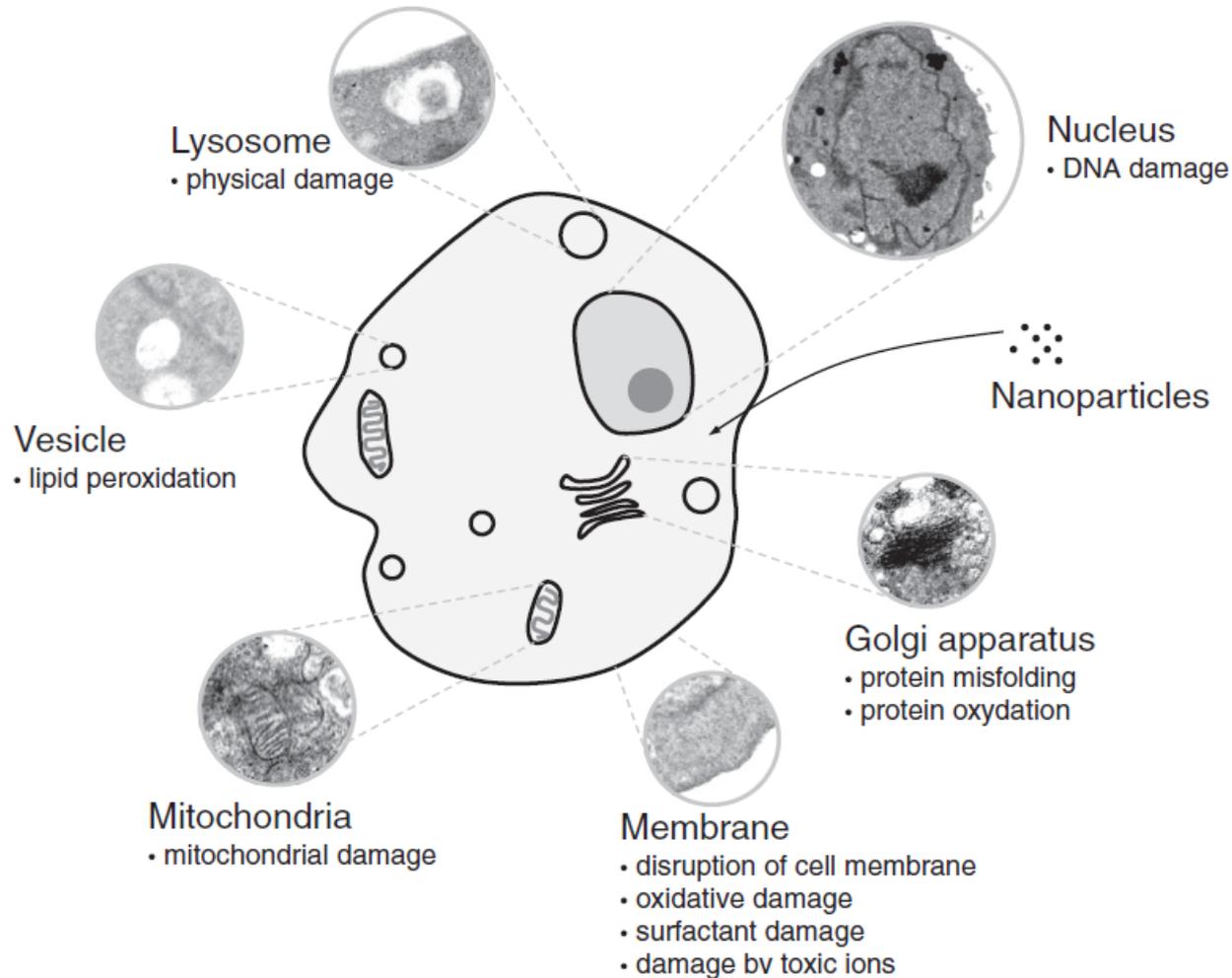
**While Soluble Particles Distribute into Lung Fluids,
Insoluble Particles can be Retained For Long Periods**



Nanoparticle entry route into the body via the lung, particle accumulation in the liver and the most vulnerable site: the brain.



Nanoparticle interaction with cells: intracellular targets and nanotoxicological mechanisms.



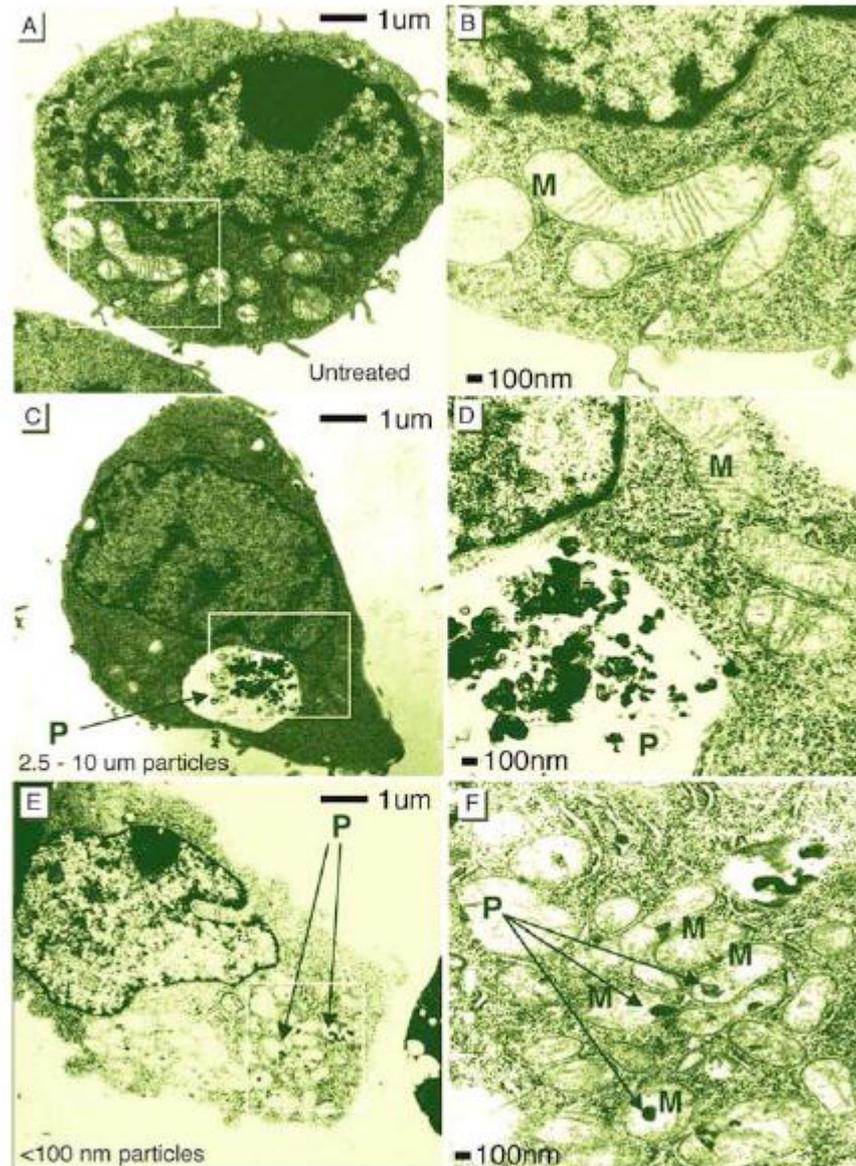
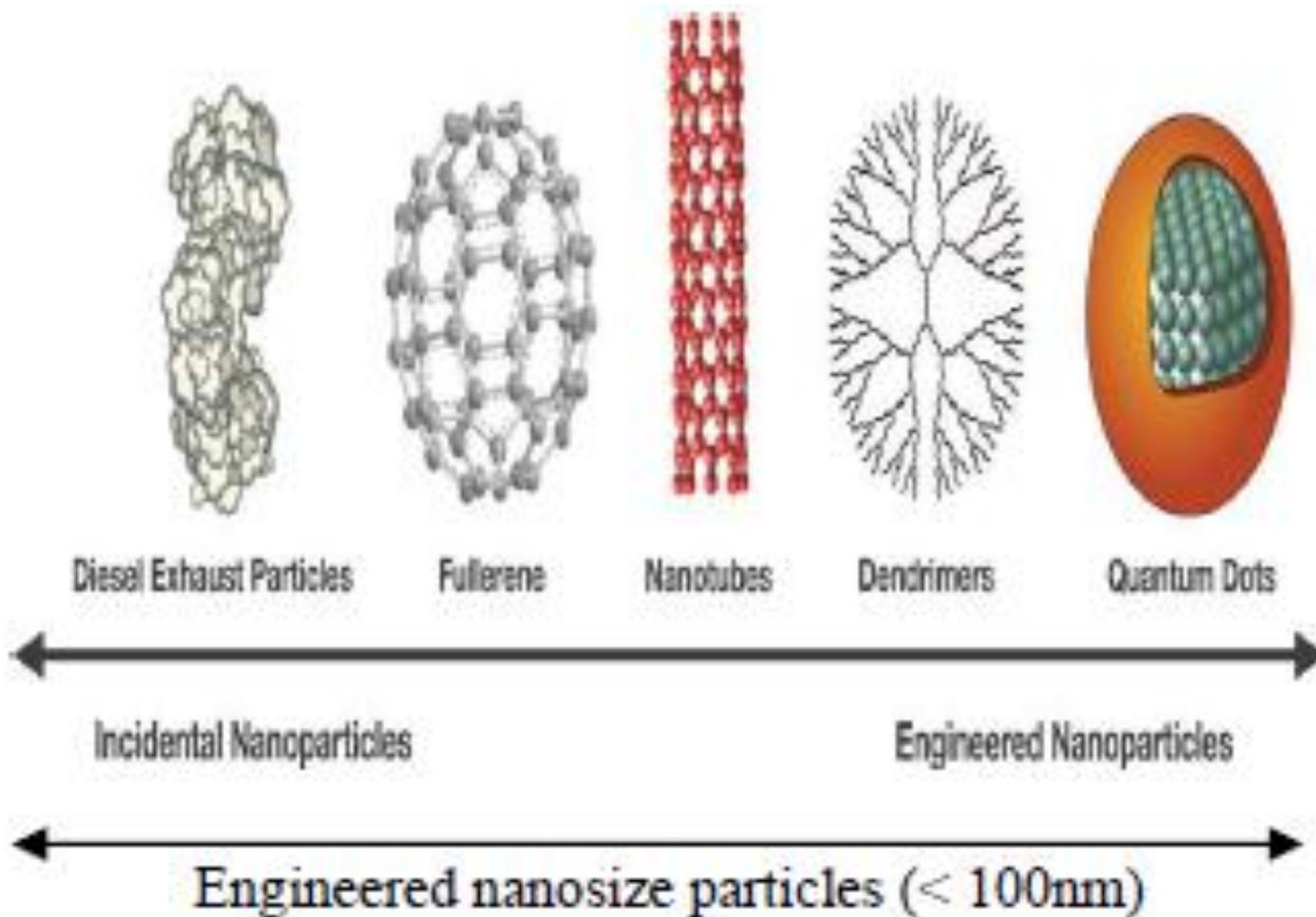


Figure 28. TEM images showing effects of environmental particles size (P) on murine macrophage cells RAW 264.7 treated with various size particles: (a,b) untreated, (c,d) 2.5 - 10 μm size particles, (e,f) particles smaller than 100 nm. M denotes mitochondria [57]. Reproduced with permission from Environmental Health Perspectives.

Typical Ambient Black Carbon Nanoparticles vs. Engineered Particles



Do Ambient UFP Play a Role in Cardiovascular Disease?

- An increase in air pollutants leads to increased mortality and hospital admissions because of cardiovascular diseases (Analitis A. et al. 2006, Zanobetti et al. 2003, Dominici et al. 2006, Peel et al. 2007)
- Exposure to elevated levels of particulate matter (PM) in ambient air leads to an increased heart rate (HR) and a decreased heart rate variability (HRV) in elderly patients (Dubowsky Adar S. et al. 2007, Luttmann-Gibson et al. 2006)
- Individuals in the >65 year-old age bracket are more susceptible to air pollution-associated heart-related morbidity and mortality
- Black and Brown Carbon are important constituents of ambient UFP.
- The role of the organic constituents of ambient PM may be associated with the effects of UFP on the heart.

Recent Findings and Implications of Air Quality-Related Health Research at UC Irvine

- Nearly 50% of deaths are associated with heart disease.
- Ultrafine PM (UFP) is more effective than Fine PM in promoting atherosclerosis.
- Biomarkers of heart disease are associated with organic (OC) and elemental carbon (EC) components of UFP.
- UFP may be important because large surface area may act as a “carrier” that brings chemicals into areas that they couldn’t ordinarily reach.

Epidemiology

- Delfino – Cardiovascular effects of UFP, association of biomarkers with adverse effects
- Wu - Land use regression for traffic related adverse responses
- Edwards - Exposure and risk assessments.

- APHEL – Near road exposures promote airway allergies; PM exposure accelerates atherosclerosis.

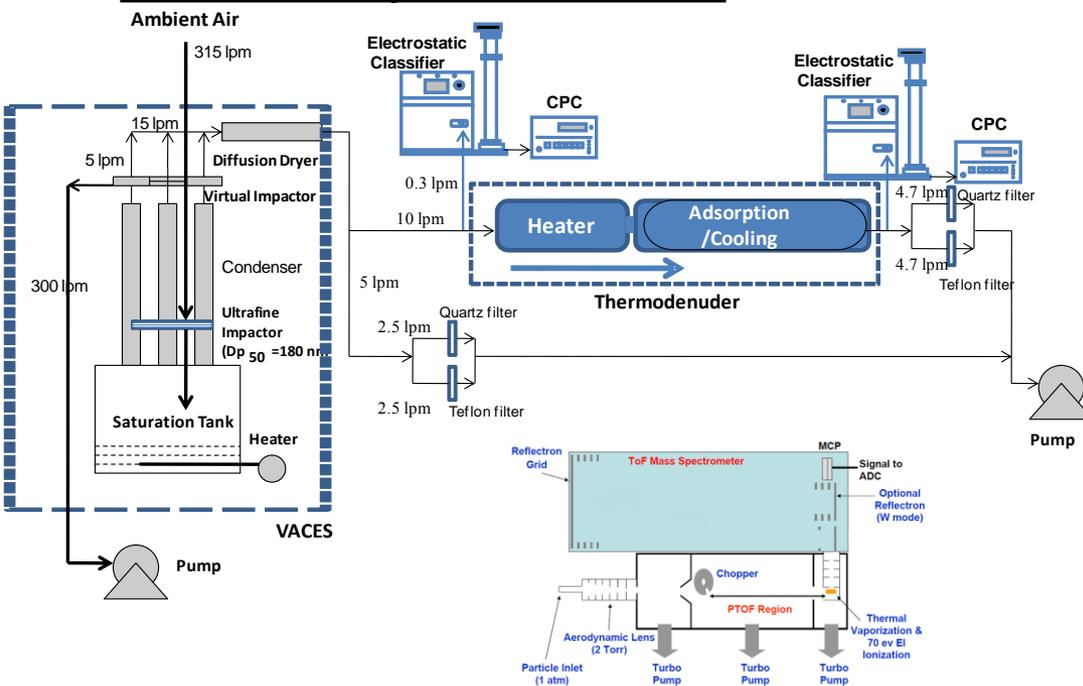
- AirUCI – ongoing characterization of ambient aerosols.
- UCLA - in vitro toxicology assays.
- USC - Characterization of ambient PM organics.

Cardiovascular Study

- Methods

Testing a Specific Mechanism by which PM Exposure Exacerbates Heart Disease

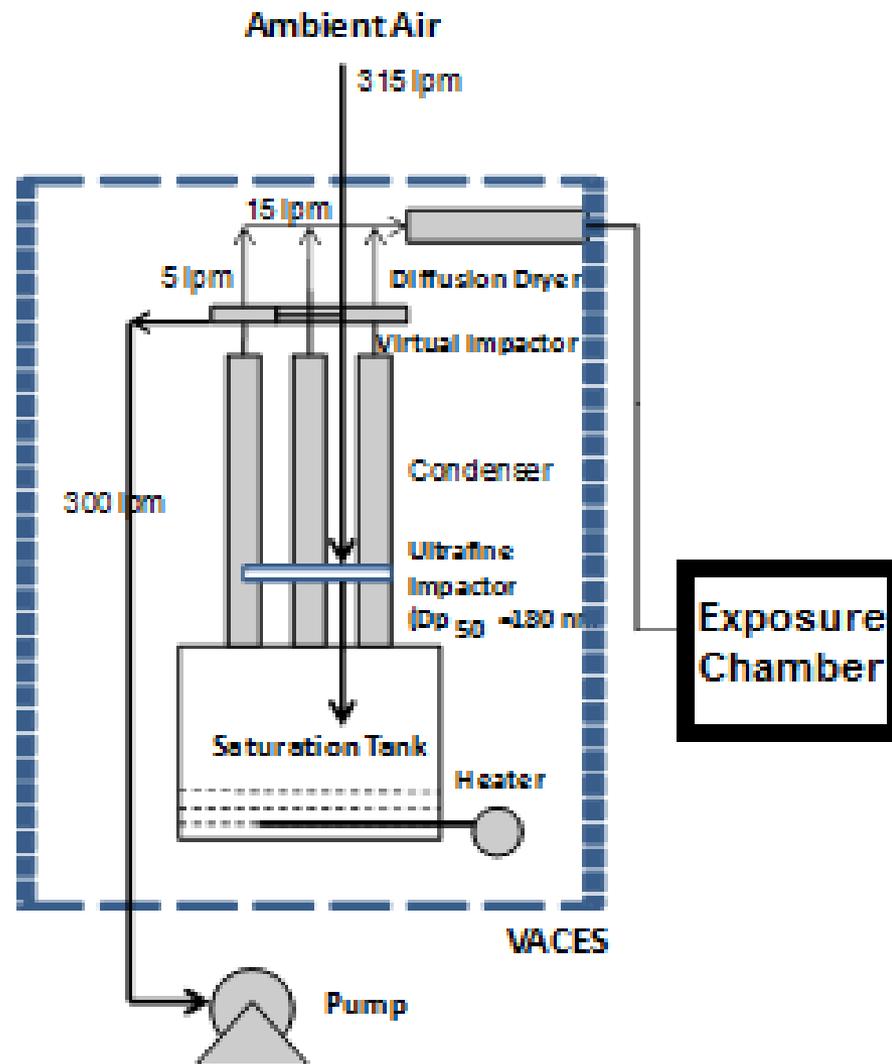
- Human biomarker study (Delfino) indicated importance of UFP organic carbon (OC) constituents related to coronary artery disease.
- We had previously shown that UFP accelerates atherosclerosis in mice.
- We have also shown that PM is less reactive, in vitro, when we remove the organic constituents from UFP using a denuder (which works analogously to modern diesel afterburner emission controls).
- So we tested the hypothesis that removal of the OC from UFP would block the acceleration of atherosclerosis.



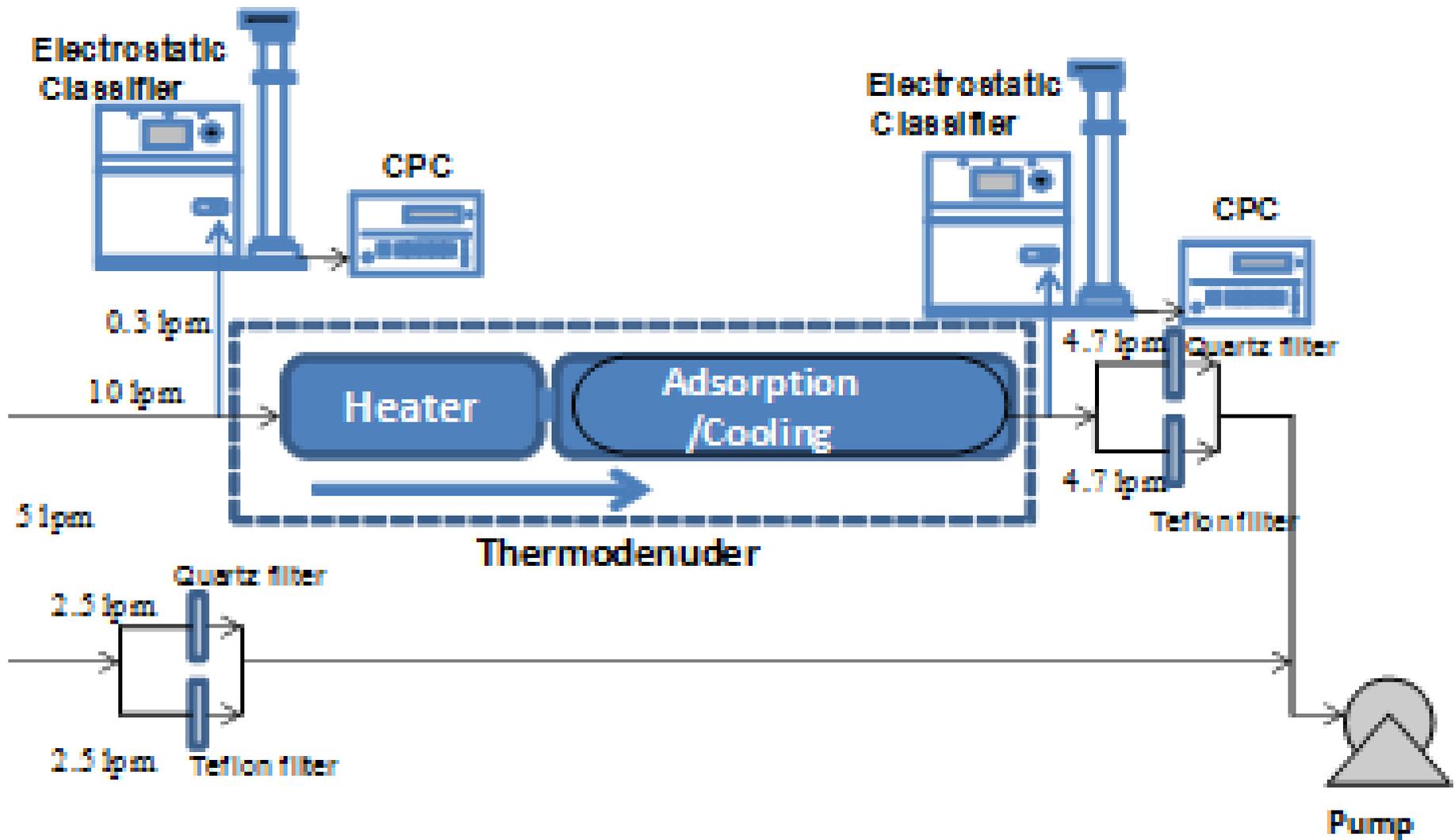
1. We exposed mice in LA to air, denuded and undenuded PM.
2. We characterized the PM.
3. We examined serum biomarkers and arteries
4. We analyzed changes in heart rate and heart rate variability



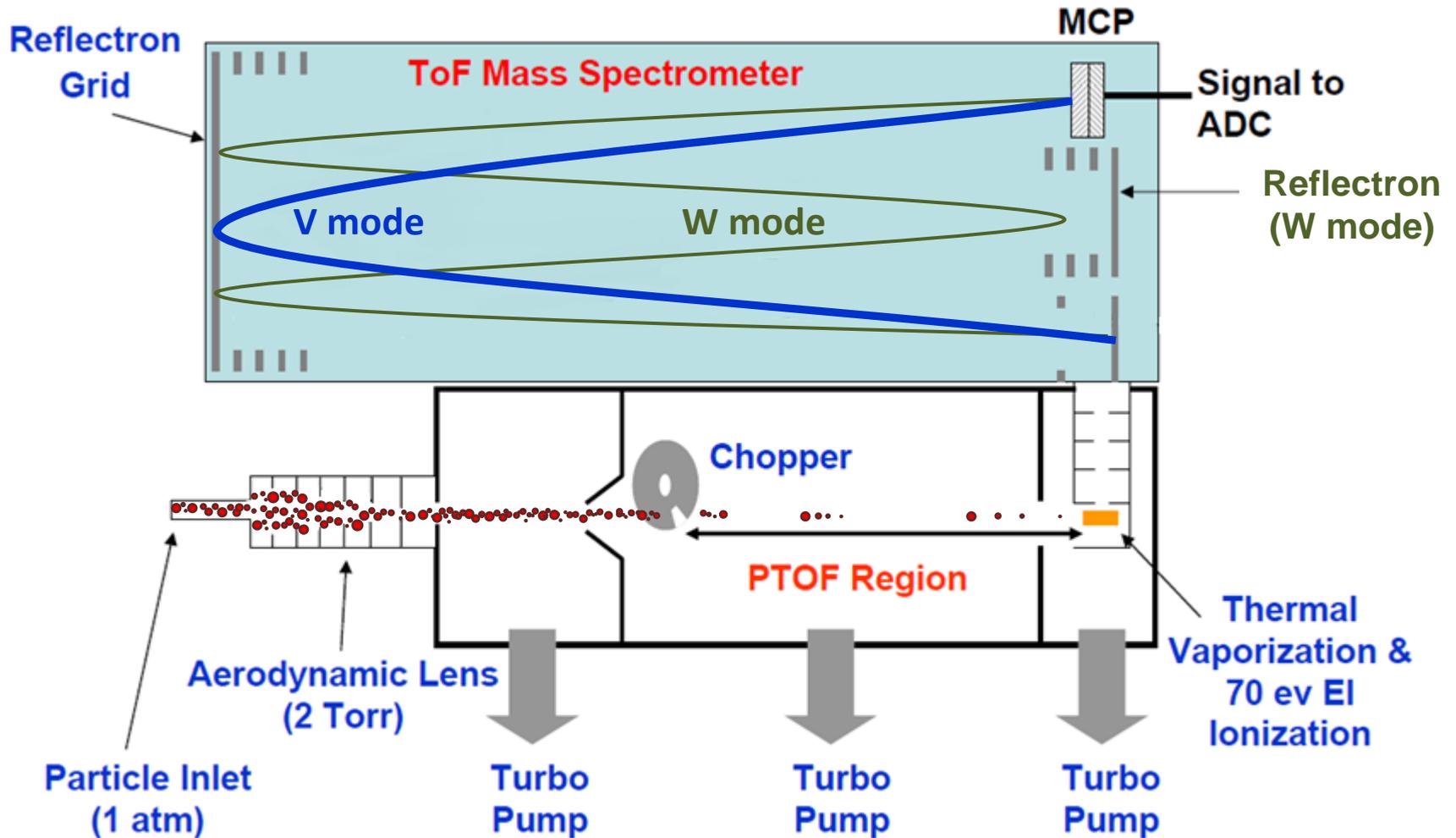
Particle Concentrator (VACES)



Thermodenuder

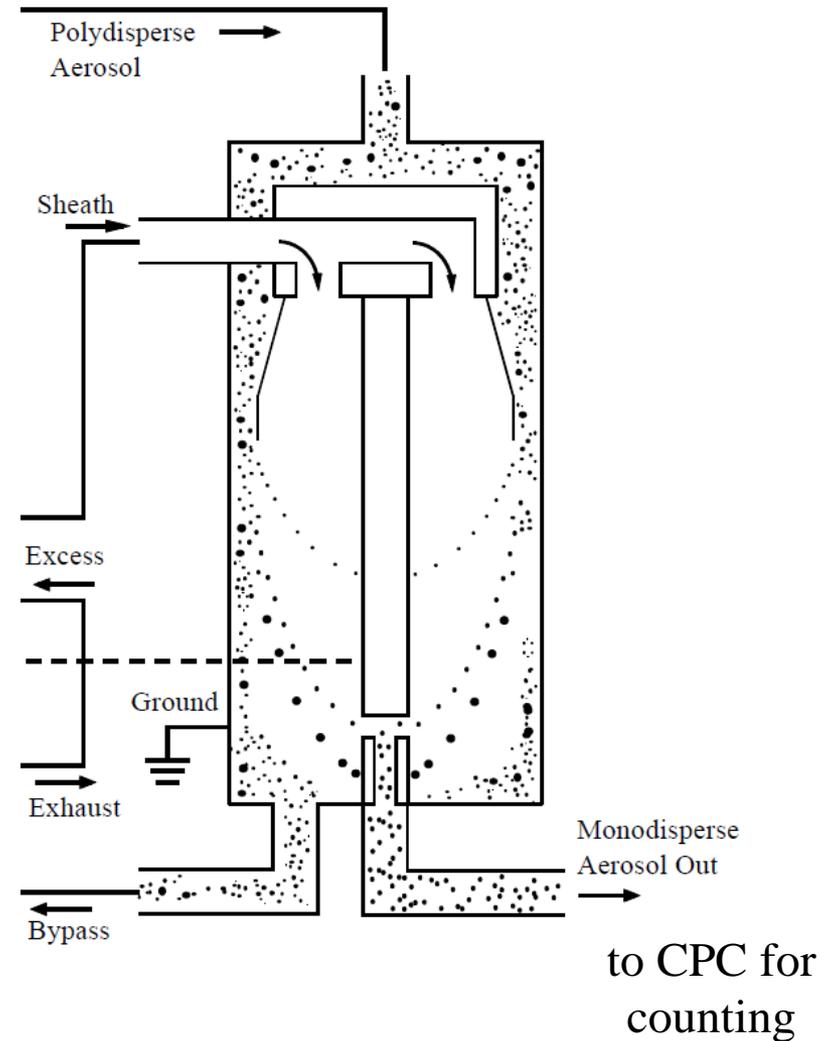


- AMS provides real time high resolution mass spectra of particles as well as particle size distributions (aerodynamic diameter).

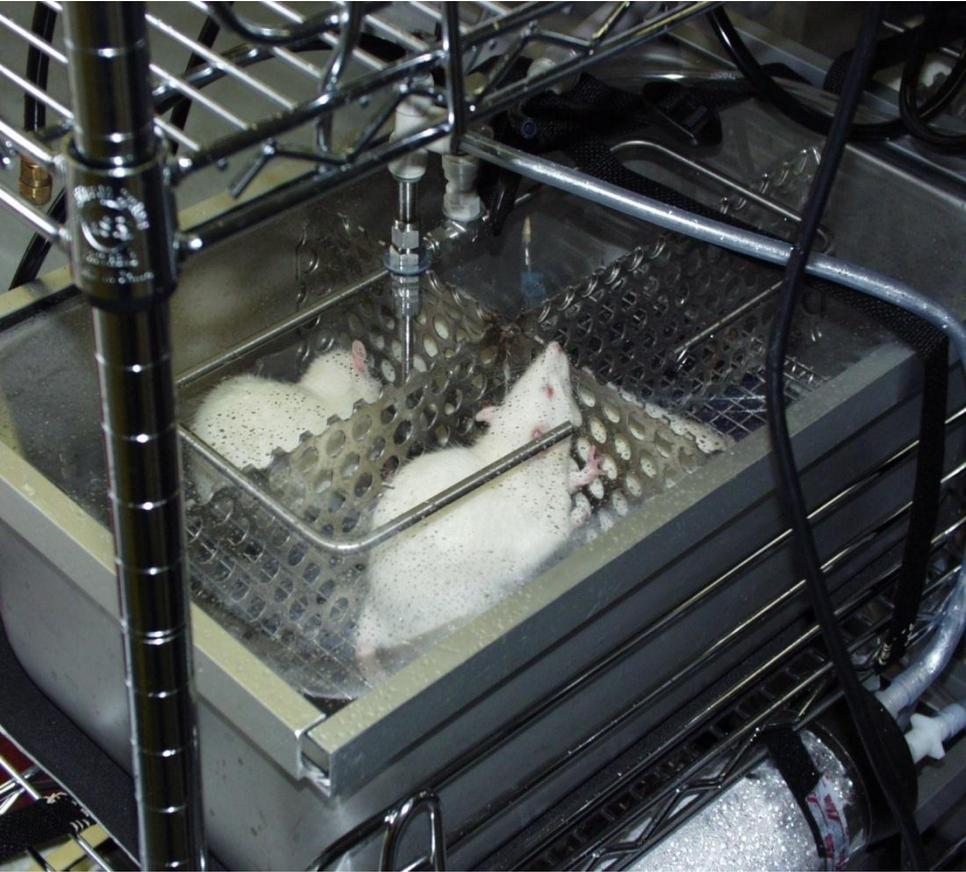


Scanning Mobility Particle Size Spectrometer (SMPS)

- SMPS measures electrical mobility diameter of polydisperse aerosol samples.
- Size distributions and particle concentrations were measured before and after the particle concentrator.
- AMS data collected of ambient air and particles concentrated by particle concentrator.



Mice were exposed to Purified Air, undenuded CAPs or denuded CAPs in Sealed Chambers



The Sealed Chambers Can Be Placed Onto Racks and Transported to USC for the Exposures



ECG Telemetry Transponders were Implanted to provide physiology data before, during and after exposures over the 8 week exposure period.

Exposure Protocol

- ApoE-/- mice were surgically implanted with ECG telemetry devices.
- Mice were transported to the exposure site while breathing purified air.
- Mice were exposed 6 hr per day (8AM to 2 PM) 4 days per week for 8 weeks at a site near US110.
- Mice were transported to UC Irvine and housed in filtered air-supplied caging systems.
- ECG data were monitored during exposures and while the mice were in housing (21 hr / day).
- All animal protocols were approved by the Institutional Animal Care and Use Committee.

The Exposure Site was Proximal to Heavily Trafficked Highways



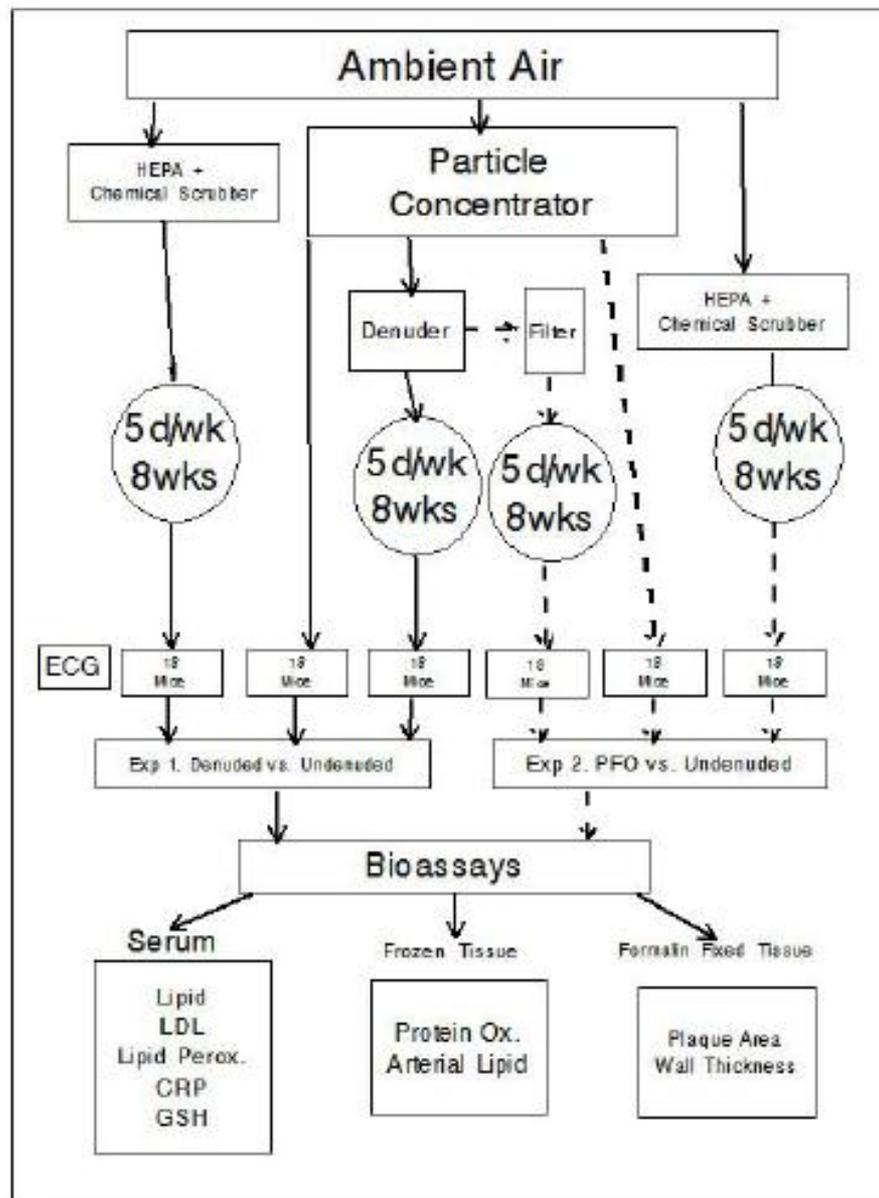
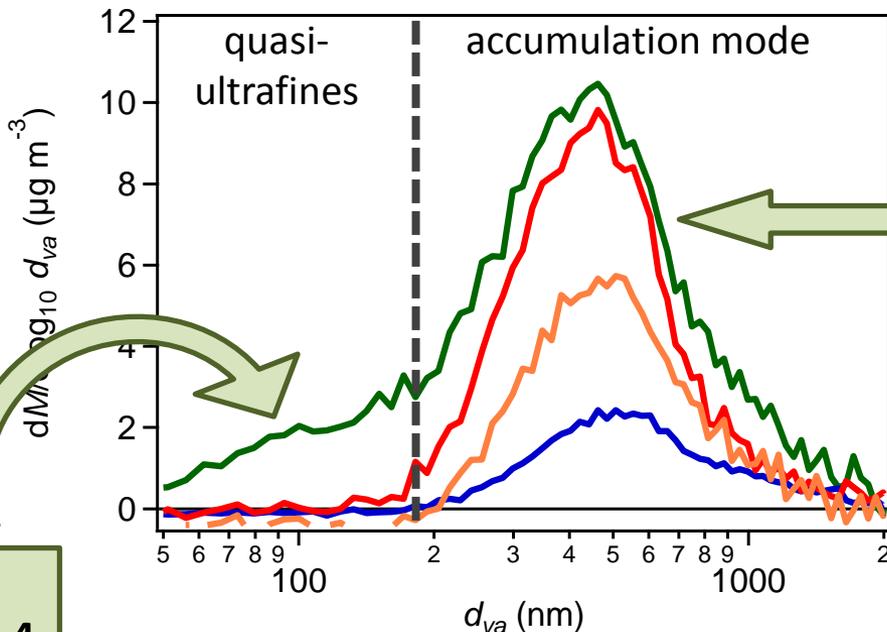


Figure 5 Schematic Diagram of Overall Exposure Design.

Cardiovascular Study

- Methods
- Results

Health-related characteristics of Ultrafine PM



ultrafines
less oxygenated
(to denuder)

$$\frac{m/z\ 44\ (CO_2^+)}{m/z\ 55\ (C_4H_7^+)} \cong 0.4$$

When you denude the UFP

Organics
Sulfate
Ammonium
Nitrate

larger particles
oxygenated

$$\frac{m/z\ 44\ (CO_2^+)}{m/z\ 55\ (C_4H_7^+)} \cong 4$$

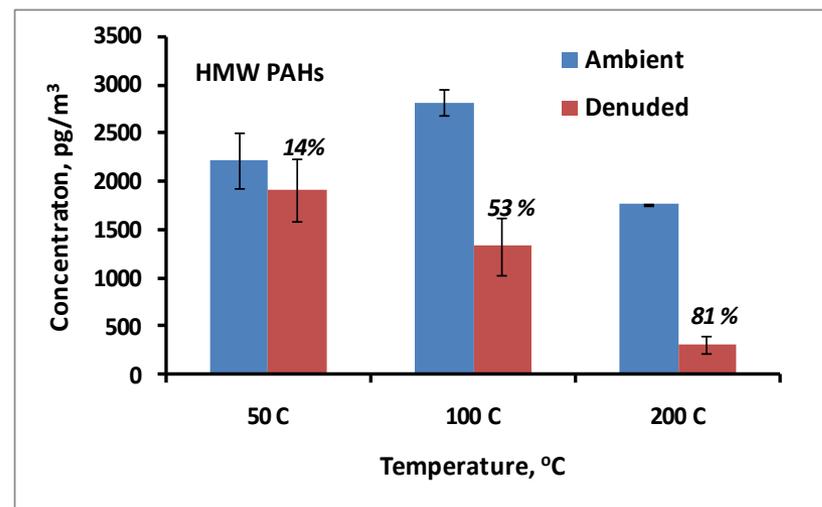
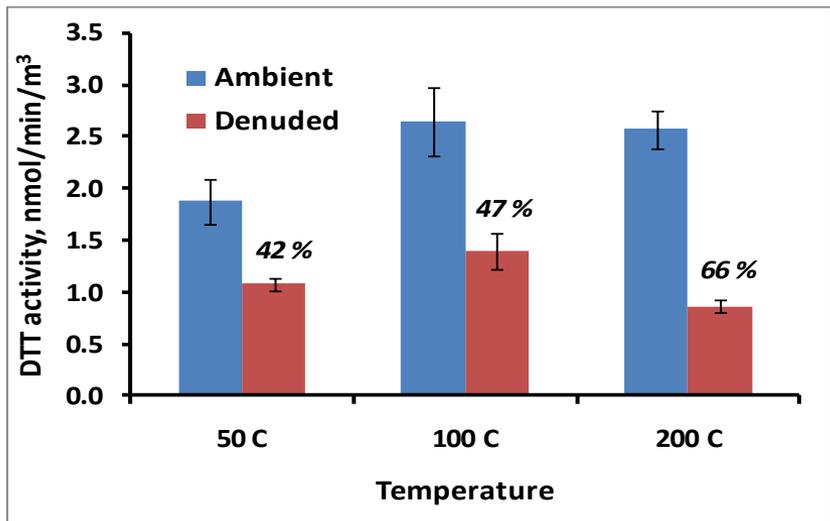


Table 1. Chemical Composition of Exposure Atmospheres (Undenuded s. Denuded)

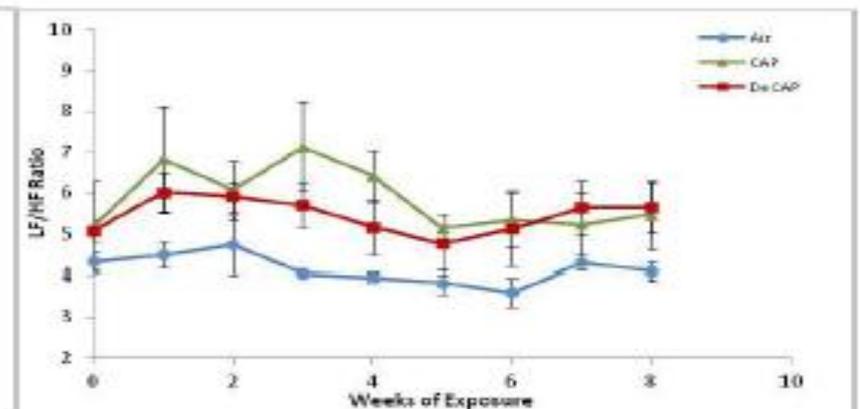
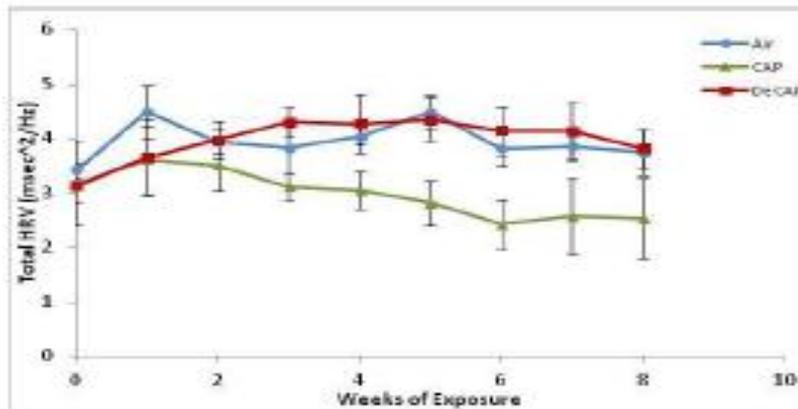
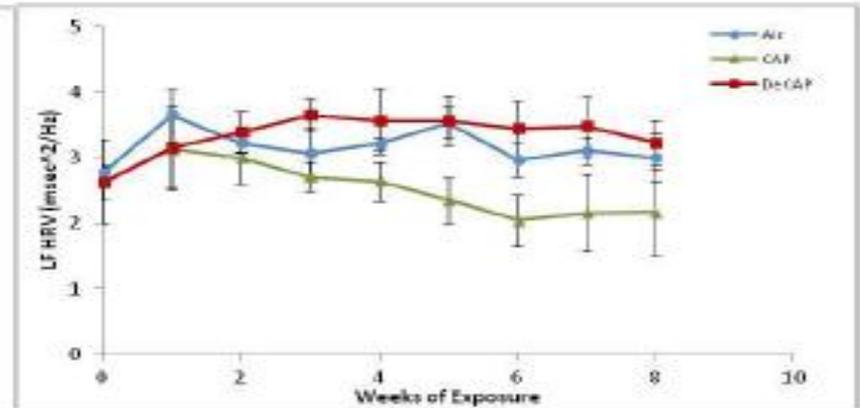
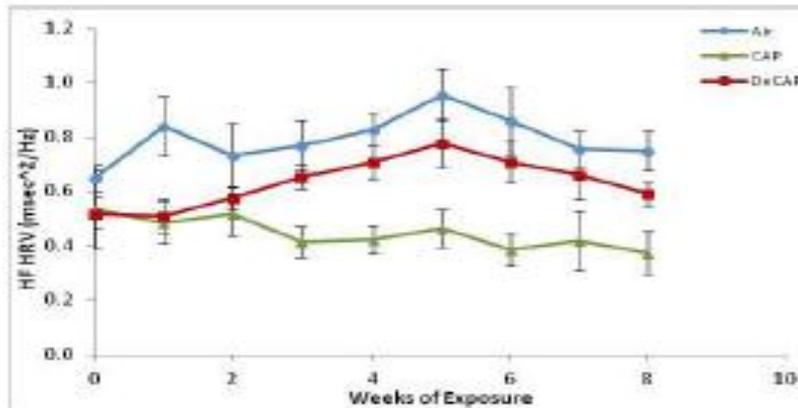
		Particle Composition				Ratio of Denuded/Undenuded
		Total UFP (Undenuded)		Thermal denuded (Denuded)		
		Concentration Mean	Uncertainty S.E.	Concentration Mean	Uncertainty S.E.	
Total UFP, $\mu\text{g}/\text{m}^3$		58.20		28.65		49%
ECOC, $\mu\text{g}/\text{m}^3$	OC	25.382	1.522	8.826	0.716	35% ^{**1}
	EC	1.472	0.371	2.008	0.392	136% ns
	TC	26.855	1.724	10.834	0.953	40% ^{**}
WSOC, $\mu\text{g}/\text{m}^3$		5.701	0.219	2.322	0.142	41% ^{**}
IC, $\mu\text{g}/\text{m}^3$	Chloride	0.027	0.039	0.100	0.041	368% ns
	Nitrate	0.359	0.049	0.214	0.037	60% [*]
	Sulfate	1.959	0.206	2.401	0.250	123% ns
	Ammonium	1.372	0.145	1.171	0.126	85% ns
	Potassium $\mu\text{g}/\text{m}^3$					
	Sodium $\mu\text{g}/\text{m}^3$					
	Phosphate $\mu\text{g}/\text{m}^3$			0.119	0.086	

Table 1. Chemical Composition of Exposure Atmospheres (Undenuded s. Denuded)

		Particle Composition				Ratio of Denuded/Undenuded
		Total UFP (Undenuded)		Thermal denuded (Denuded)		
		Concentration Mean	Uncertainty S.E.	Concentration Mean	Uncertainty S.E.	
PAH, ng/m ³	Naphthalene	≤0.018	≤0.018	≤0.018	≤0.018	86% ns 320% ns 76% ns 29% **
	Acenaphthylene	≤0.018	≤0.018	≤0.018	≤0.018	
	Fluorene	≤0.018	≤0.018	≤0.018	≤0.018	
	Phenanthrene	0.250	0.071	0.216	0.064	
	Anthracene	0.023	0.020	0.075	0.026	
	Fluoranthene	0.142	0.035	0.108	0.030	
	Pyrene	0.326	0.071	0.095	0.029	
	Methylfluoranthene	≤0.018	≤0.018	≤0.018	≤0.018	
	9-Methylanthracene	≤0.018	≤0.018	≤0.018	≤0.018	
	Benzo(ghi)fluoranthene	≤0.018	≤0.018	≤0.018	≤0.018	
	Cyclopenta(cd)pyrene	≤0.018	≤0.018	≤0.018	≤0.018	
	Benzo(a)anthracene	≤0.018	≤0.018	≤0.018	≤0.018	
	Chrysene	≤0.018	≤0.018	≤0.018	≤0.018	
	1-Methyl chrysene	≤0.018	≤0.018	≤0.018	≤0.018	
	Retene	≤0.018	≤0.018	≤0.018	≤0.018	
	Benzo (b)fluoranthene	0.912	0.183	0.028	0.019	3% **
	Benzo (k)fluoranthene	≤0.018	≤0.018	≤0.018	≤0.018	0% ** 0% **
	Benzo(e)pyrene	0.765	0.154	≤0.018	≤0.018	
	Benzo(a)pyrene	0.788	0.159	≤0.018	≤0.018	
	Perylene	≤0.018	≤0.018	≤0.018	≤0.018	0% ns 13% ** 0% ns
	Indeno(123-cd)pyrene	0.096	0.027	≤0.018	≤0.018	
	Benzo(ghi)perylene	0.216	0.047	0.028	0.019	
	Dibenzo(ah)anthracene	0.023	0.019	≤0.018	≤0.018	11% **
Picene	≤0.018	≤0.018	≤0.018	≤0.018		
Coronene	0.204	0.060	0.022	0.031		
Dibenzo(ae)Pyrene	≤0.018	≤0.018	≤0.018	≤0.018		

Ambient PM Exposure Causes Reduced Heart Rate Variability – Removing the Organic Constituents Blocks The Effect

Heart Rate Variability



2009
Decrease in
HF HRV
>50%
Baseline

Air

CAPS

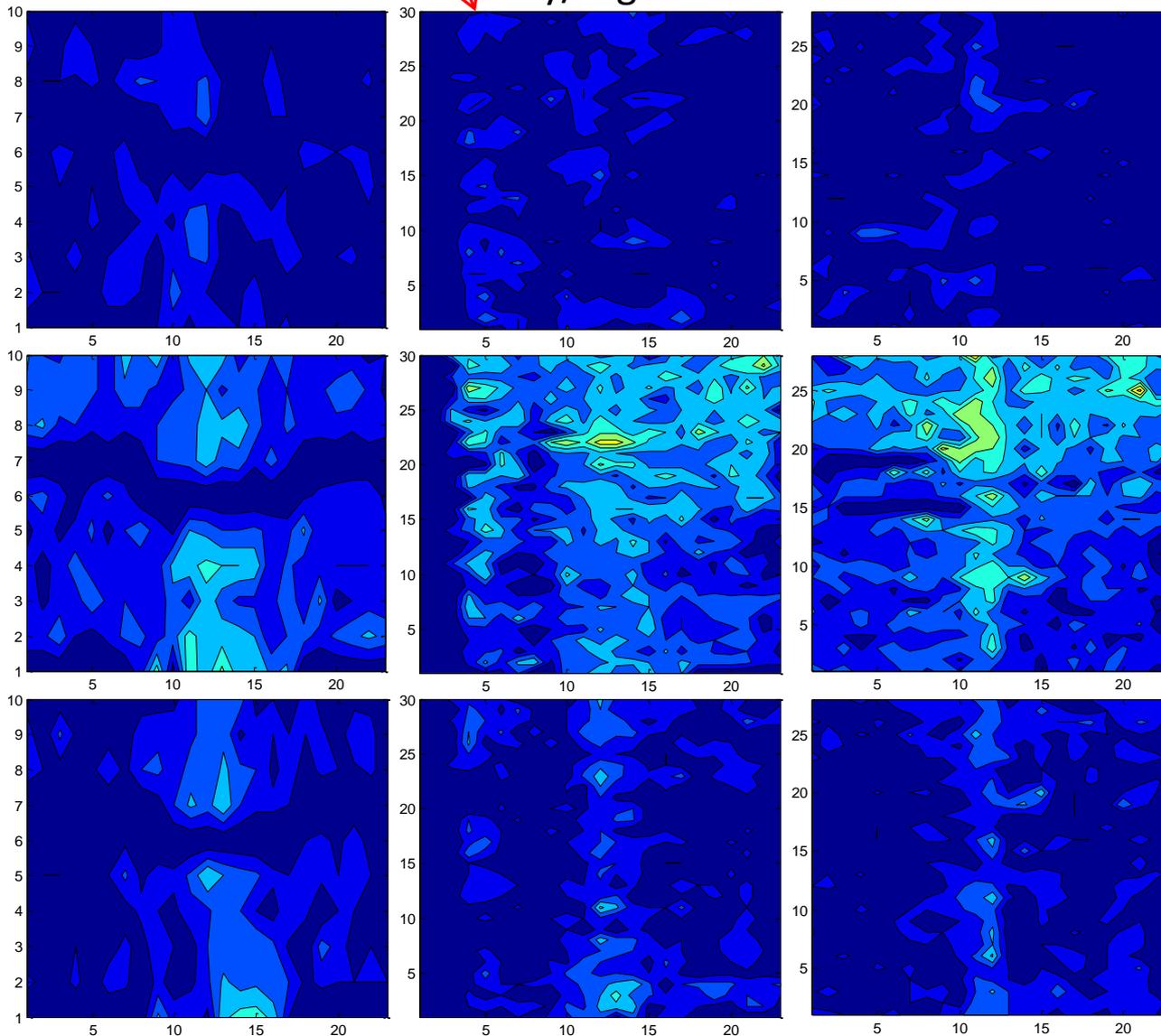
DeC
APS

Baseline

During exposure

Exposure
Day/Night

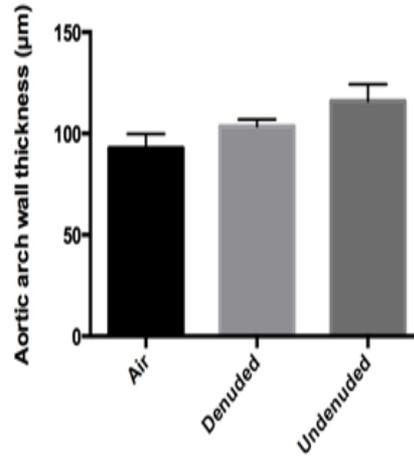
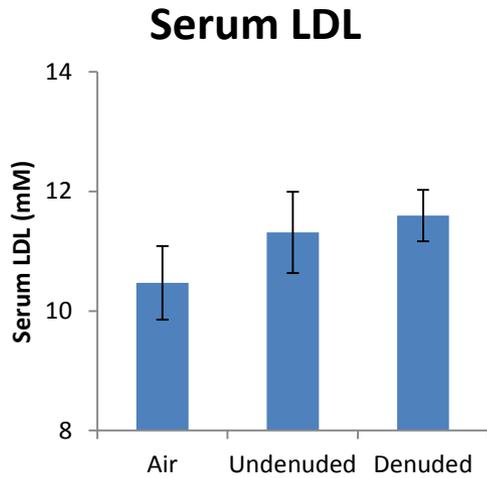
Lab Day/Night



Day of
Exposure

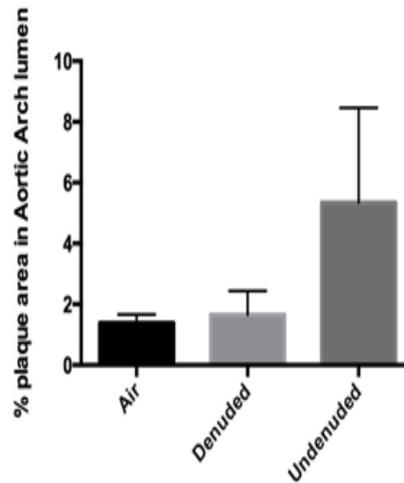
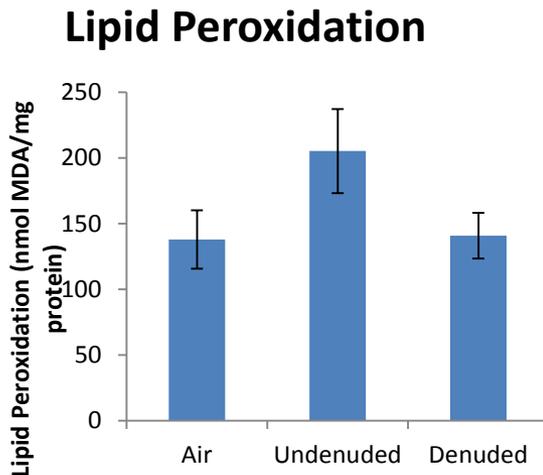
Hour of Day (0=6AM)

Exposure raises cholesterol but the organic fraction oxidizes the lipids promoting atherosclerosis



Air

Denuded



Undenuded

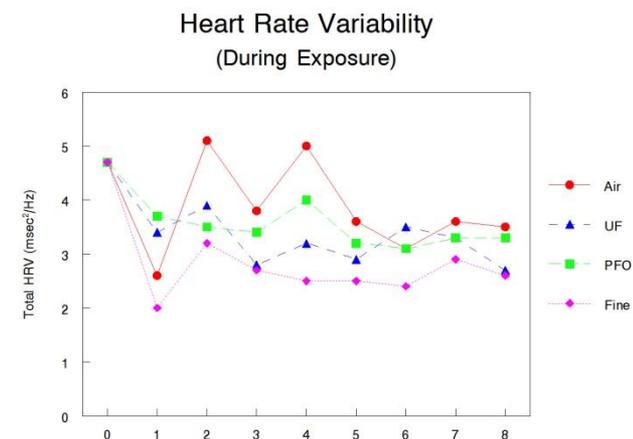
Aortic Arch 2x



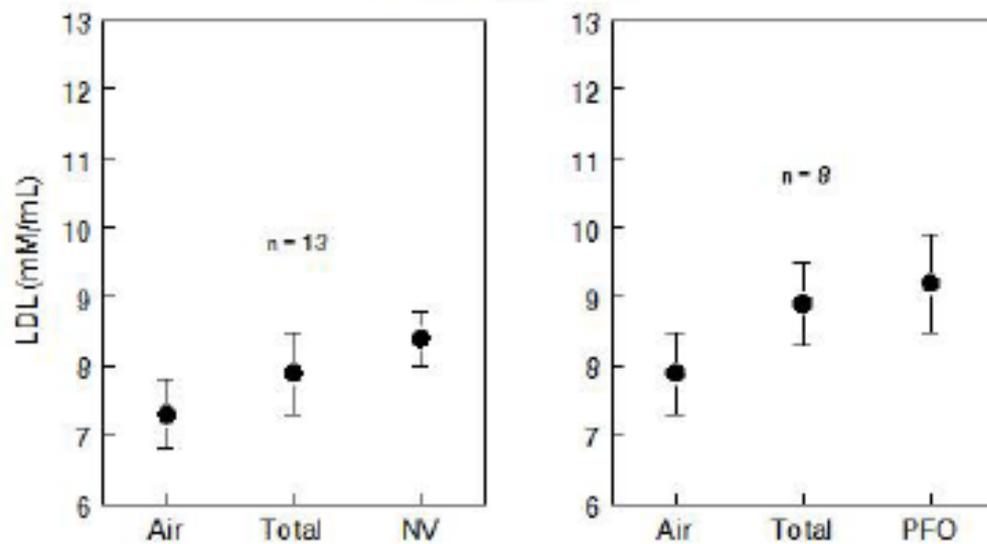
Particle Free Organics had an Independent Effect

Table 3. Effects of Particle Free Organic (PFO) compounds and Undenuded PM on Heart Rate Variability (Indexed as % Change From Baseline \pm SE)

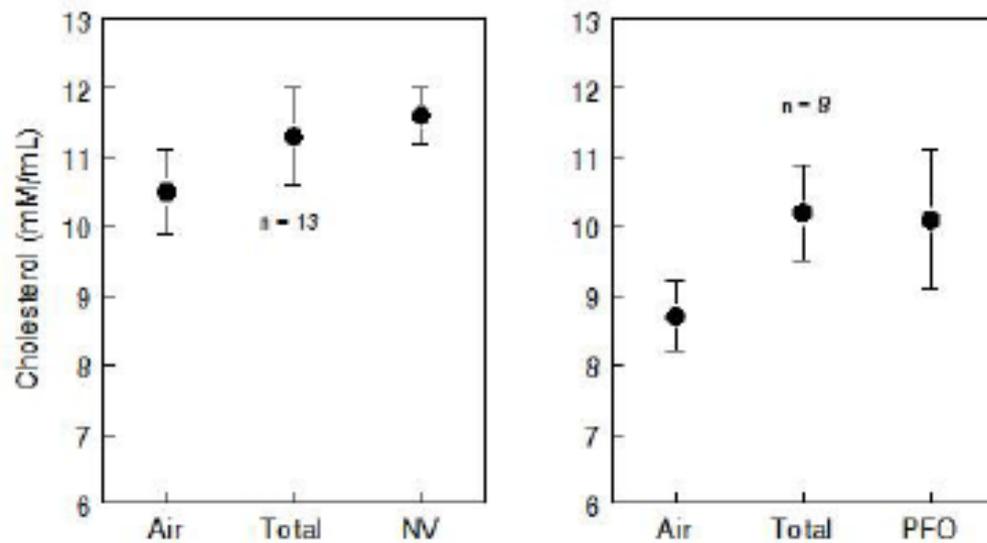
LF/HF Ratio			
Week	Purified air	PFO	Undenuded
1	-6.1 \pm 5	12.6 \pm 17.8	4.2 \pm 17.8
2	6.9 \pm 2	-0.2 \pm 16.6	6.9 \pm 10.5
3	14.5 \pm 10	26.75 \pm 19.0	-5.8 \pm 7.6
4	3.6 \pm 2	49.5 \pm 24.8	16.8 \pm 6.3
5	7.6 \pm 1	24.0 \pm 15.3	7.6 \pm 22.6
6	-0.5 \pm 5	33.7 \pm 19.7	18.8 \pm 12.3
7	5.4 \pm 1	51.1 \pm 27.2	18.2 \pm 18.3
8	-7.6 \pm 8	62.3 \pm 33.6	21.7 \pm 24.3
Average \pm S.E.	3.0 \pm 2.6	32.4 \pm 7.4	11.1 \pm 3.2
One-Way Anova Results	<p>I-----I I-----I</p> <p>$p \geq 0.005$ $p \leq 0.05$</p> <p>I-----I</p> <p>$p \geq 0.10$</p>		



Serum LDL



Serum Cholesterol



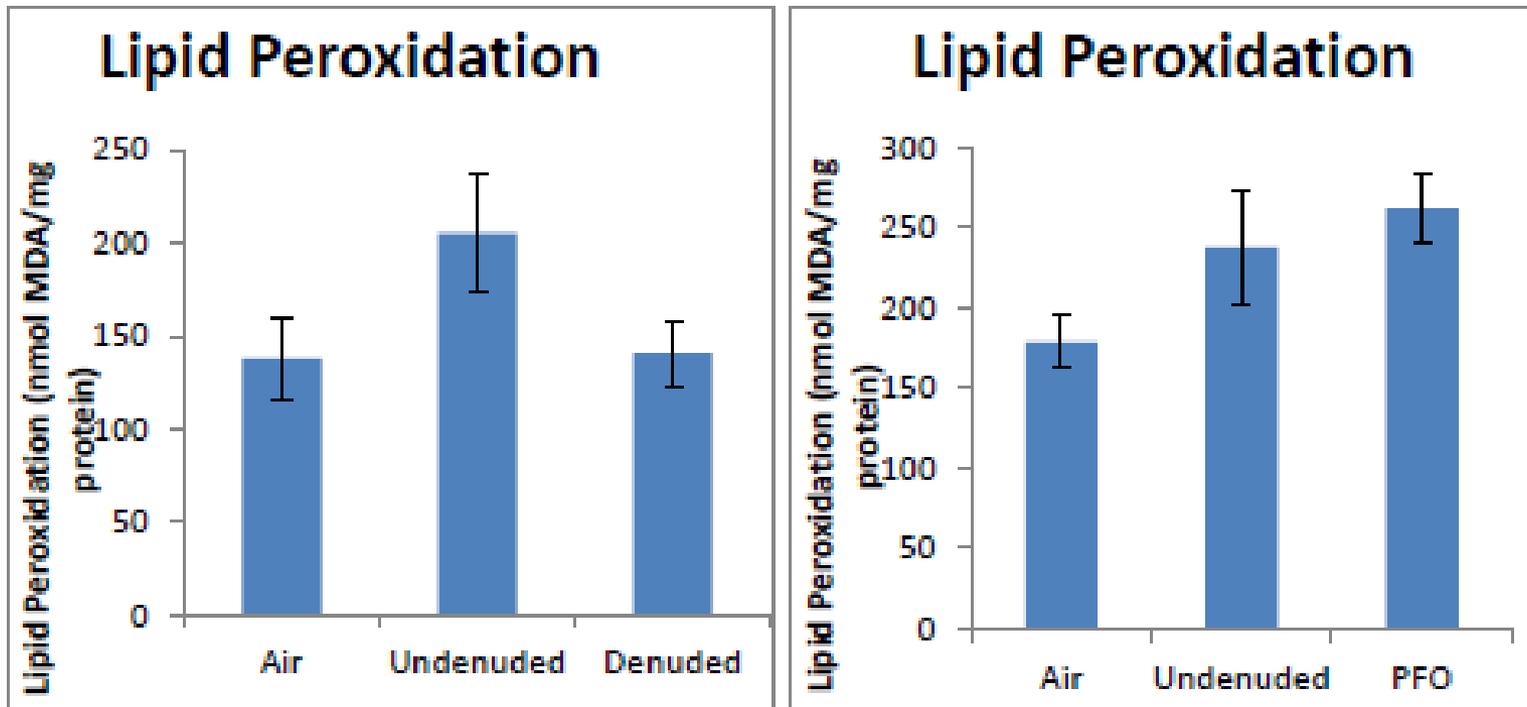


Figure 10. Serum Lipid Peroxidation Levels in Mice Exposed to Either Denuded PM, Undenuded PM and Particle Free Organics (PFO)

Cardiovascular Study

- Methods
- Results
- Conclusions

Conclusions

- The VACES and the Dekati Thermodenuder can be used in tandem to deliver undenuded ultrafine ambient PM (UFP, $d_p \leq 0.18 \mu\text{m}$), denuded UFP and Particle Free Organic Vapor (PFO; consisting of organic compounds stripped from the PM by the denuder) to genetically modified, apoE-/-, mice in a mobile rodent exposure system;
- Exposures to undenuded PM accelerated the development of atherosclerotic plaques;
- Exposures to undenuded PM or to PFO induced decreases in heart rate variability;
- The organic constituents of UFP are important contributors to atherosclerotic plaque development and significantly accelerate the growth of arterial plaques after an 8 week exposure;

Conclusions

- Exposure to both organic and inorganic constituents of UFP raise serum concentrations of cholesterol and low density lipoprotein-cholesterol (LDL), but
- Exposures to denuded UFP (PM denuded of most organic constituents) did not promote serum lipid peroxidation while exposures to undenuded UFP or to PFO did promote serum lipid peroxidation.
- Progressive losses in HRV were seen with CAPs but not with denuded CAPs.
- This study has demonstrated that the semi-volatile PM fraction of ambient ultrafine particulate matter is an important contributor to the development of atherosclerosis and heart disease.
- Thermal denuding technology such as afterburner emission controls not only reduce pollution but reduce the toxicity of the residual particles.

Acknowledgements



- Research using the AMS and SMPS was through AirUCI and funded by the National Science Foundation.



- L.W. thanks Mike Ezell for SMPS measurements, Prof. Nizkorodov for loan of the CPC, and Dr. Veronique Perraud and Emily Bruns for helping move the AMS.



Moving the AMS is a group effort!



Health studies at are currently sponsored by the California Air Resources Board, the South Coast Air Quality Management District and the NIEHS



I want to thank my collaborators

- Costas Sioutas
- Andrew Keebaugh
- Lisa Wingen
- Loyda Mendez
- Payam Pakben

Questions and Discussion

