CALIFORNIA
Air Resources Board

Chair's Air Pollution Seminar

January 12, 2010

Cardiovascular Response to Freeway Air: Results of an On-Road Exposure Study

William C. Hinds, ScD.

INTRODUCTION

Project Overview

- Human subjects
  - 19 subjects
  - Over age of 60
  - Healthy
- 2-hour exposure
  - Filtered or unfiltered
  - I-710 or I-405 freeways
  - Detailed physical characterization of aerosol
- Short term indicators of exposure or response to UFP on freeways
  - HRV + cardiac rhythm (24 hour)
  - Blood biomarkers (before, after, next day)

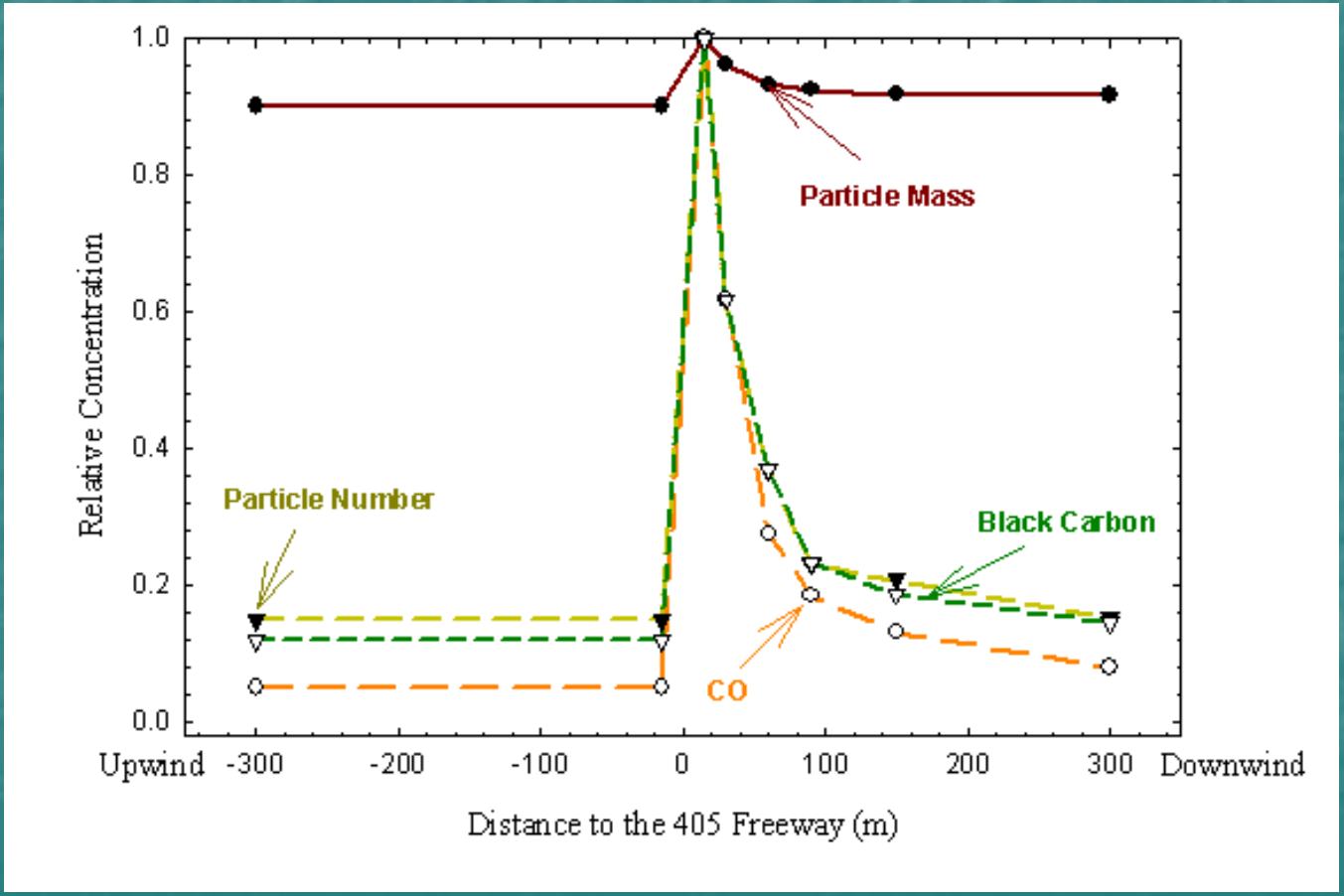
Impetus for Study

- High concentration of ultrafine particles on or near freeways (Zhu et al, 2002)
  - For typical LA commuter bulk of daily exposure occurs on freeway
- Change in HRV associated with PM-2.5 for NC highway patrol (Riediker et al, 2004)
- Risk of MI increases with time spent in traffic preceding 2 hours (Peters et al, 2004)

Impetus for Study

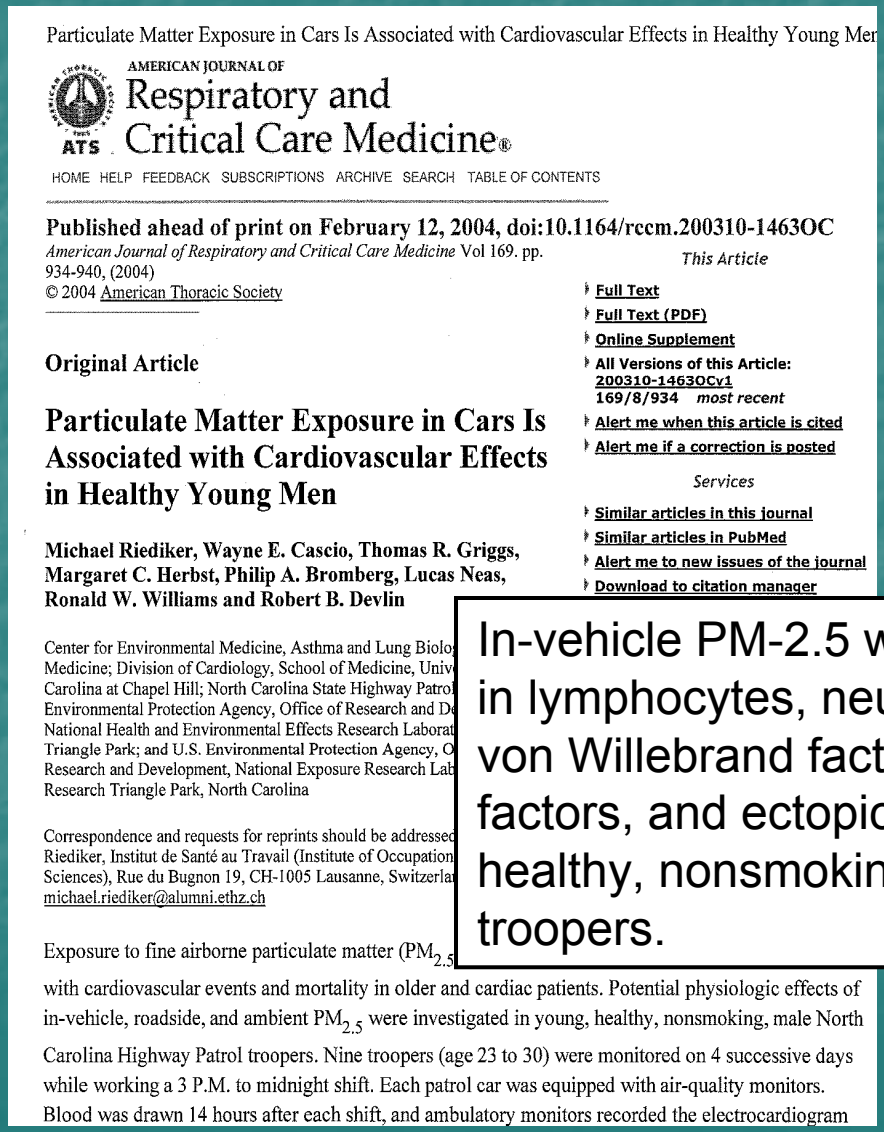
Impetus for Study

PREVIOUS STUDY: Relative Particle Number, Mass, Black Carbon, CO Concentration, vs. Downwind Distance from Freeway 405 during daytime.



Yifang Zhu, William C. Hinds, Seongheon Kim and Constantinos Sioutas "Concentration and size distribution of ultrafine particles near a major highway", 2002, *J. of Air and Waste Management Association*, 52:1032-1042.

Impetus for Study



Particulate Matter Exposure in Cars Is Associated with Cardiovascular Effects in Healthy Young Mer

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American Journal of Respiratory and Critical Care Medicine Vol 169. pp. 934-940, (2004)

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Original Article

Particulate Matter Exposure in Cars Is Associated with Cardiovascular Effects in Healthy Young Men

Michael Riediker, Wayne E. Cascio, Thomas R. Griggs, Margaret C. Herbst, Philip A. Bromberg, Lucas Neas, Ronald W. Williams and Robert B. Devlin

Center for Environmental Medicine, Asthma and Lung Biolo
Medicine; Division of Cardiology, School of Medicine, Univ
Carolina at Chapel Hill; North Carolina State Highway Patro
Environmental Protection Agency, Office of Research and D
National Health and Environmental Effects Research Laborat
Triangle Park; and U.S. Environmental Protection Agency, O
Research and Development, National Exposure Research Lab
Research Triangle Park, North Carolina

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Exposure to fine airborne particulate matter ($PM_{2.5}$
with cardiovascular events and mortality in older and cardiac patients. Potential physiologic effects of in-vehicle, roadside, and ambient $PM_{2.5}$ were investigated in young, healthy, nonsmoking, male North Carolina Highway Patrol troopers. Nine troopers (age 23 to 30) were monitored on 4 successive days while working a 3 P.M. to midnight shift. Each patrol car was equipped with air-quality monitors. Blood was drawn 14 hours after each shift, and ambulatory monitors recorded the electrocardiogram

In-vehicle PM-2.5 was associated with changes in lymphocytes, neutrophils, C-reactive protein, von Willebrand factor, heart rate variability factors, and ectopic beats in a group of young, healthy, nonsmoking male Highway Patrol troopers.

Impetus for Study

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

◀ Previous Volume 351:1721-1730 October 21, 2004 Number 17 Next ▶

Exposure to Traffic and the Onset of Myocardial Infarction

Annette Peters, Ph.D., Stephanie von Klot, M.P.H., Margit Heier, M.D., Ines Trentinaglia, B.S., Allmut Hörmann, M.S., H. Erich Wichmann, M

ABSTRACT

Background An association b
exacerbation of cardiovascula
designed to assess whether e

Methods We conducted a cas
identified with the use of data
Myocardial Infarction Registry
1999 to July 2001. There wer
infarction were known who ha
registry's standardized interview, and provided information on factors that may have triggered the
myocardial infarction. Data on subjects' activities during the four days preceding the onset of

"Time spent in traffic (including time in cars, on public transport, or riding bicycles) 1 or 2 hours earlier increased the relative risk of MI onset by 2- to 3-fold compared with control periods."

Overall Objectives

- Determine if exposure to freeway air changes HRV or blood chemistry
- Determine if these changes increase with increases in fine or ultrafine particle exposure
- Provide data for estimating in-vehicle exposure to ultrafine particles on freeways

Specific Objectives

- Develop a near real-time, mobile instrumentation system for in-vehicle measurement
  - Concentration and size distribution of UFP
  - Other vehicle-related air pollutants
  - Heart rate variability and measures of cardiovascular health
- Expose subjects to filtered and unfiltered freeway air
  - Gasoline dominated freeway
  - Diesel dominated freeway
  - Rigorous double blinding
- Analyze physiological and environmental data
  - Draw conclusions on health response
  - Write up papers and reports

Team Leaders

- PI: William Hinds – UCLA
  - Overall Coordination
  - Environmental Instruments and Measurements
  - Van Modifications and operation
- William Linn – LAREI
  - Subject Recruitment and Screening
  - Lung function
  - Blood samples
  - Holter monitors
  - Physiologic Measurements
- Yifang Zhu - Texas A&M Kingsville
  - Instrument Calibration
  - Data management
- Wayne Cascio - E. Carolina Medical School
  - Cardiac Measurement and Analysis
  - Biomarker analysis
- Daniel Stram - USC
  - Biostatistics

METHODS

Experimental Design

Subjects (60 or older) were exposed, 1 or 2 at a time, for 2-h periods (~10:00-12:00), at 1 week intervals, random order/double-blind, to:

- **I-710 freeway (mostly diesel trucks) unfiltered and filtered**
- **I-405/105 freeway (mostly gasoline cars) unfiltered and filtered**

Environmental measurements in near real time during exposure:

- **PM-10, PM-2.5, UFP, size dist.**
- **BC, P-PAH**
- **CO, CO_2, NOx**

Responses were measured in terms of:

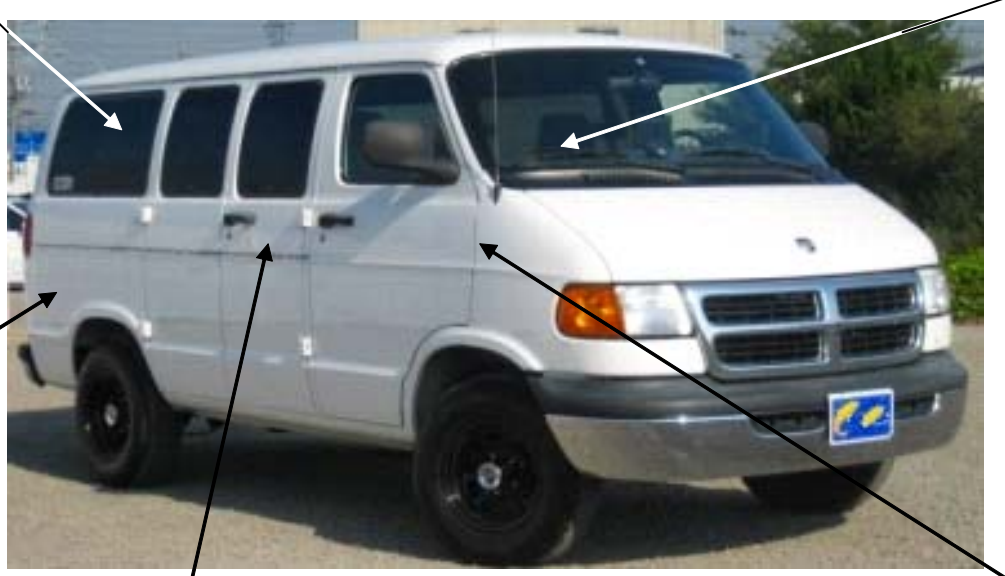
- **24-h Holter ECG (heart rate variability, arrhythmia incidence)**
- **24-h ambulatory blood pressure record**
- **Spirometry & vital signs (pre-, 0, 2, 22 h post-exposure)**
- **Blood biomarkers (pre, 2, 22 h)**
- **Symptom and time-activity diary recording**


4R15

A conventional 9-passenger van was converted to a mobile exposure chamber as shown.

Air monitoring instruments on shock mount platform replacing 3rd seat

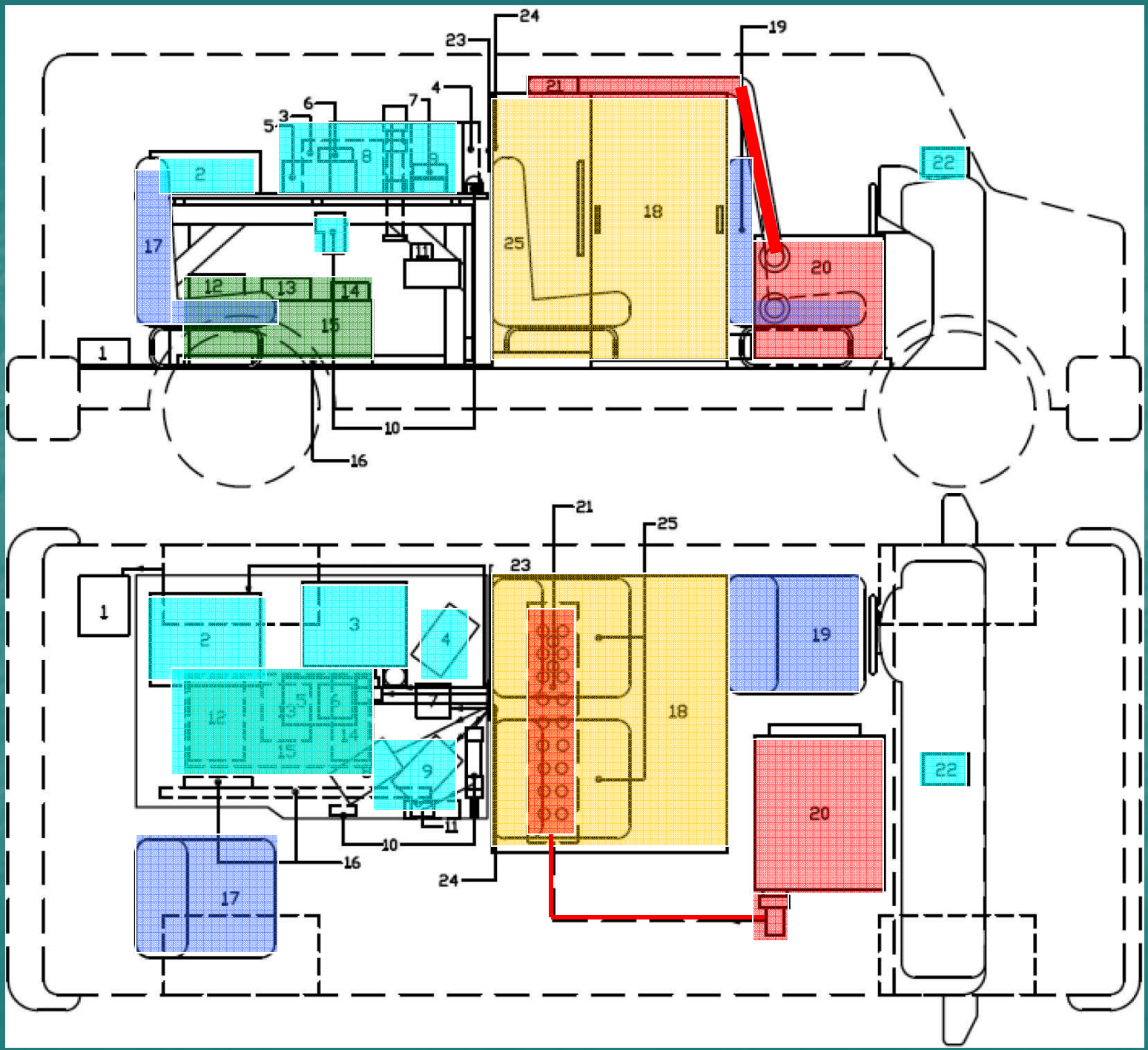
Dash-mounted camera & video recorder document traffic



Battery/inverter power supply under instrument platform

Clear plastic partitions around 2nd seat form exposure chamber with ~40 air changes per hour

HEPA filter/blower unit in front passenger seat delivers filtered or unfiltered air to chamber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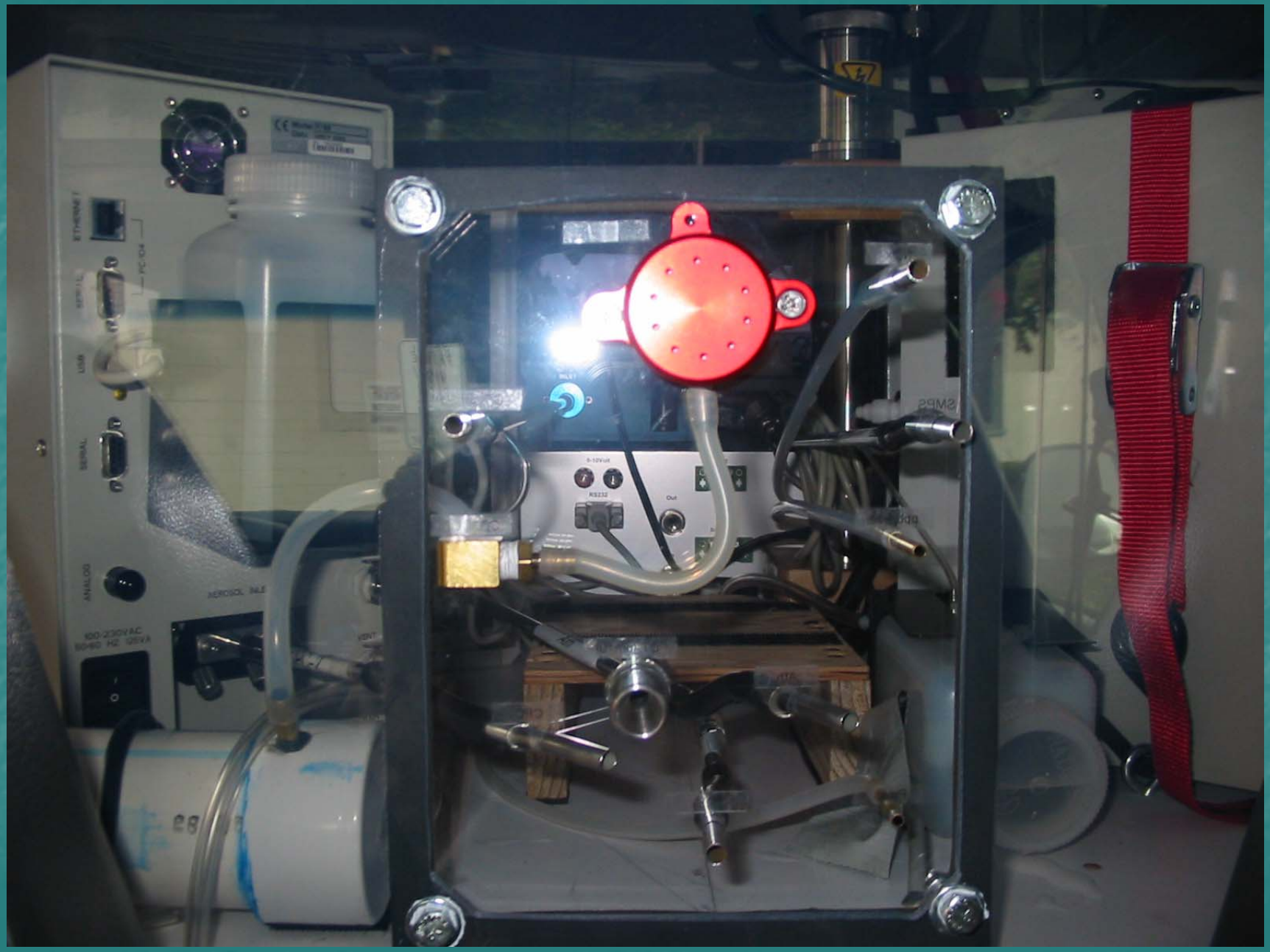
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Xantrex
Sine Wave Inverter 1000
1000 watts
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DISC
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INV
B2
B3
B4
DISC
CONN
CHG
Always charge or use at least 2 batteries at a time.
CB1 CB2 CB3 CB4
B1
B2
B3
B4

Instruments

SMPS: Particle Size Distribution

Water CPC: Total Particle Number Concentration

Dust Trak: Real time PM10, PM2.5

Q-Trak: CO, CO2, Temp, Rh

Portable Aethelometer: EC

PEM: PM2.5 Filter Samples

EcoChem PAS2000: Particle bound PAHs

API 200AU:

NO, NO_2, NOx

Environmental Parameters and Measurement methods.

	Species/Parameter	Instrument	Detection Limit	Flow Rate (L/Min)	Response Time (s)
1	Ultrafine Particle Size Distribution	TSI SMPS	Single Particle	1.5	100/200
2	Particle Number Concentration	TSI CPC	Single Particle	0.3	<2
3	PM-10 Real Time Mass	TSI Dusttrak 8520 with 10 µm inlet impactor	1 µg/m^3	1.7	60
4	PM-2.5 Real Time Mass	TSI Dusttrak 8520 with 2.5 µm inlet impactor	1 µg/m^3	1.7	60
5	Elemental Carbon	Portable Aethelometer AE-42	1 µg/m^3	5	60
6	CO, CO2, Temperature, Relative humidity	TSI Q-trak	1 ppm, 0.1°C, 1%	n/a	60
7	Particle-bound PAHs	EcoChem PAS 2000	ng/m^3	2	30
8	NO, NO_2, NOx	API 200AU	<1 ppb	1	60
9	Location and Speed	Camcorder, Garmin GPS18	10 m	n/a	1


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Aethalometer™
RUN PAUSE CHECK ERROR STOP
Condensation
Particle Counter
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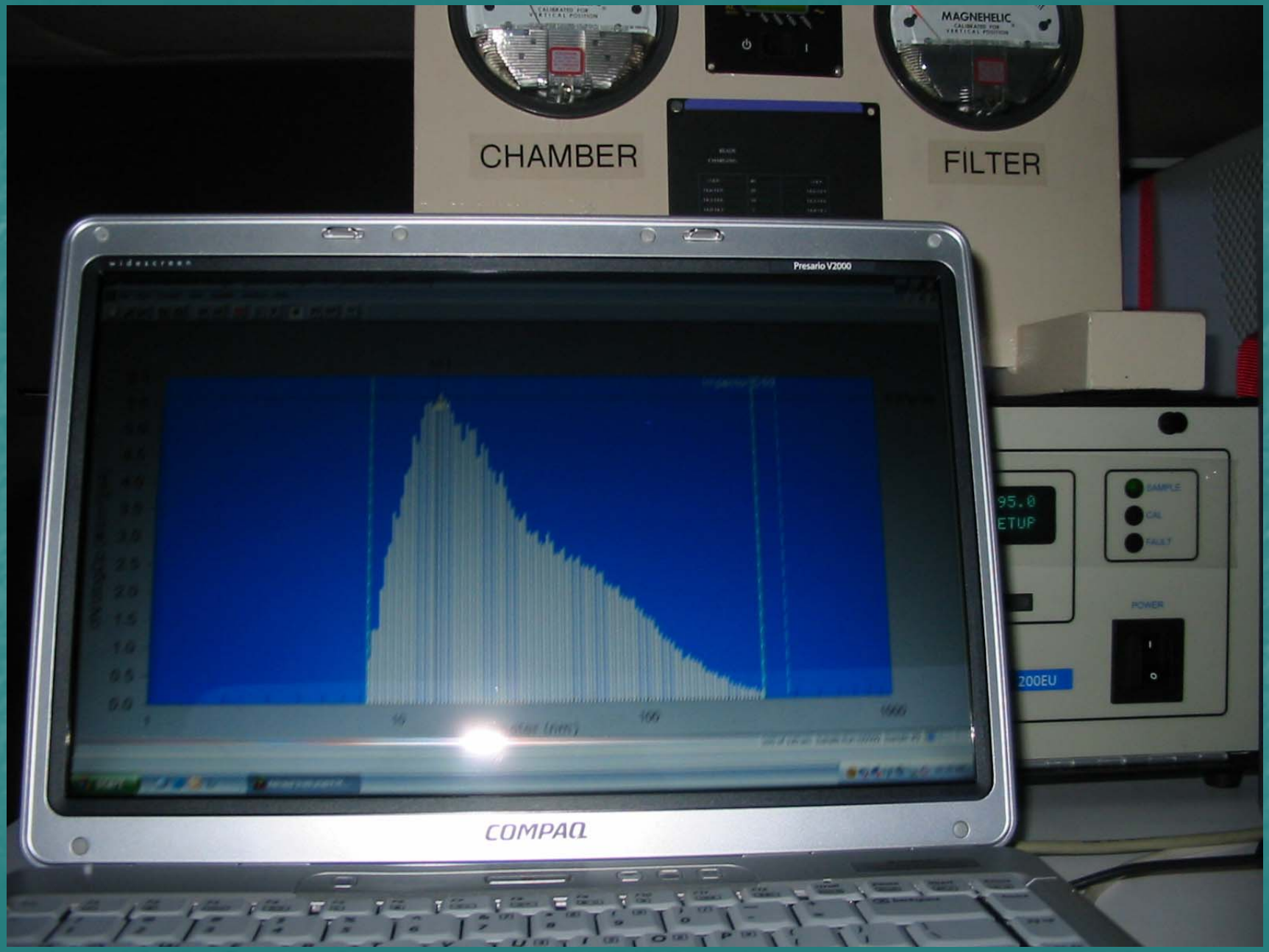
COMPAQ
GPS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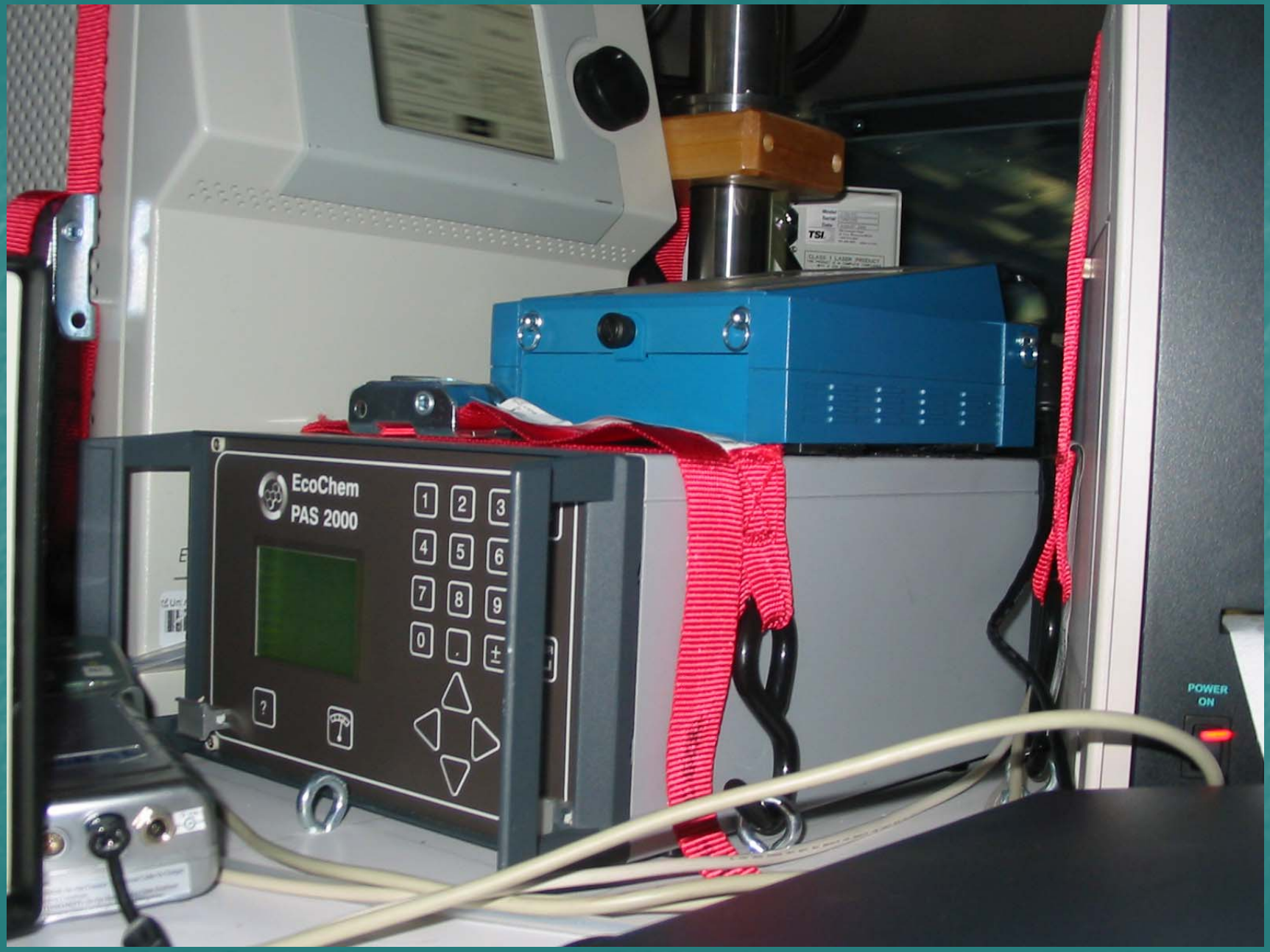
EcoChem
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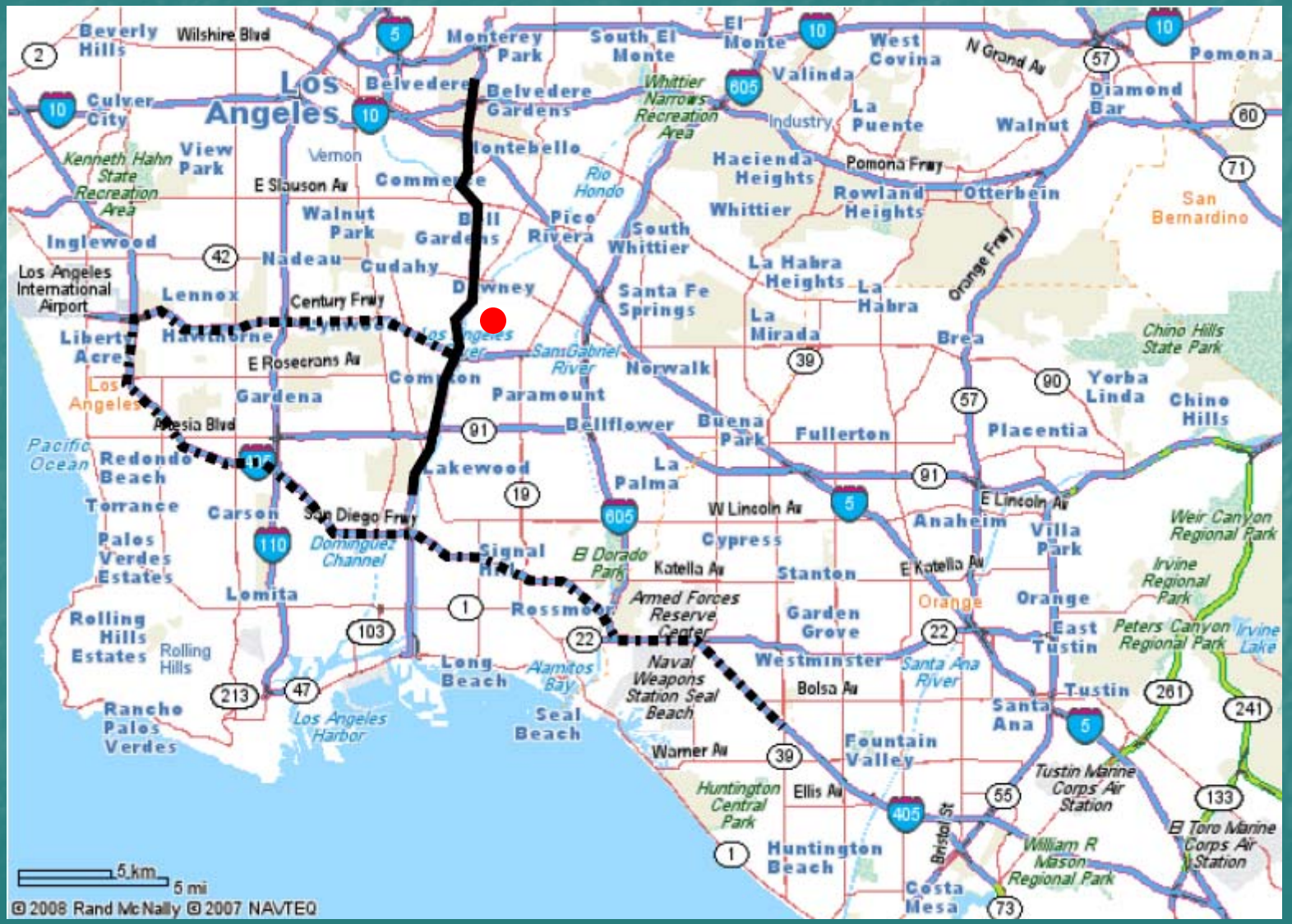
Exposure Routes



I-405 and I-710 Freeways

Zhu et al., 2002 "Concentration and size distribution of ultrafine particles near a major highway", *J. of Air and Waste Management Association*, 52:1032-1042.

Zhu et al., 2002 "Study of Ultrafine Particles near a Major Highway with Heavy-duty Diesel Traffic", 2002, *Atmospheric Environment*, 36: 4323-4335.

Subject Characteristics

ID #	Sex	Ethnicity	Height (in)	Weight (lb)	Age (y)
2676	F	White	62	156	73
2692	F	White	60.5	138	75
2675	F	White	64	232	65
2680	F	White	66	250	69
2683	F	White	66.5	150	77
2705	M	White	73	142	83
2694	M	Hispanic	70	209	70
2674	M	White	67	158	73
2691	M	Asian	67	186	75
2681	F	White	63.5	129	71
2677	F	Asian	60	141	73
2707	M	White	73	223	65
2713	M	White	71	208	64
2710	F	White	61	128	61
2708	M	White	72	225	68
2709	M	White	68	191	70
2716	M	White	68.5	184	74
2842	M	Hispanic	67	184	66
2841	M	White	66	165	76

Physiological Measurements

- 12 lead Holter ECG monitor (24-hour)
  - HRV, Arrhythmias
- Ambulatory blood pressure monitor (24-hour)
- Spirometry
  - Lung function – FVC, FEV-1, MMF, Resistance, resonant freq.
- Pulse oximeter – fingertip
  - Arterial Oxygen saturation, pulse rate
- Symptom score
- Time – activity diary record
- Blood draw – biochemical analysis

Biomarkers

Regular blood chemistry
- uric acid
- hematocrit
- MCV
- MCH
- MCHC
- Neutrophils
- lymphocytes
- lymphocyte counts

Cytokines
- IL-1b
- IL-6
- IL-8
- IL-10
- MCP-1
- TNF-a

Acute phase response
- Fibrinogen
- CRP

Vascular injury/repair
- Soluble E-selectin
- Soluble ICAM
- Soluble VCAM
- MMP-9
- PAI-1
- Myeloperoxidase
- VEGF
- vWF

Vasoactive peptides and other molecules
- Endothelin-1
- Angiotensin II
- ACE
- Plasminogen
- NT pro-BNP

Biomarkers

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- VEGF
- vWF

Vasoactive peptides and other molecules
- Endothelin-1
- Angiotensin II
- ACE
- Plasminogen
- NT pro-BNP

Exposure Sequence

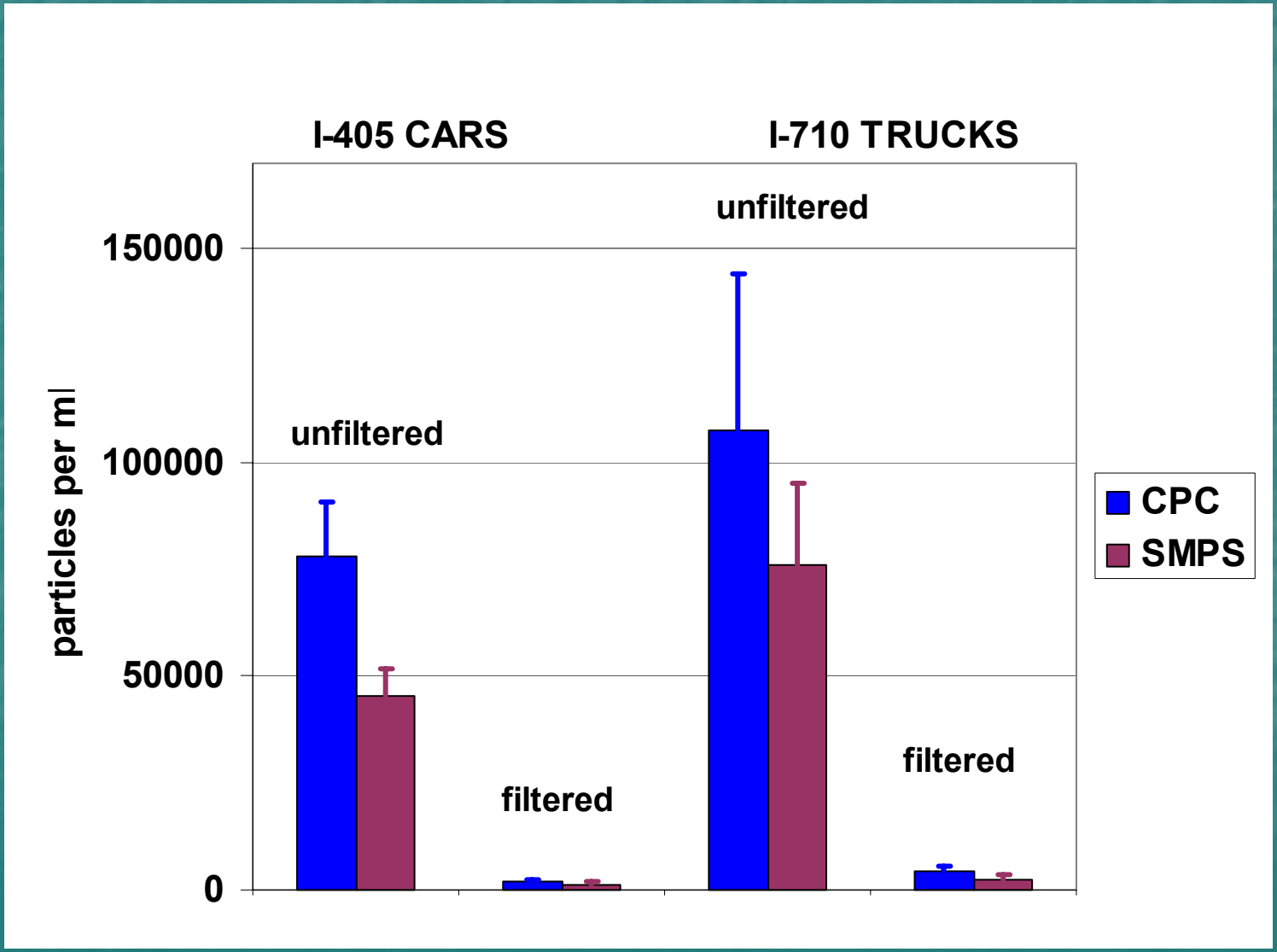
Table 2. Sequence of Procedures for Each Exposure Session

Day	Time	Activity
Day 1		
	08:00	Arrive at lab; rest in clean air; equipment hookup.
	09:00	Pre-exposure cardiopulmonary examination; symptom recording; SpO2; spirometry; blood draw; start Holter ECG and ambulatory blood pressure monitor ("pre" testing).
	10:00	Resting exposure for 2 hr in van on freeway; record symptoms every 15 minutes.
	12:30	Return to lab; rest in clean air; symptom recording; SpO2; Spirometry ("post" testing).
	14:30	Symptom recording; SpO2; spirometry; blood draw ("hour 2" testing); leave laboratory; fill out time-activity diary through the following morning.
Day 2		
	08:00	Arrive at lab; rest in clean air; post-exposure cardiopulmonary examination; symptom recording; SpO2; spirometry; blood draw ("day 2" testing).
	09:00	Discharge from laboratory.

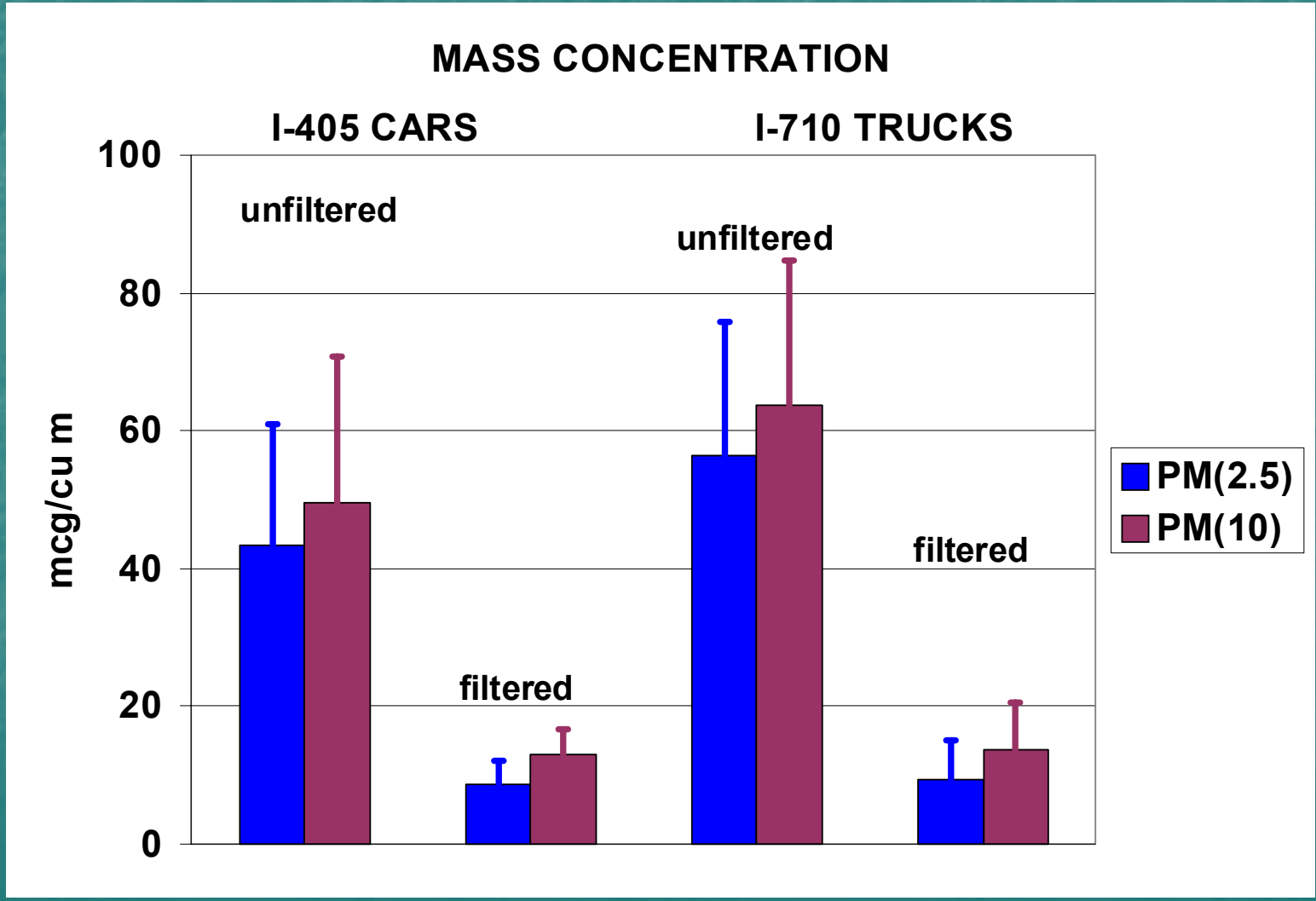
Exposures continued one per week for four weeks.

Environmental Results

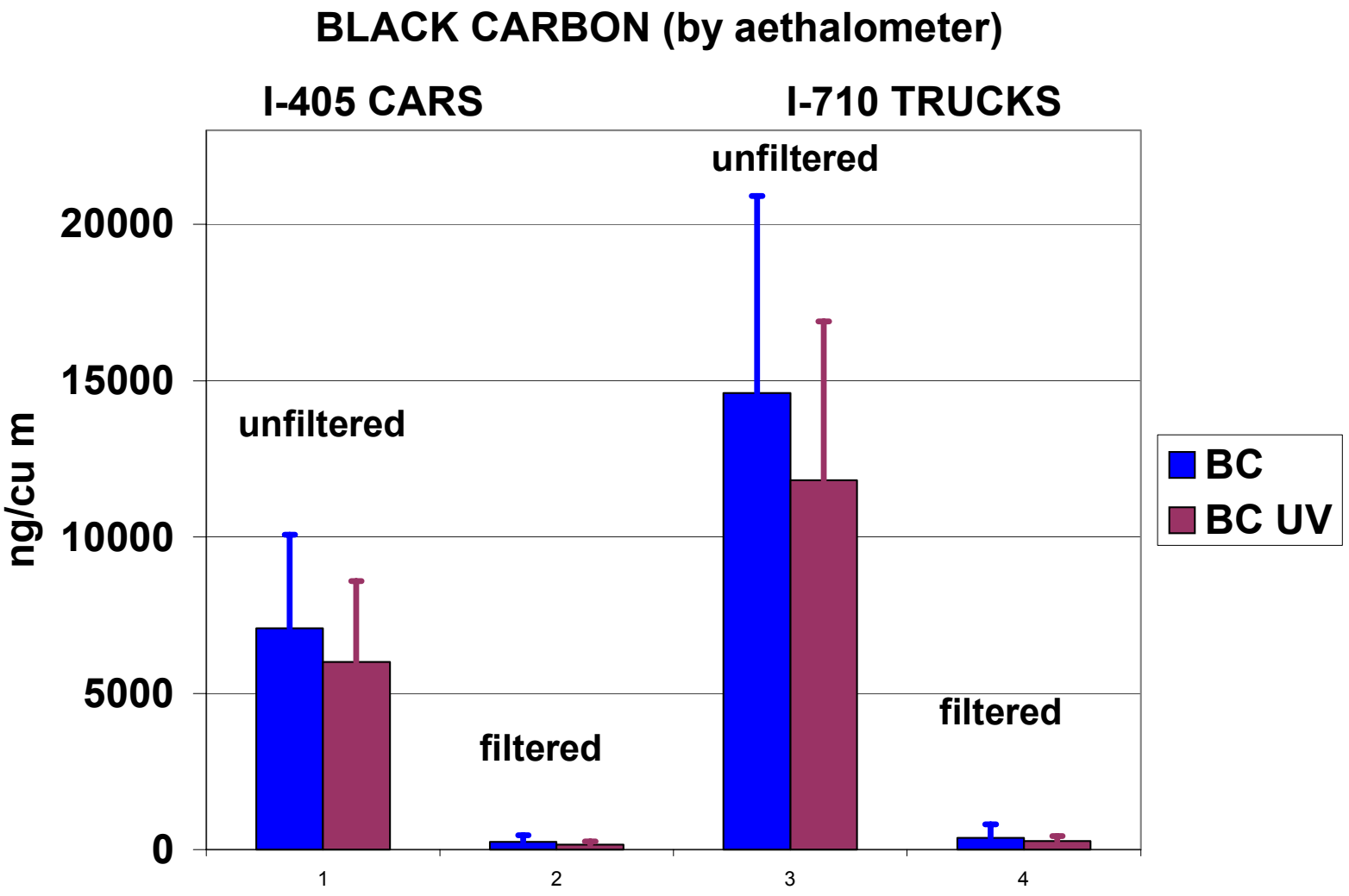
Particle Number Concentration



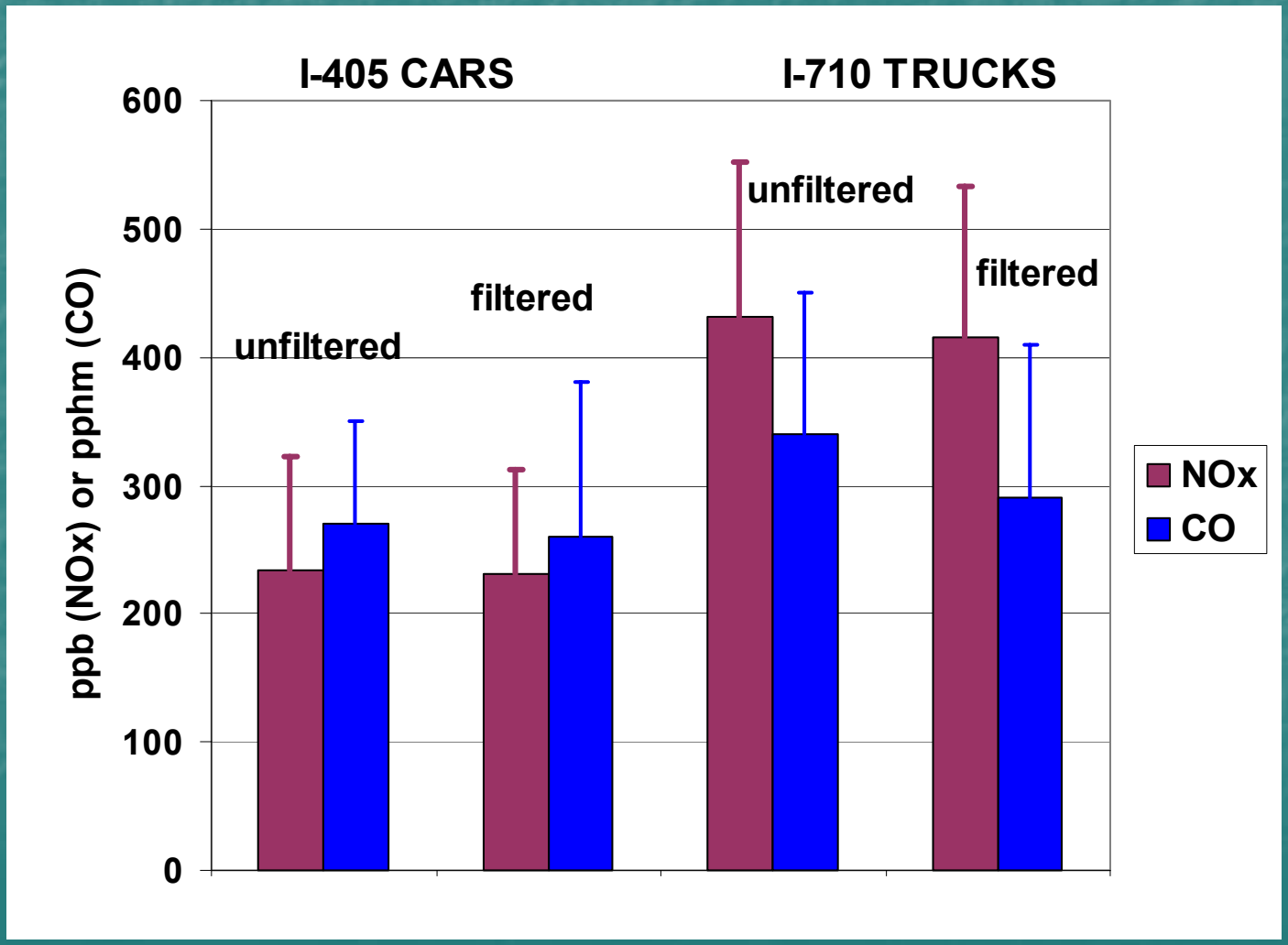
Particle Mass Concentration



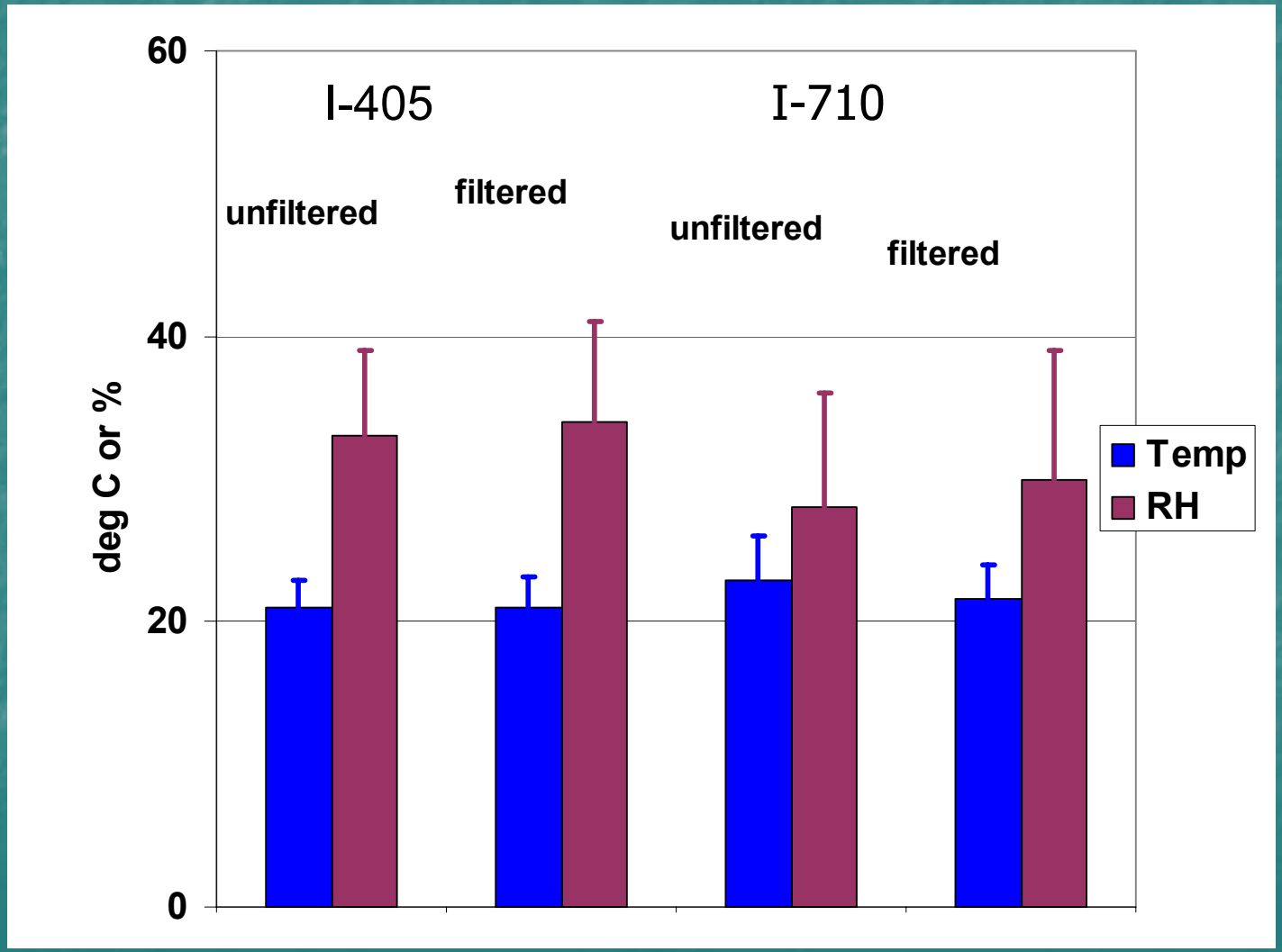
Black Carbon



OXIDES OF NITROGEN
CARBON MONOXIDE



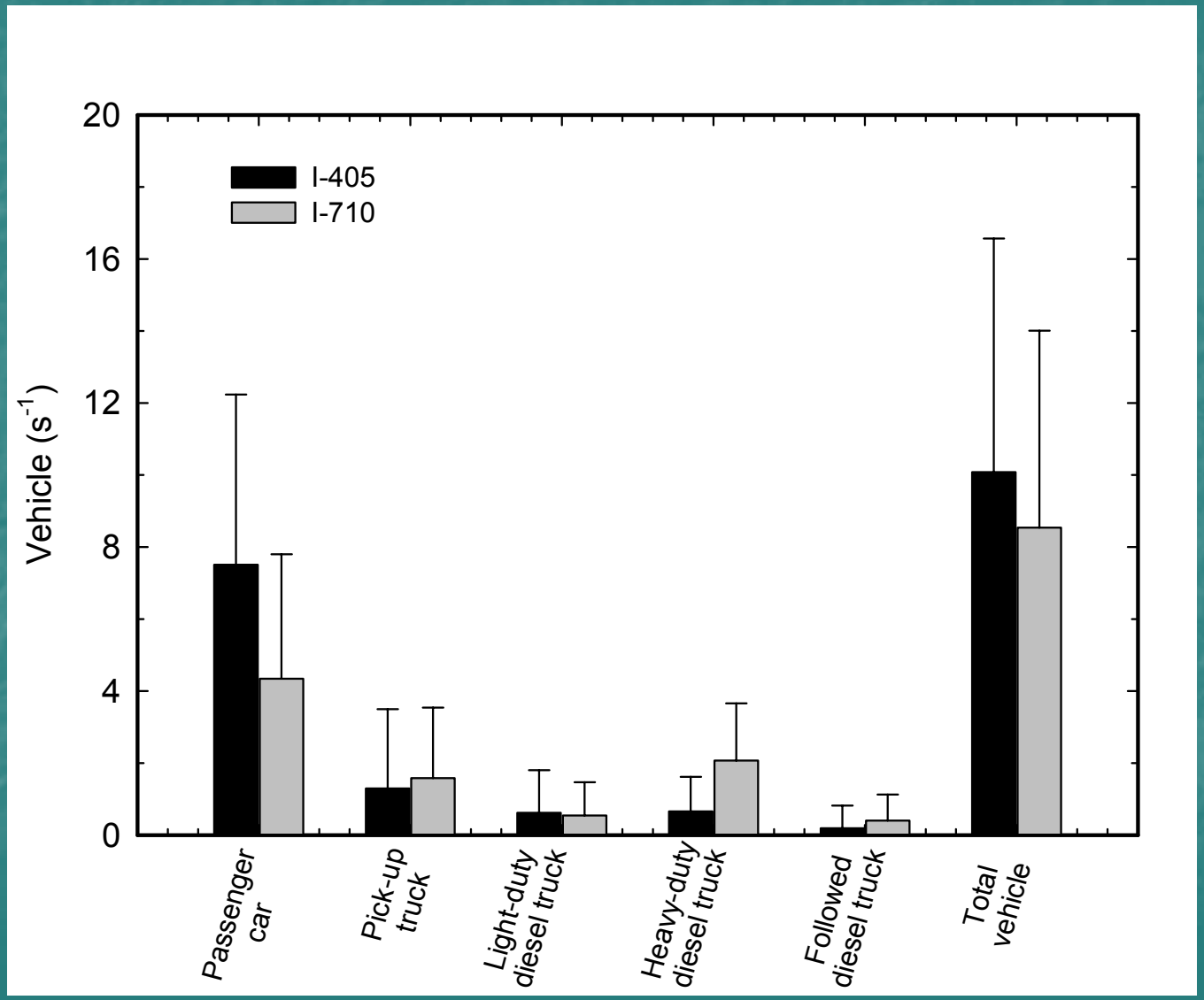
Temperature, Relative Humidity



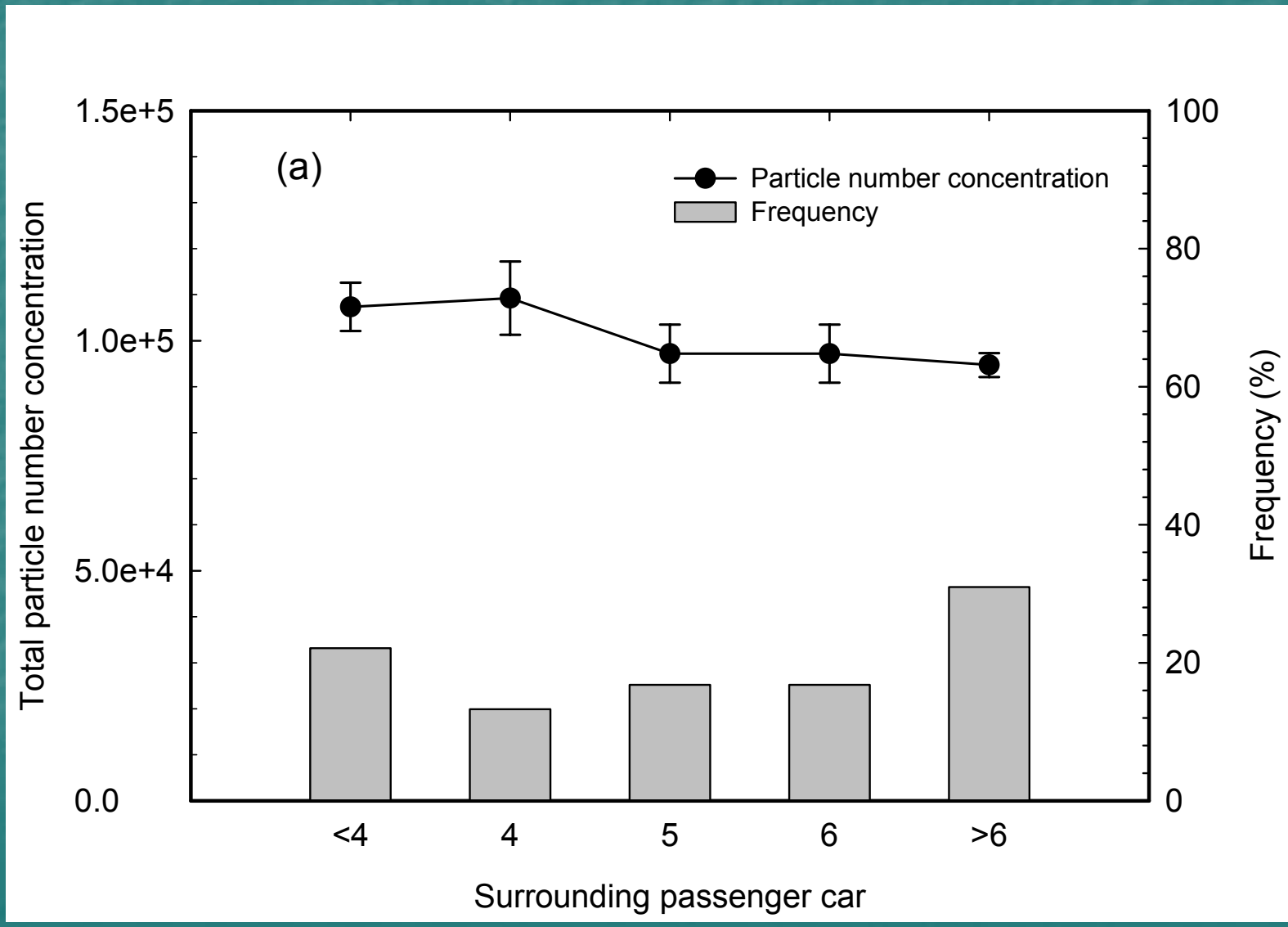
Mean Values for Environmental Measurements

Variable	Units	I-405 unfiltered	I-405 filtered	I-710 unfiltered	I-710 filtered
Particle number	count/ ml	78069 (13419)	2221 (549)	107152 (36414)	4327 (1346)
$PM_{2.5}$	µg/m³	44.5 (17.6)	8.1 (3.3)	51.4 (19.6)	9.8 (5.7)
PM_{10}	µg/m³	50.8 (21.3)	13.1 (3.2)	58.5 (21.0)	14.5 (7.0)
Black carbon	ng/m³	6214 (1268)	325 (270)	11729 3904)	663 (545)
PAH	ng/m³	148 (38)	21 (74)	250 (128)	5 (3)
NOx	ppb	234 (88)	231 (82)	431 (121)	415 (118)
CO	ppm	2.7 (0.8)	2.6 (1.2)	3.4 (1.1)	2.9 (1.2)
Temperature	deg C	21.1 (1.8)	20.9 (1.8)	22.8 (2.9)	21.5 (2.4)
Rel. Humidity	%	33 (6)	35 (7)	28 (8)	30 (9)
Prior 24 hr Amb. PM_{10}	µg/m³	30.0 (9.2)	26.2 (8.6)	30.1 (8.3)	29.6 (9.7)
Prior 24 hr Amb. $PM_{2.5}$	µg/m³	24.0 (5.6)	21.7 (7.7)	21.5 (10.1)	23.6 (12.2)

Vehicle Distribution



Effect of Nearby Vehicles



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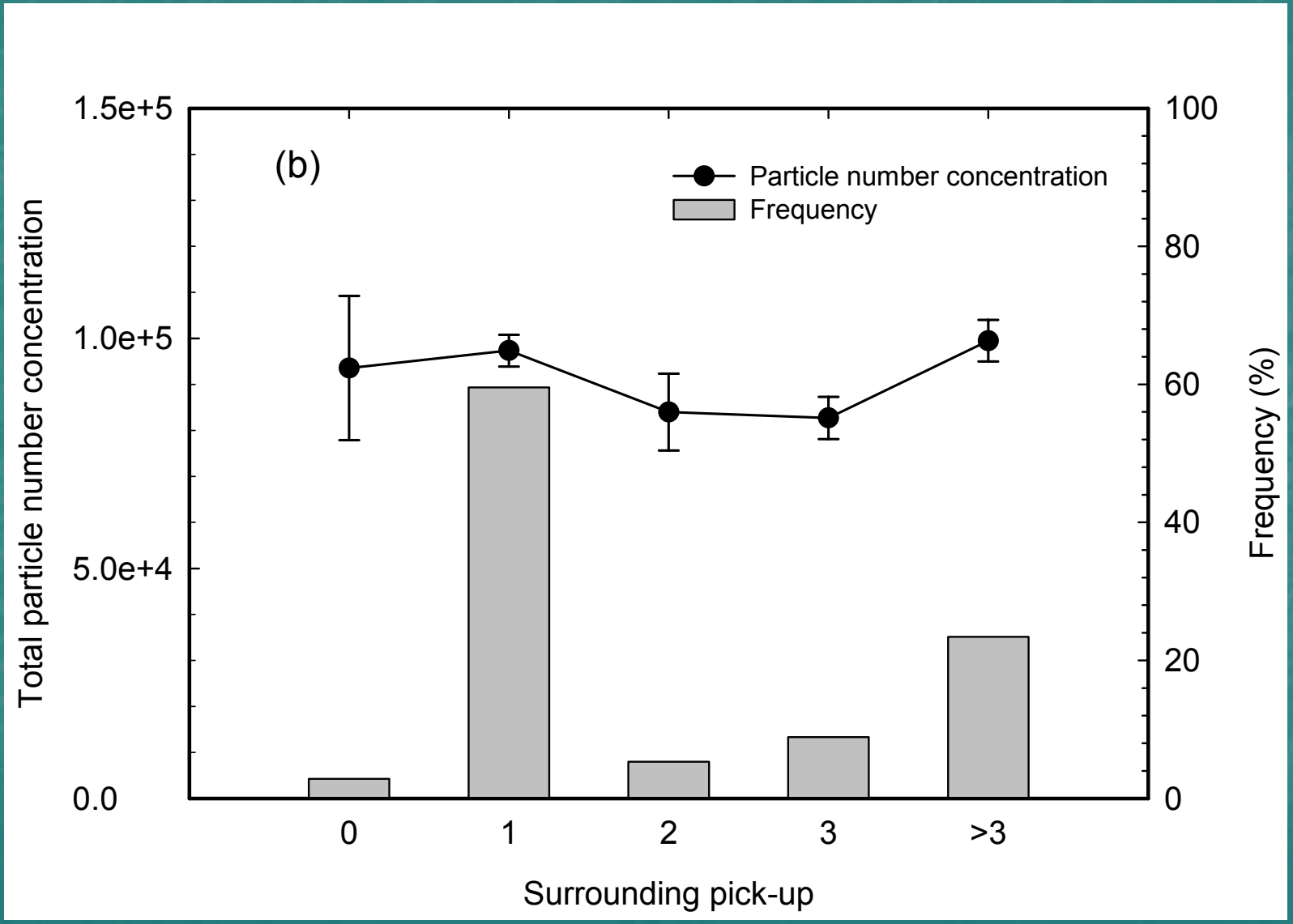
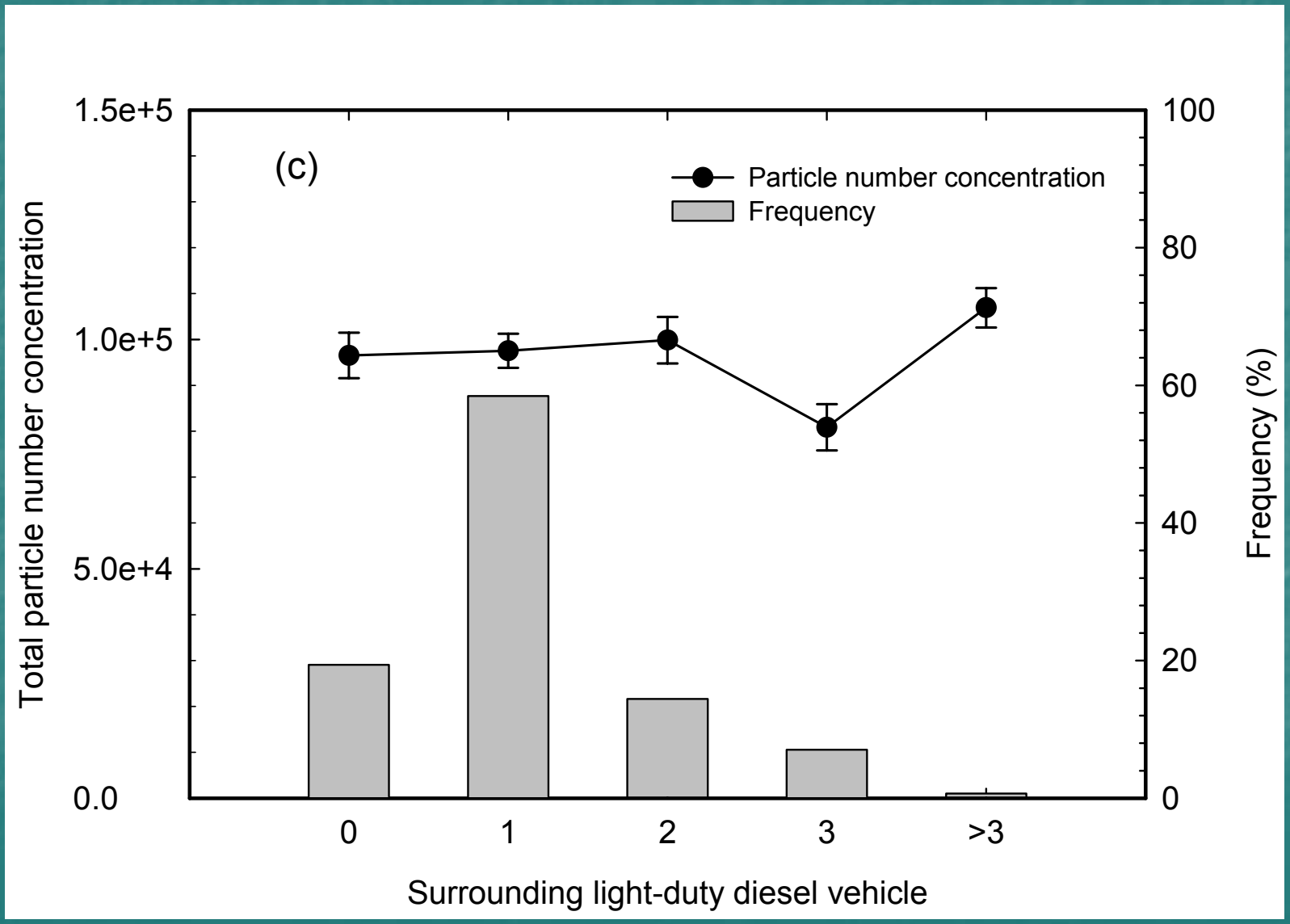
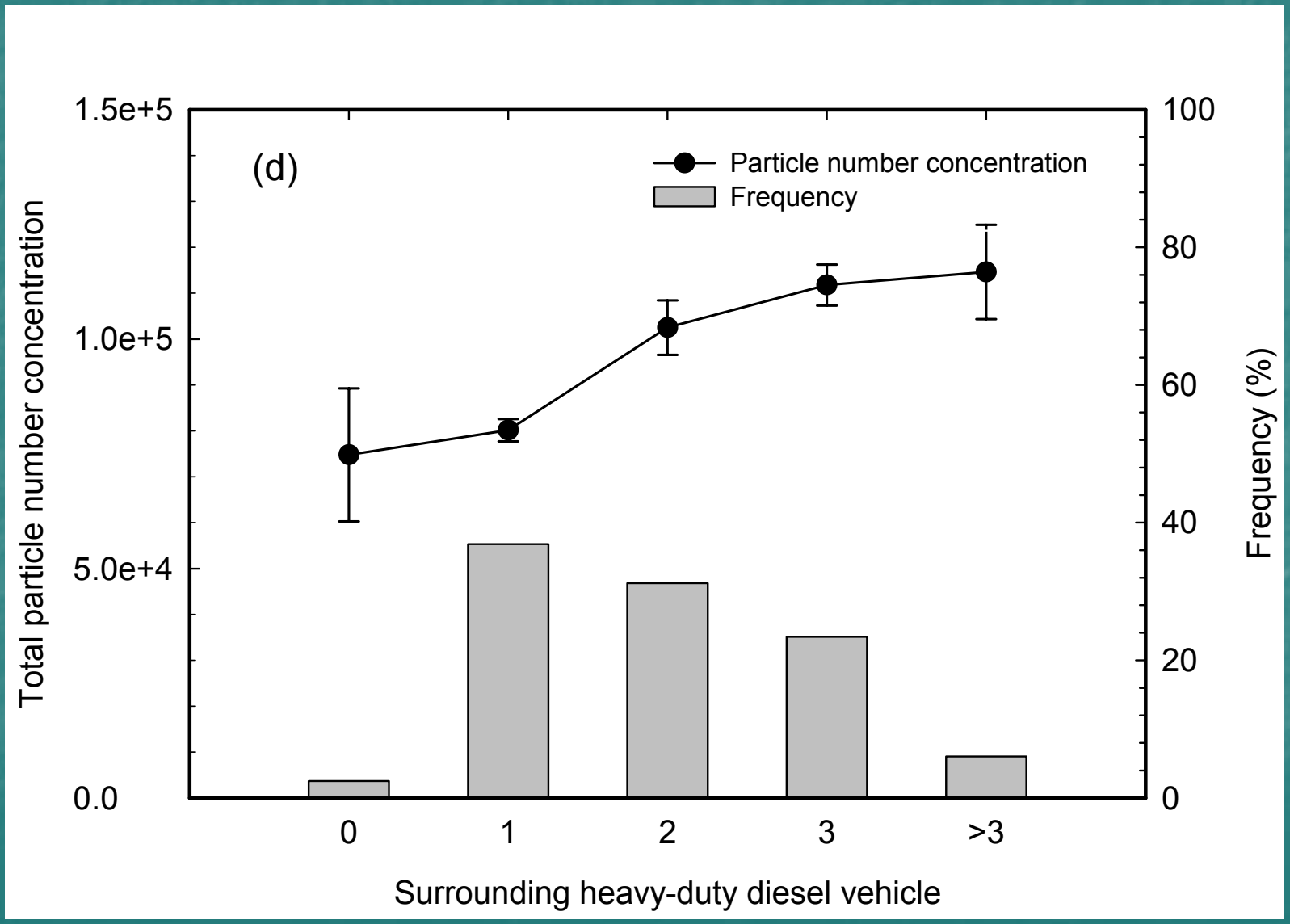


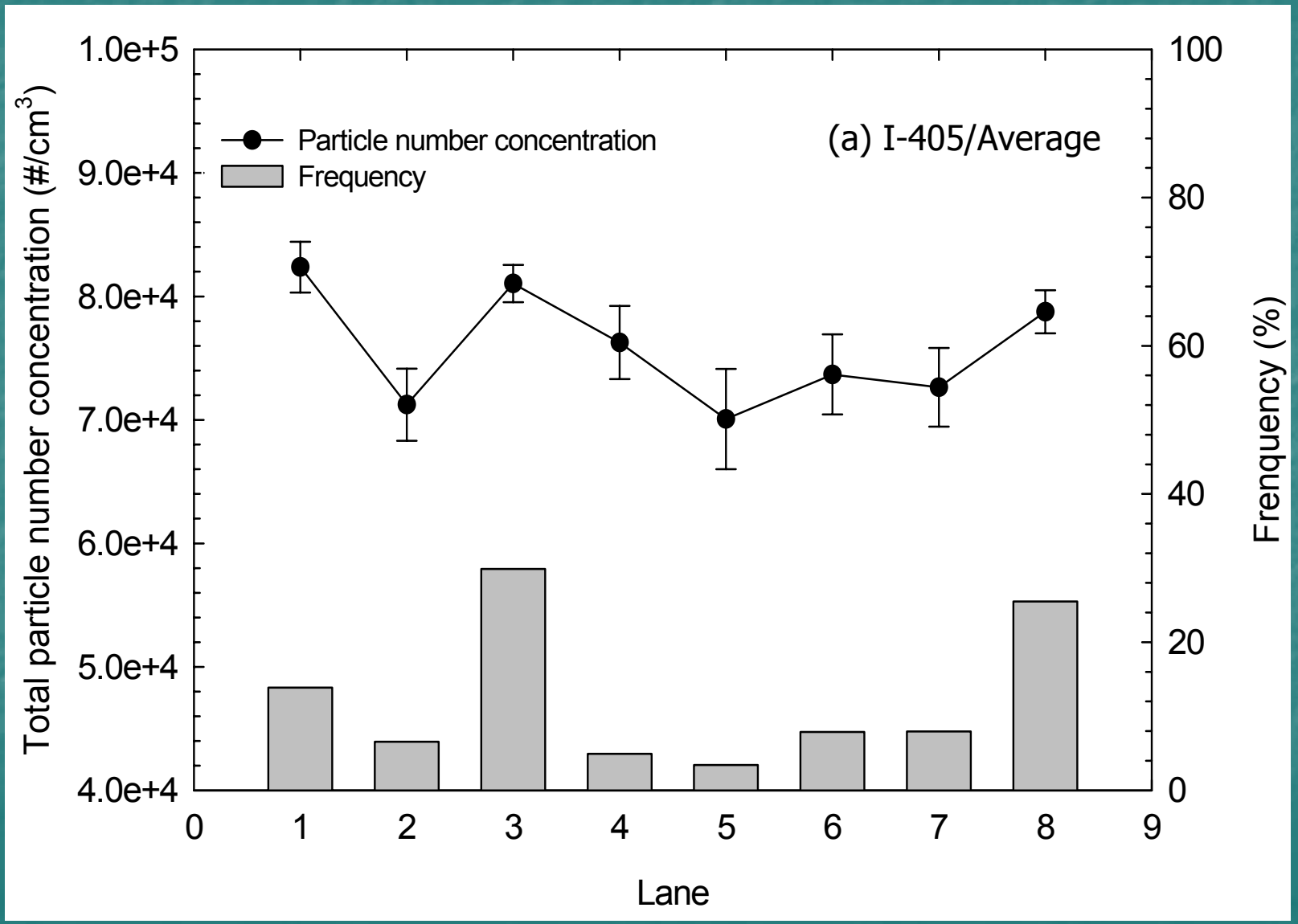
Effect of Nearby Vehicles



Effect of Nearby Vehicles



Effect of Driving Lane



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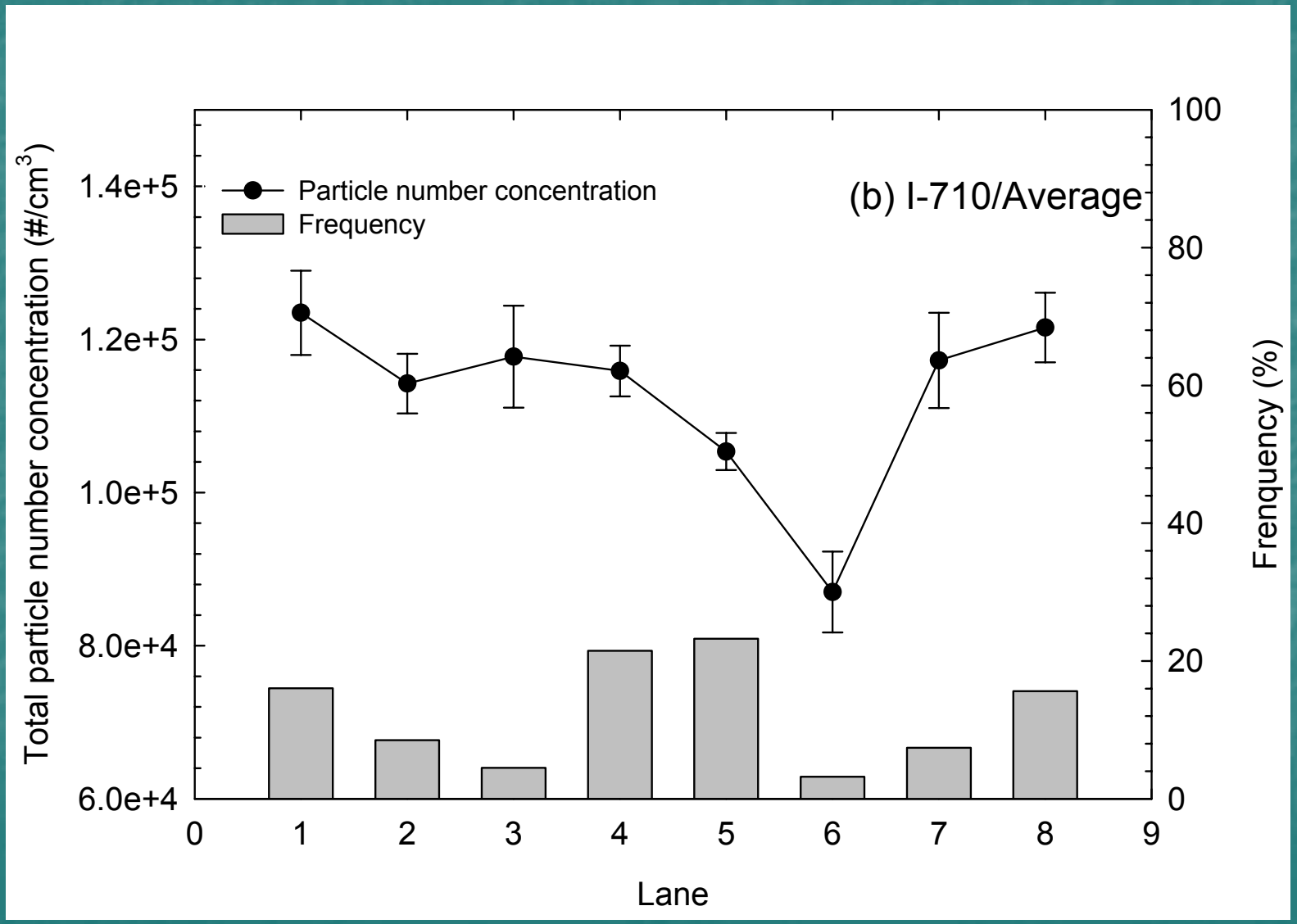

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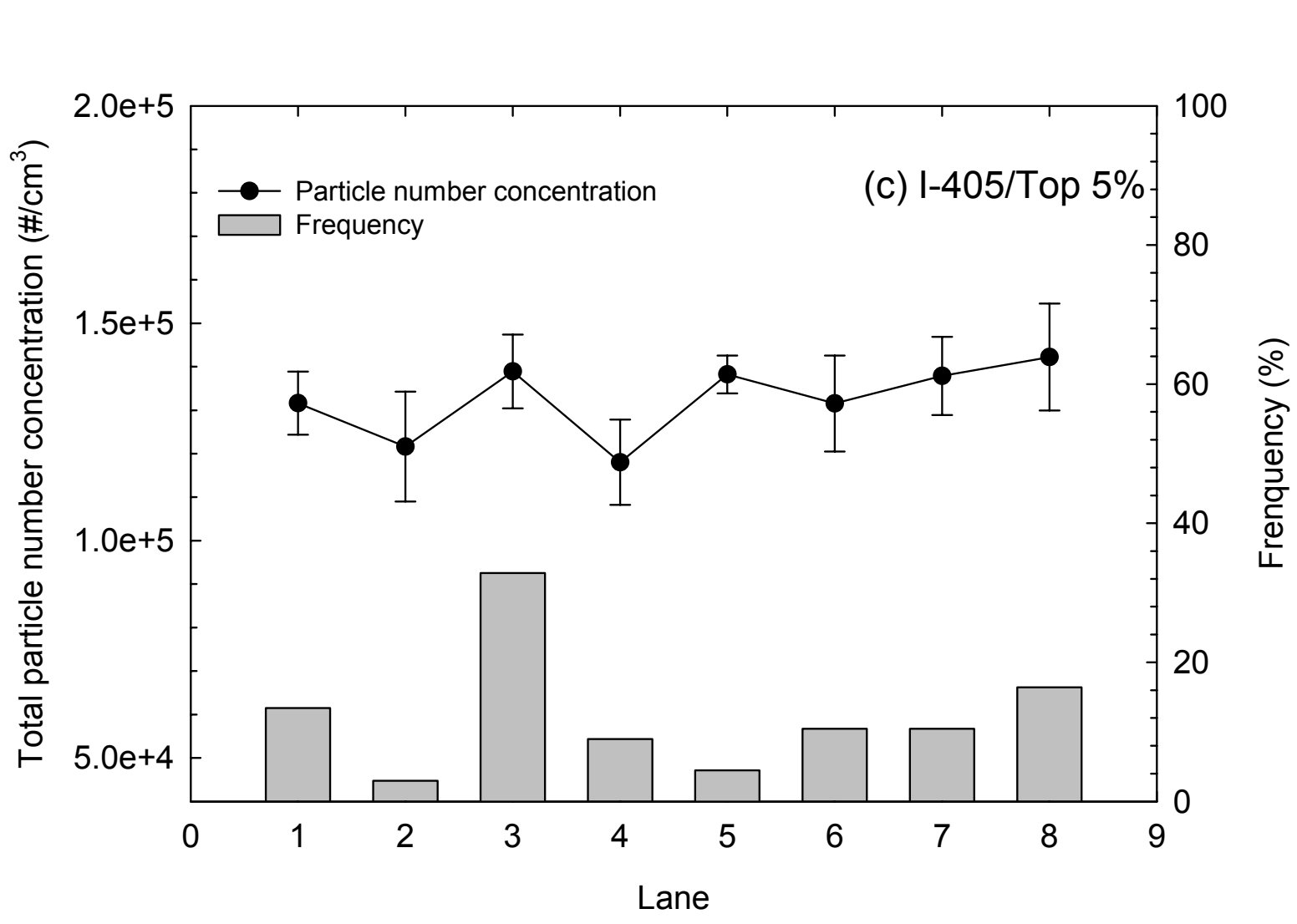
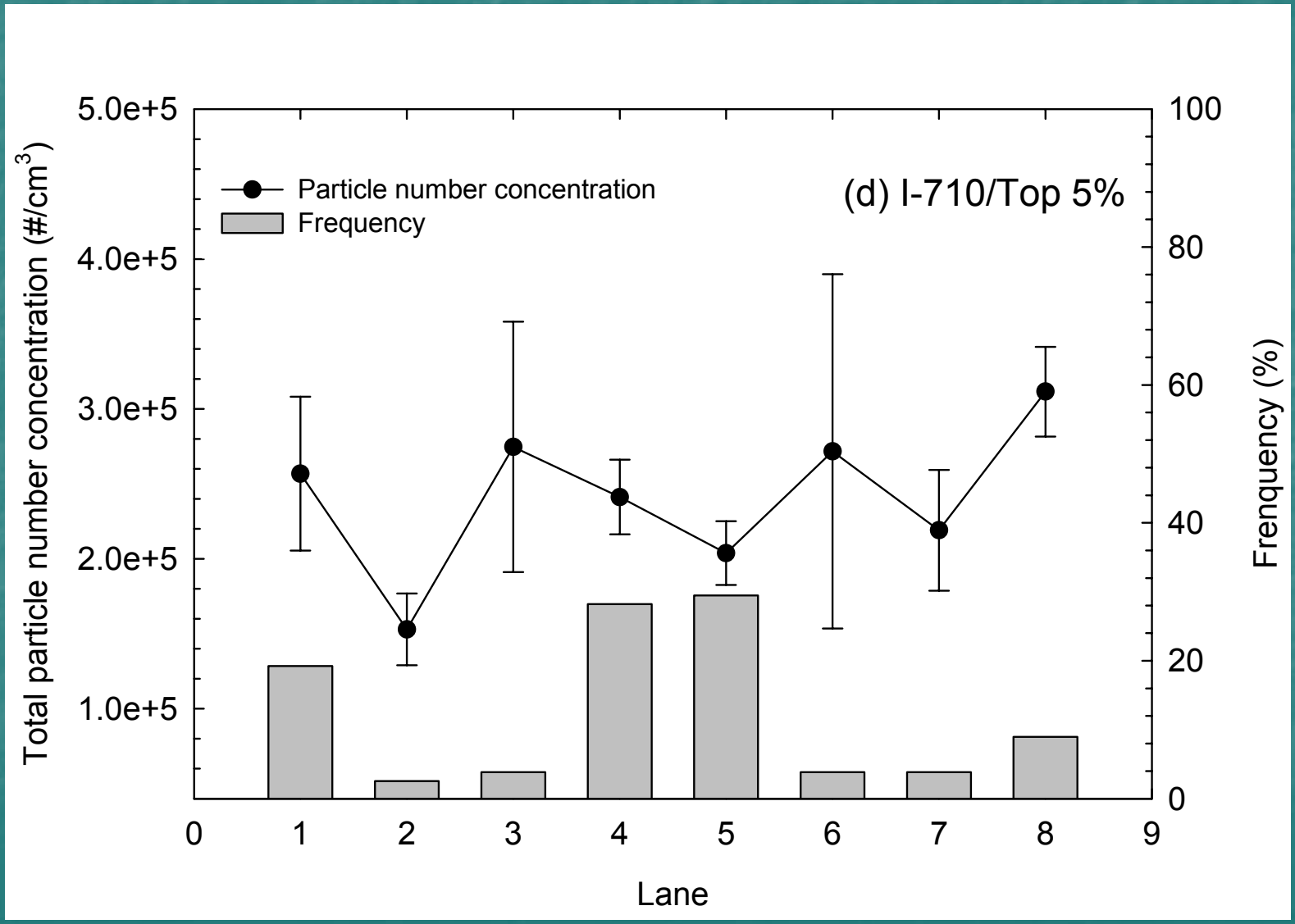
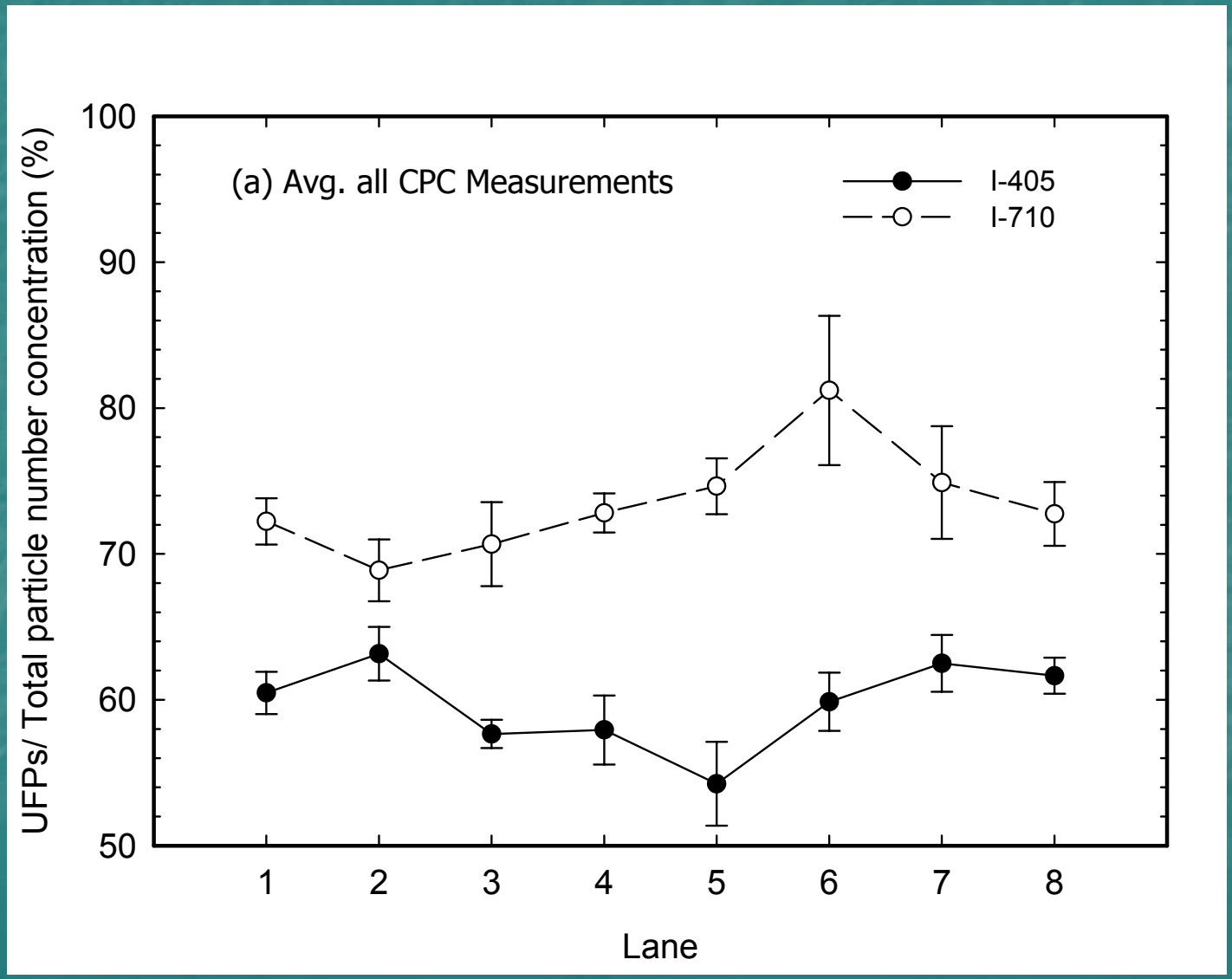


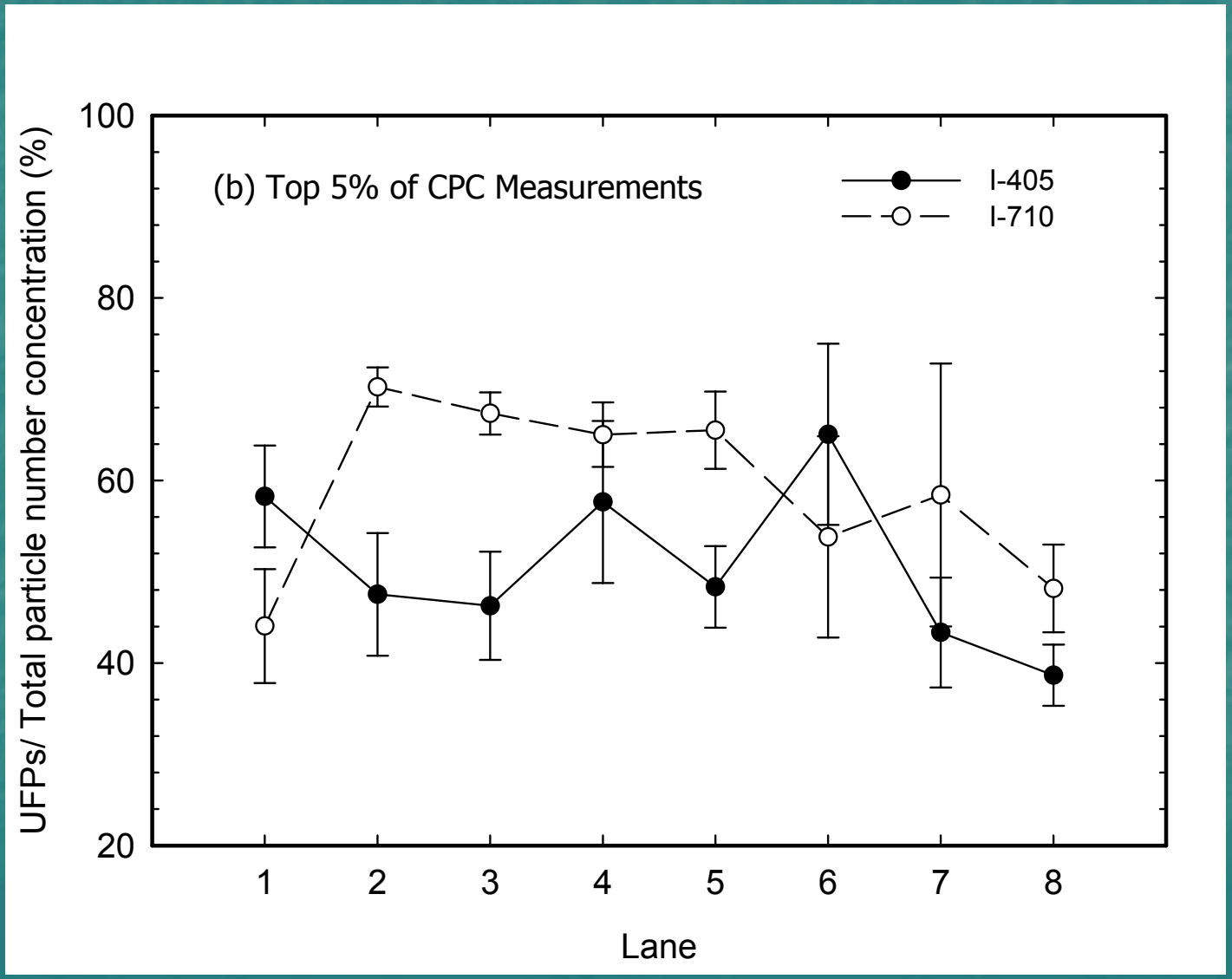
Effect of Driving Lane



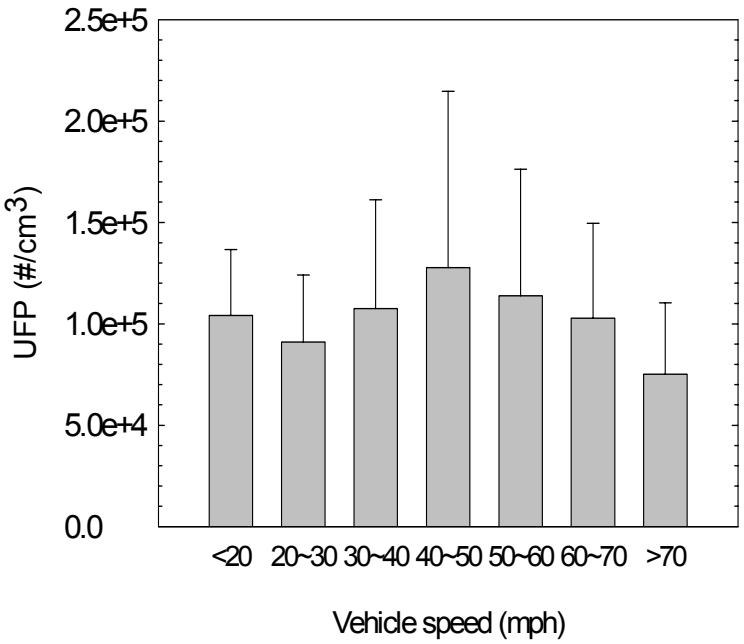
Effect of Driving Lane

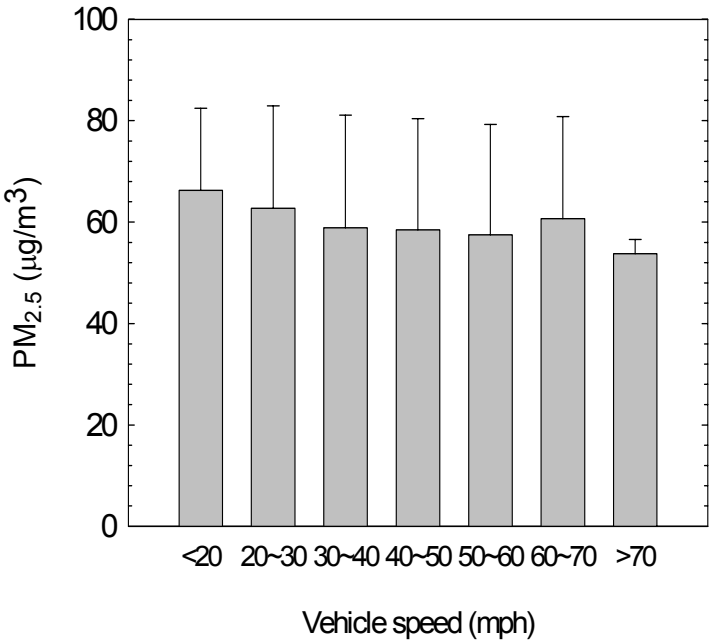


Effect of Driving Lane

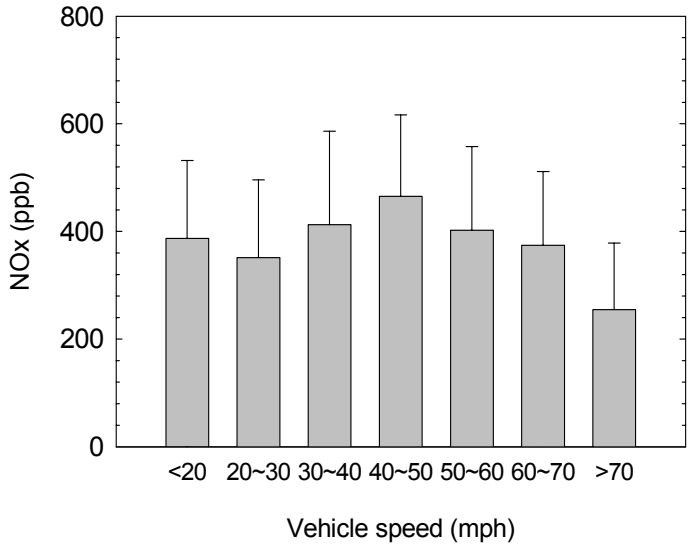


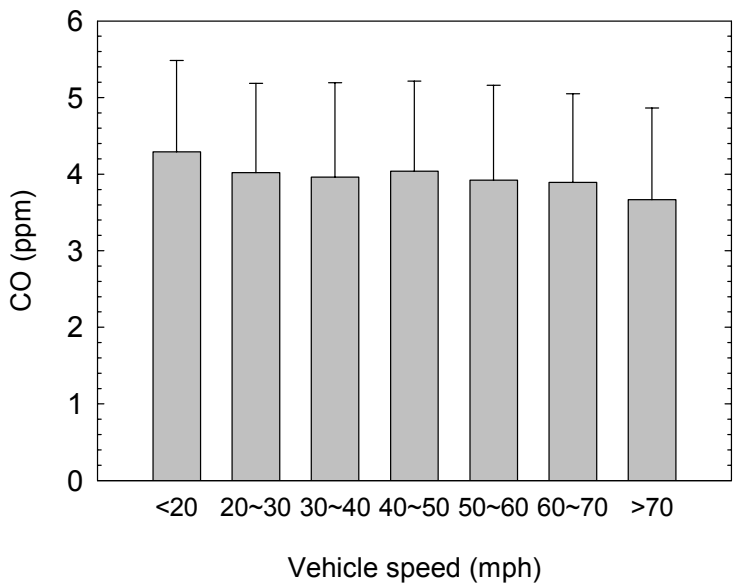
Effect of Vehicle Speed



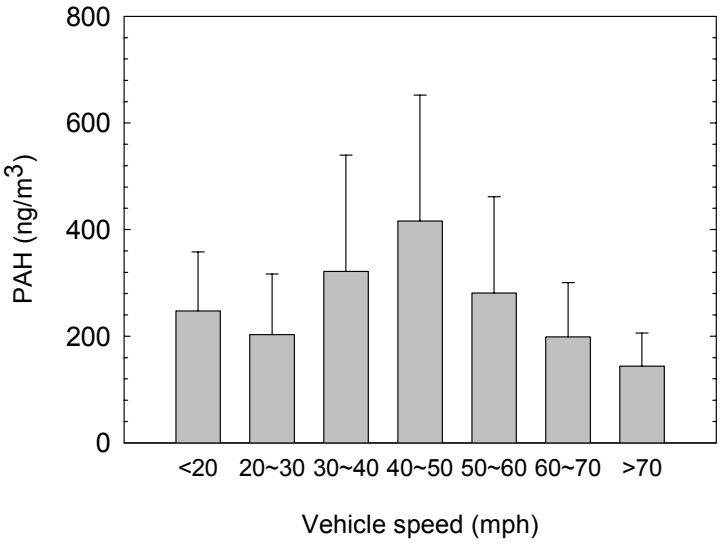


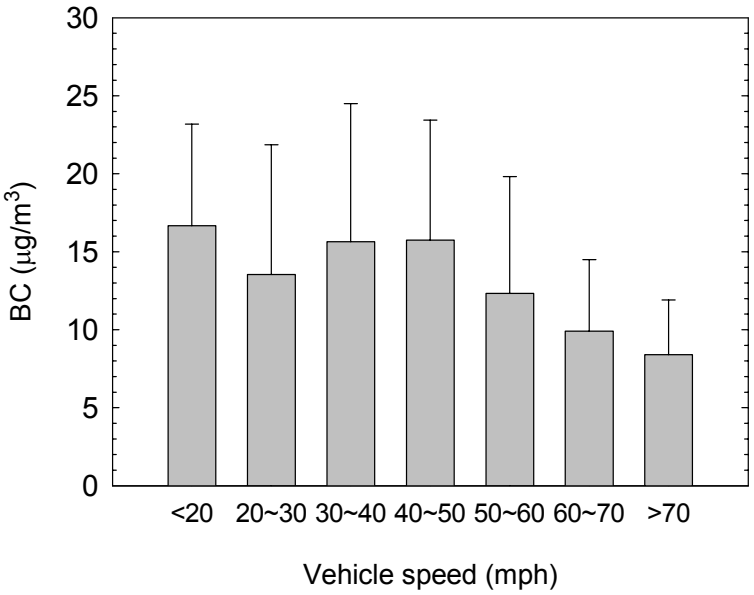
Effect of Vehicle Speed



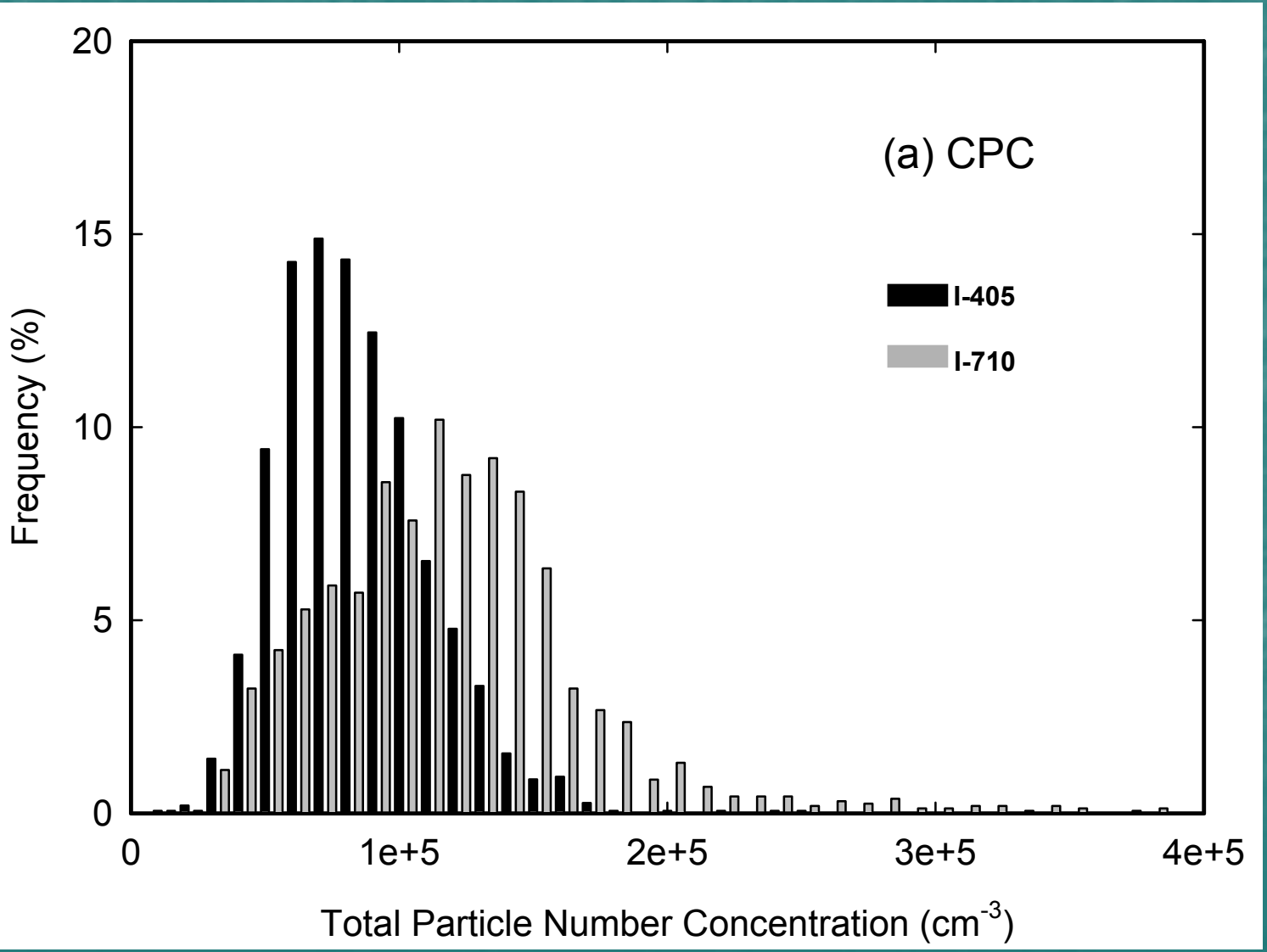


Effect of Vehicle Speed

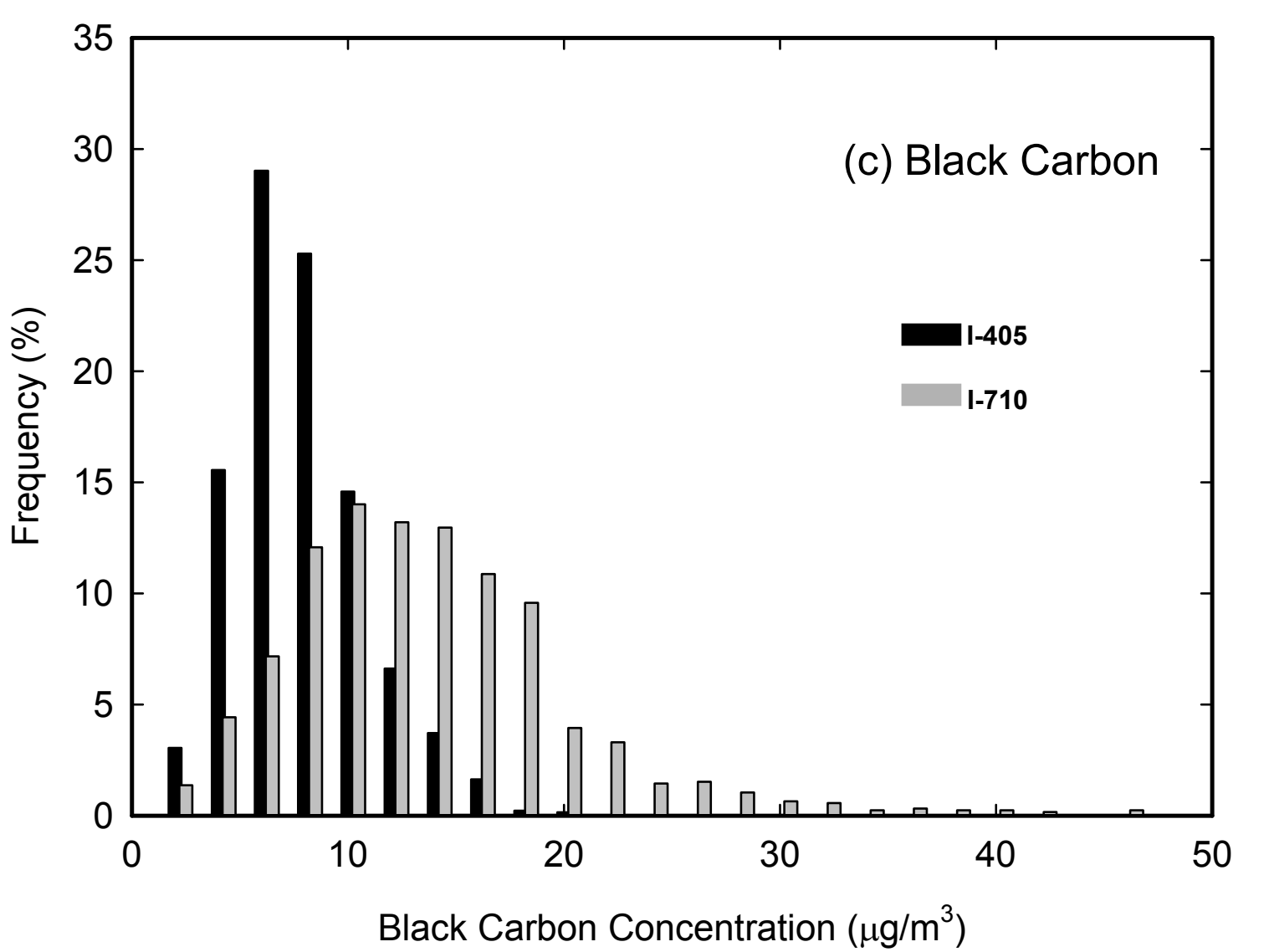




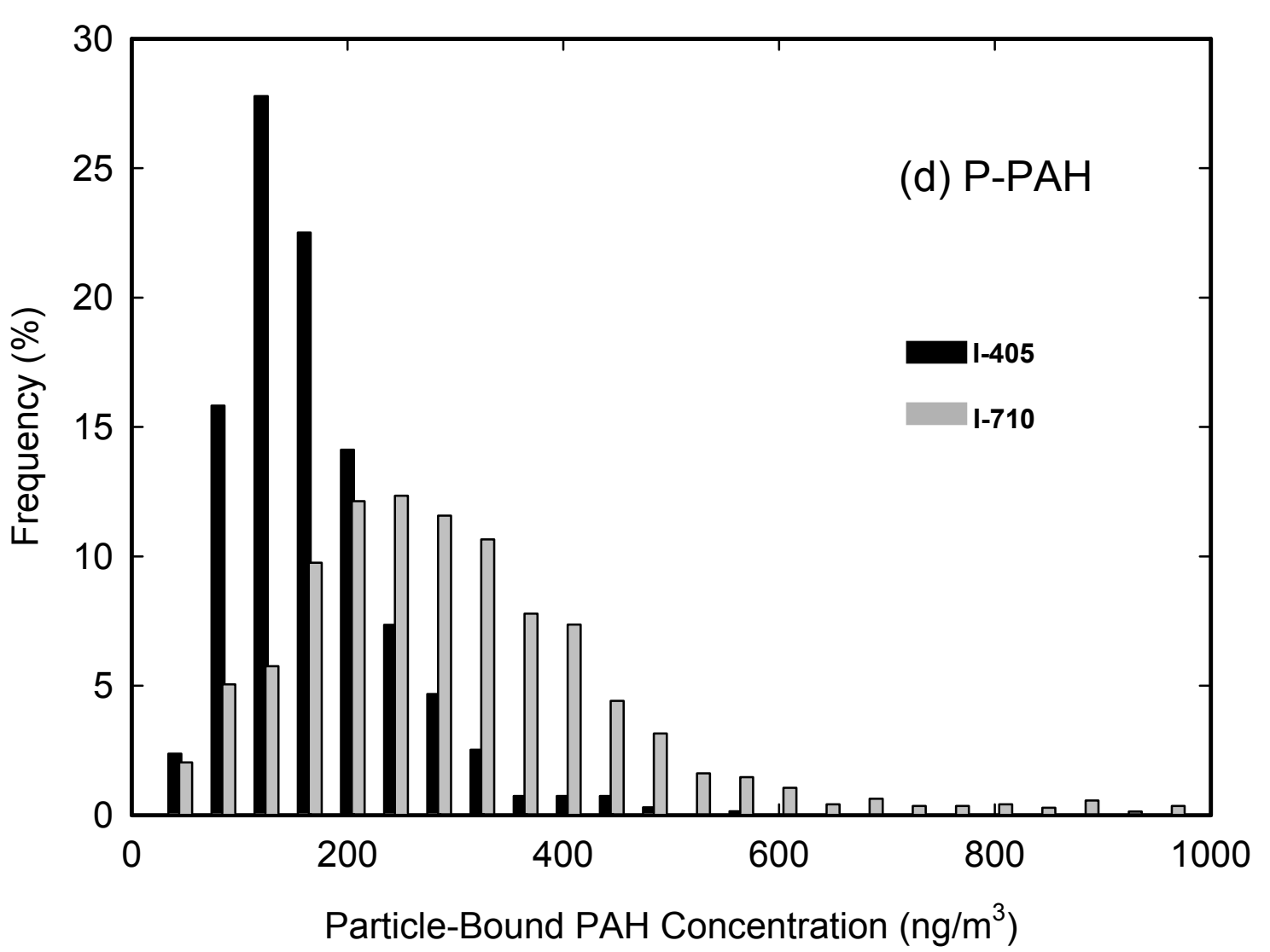
Distribution of Concentrations



Distribution of Concentrations



Distribution of Concentrations



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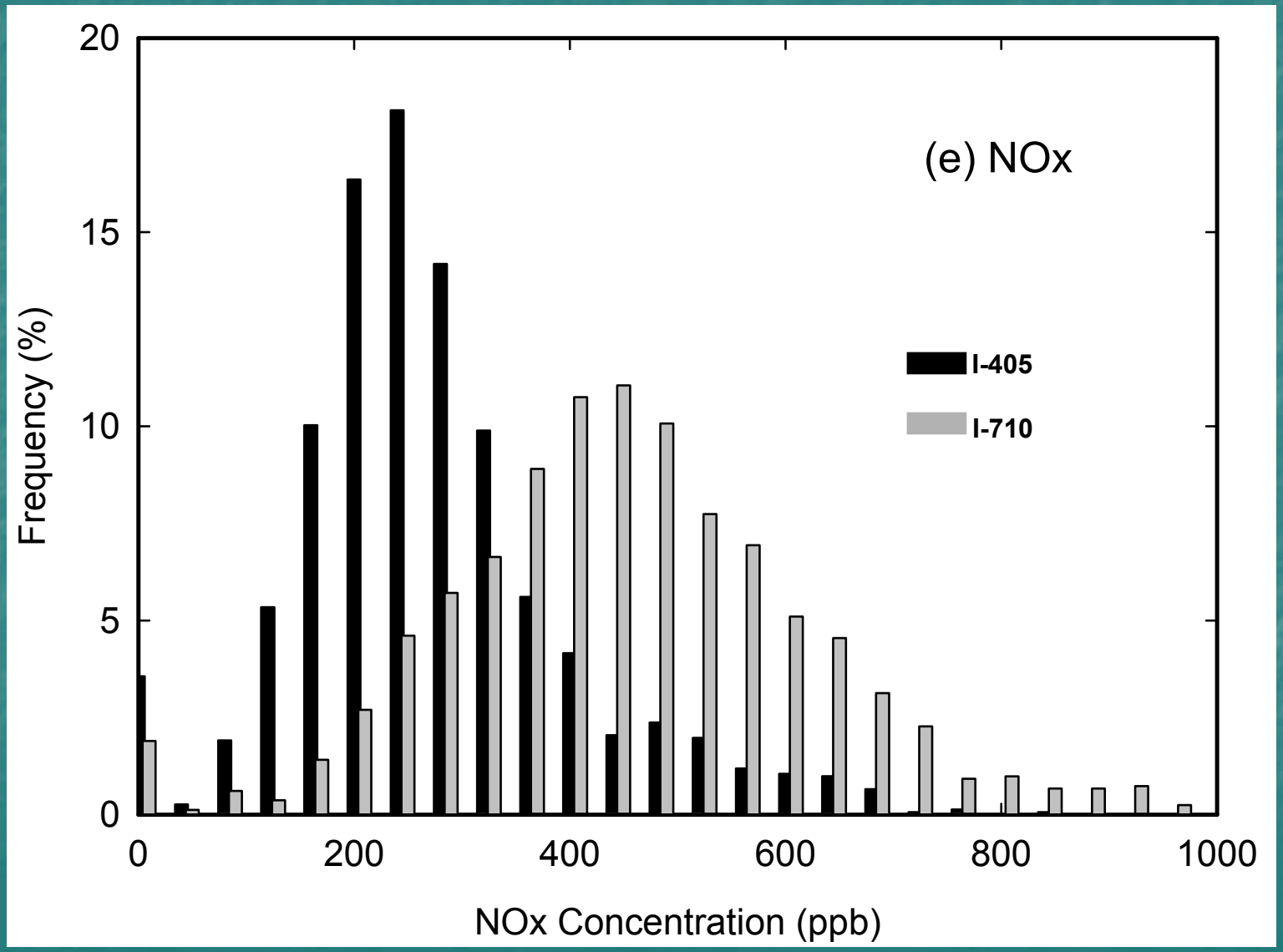
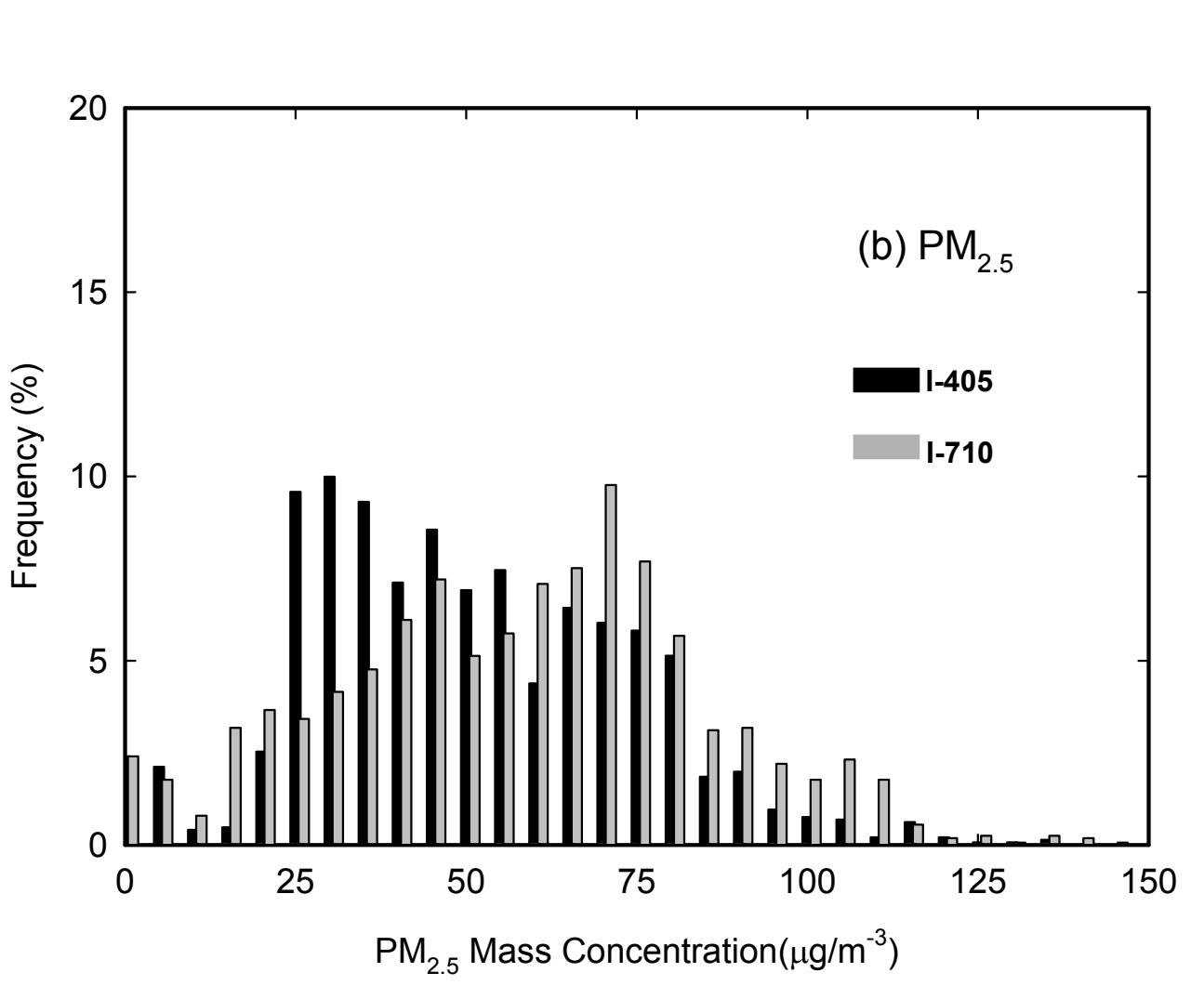
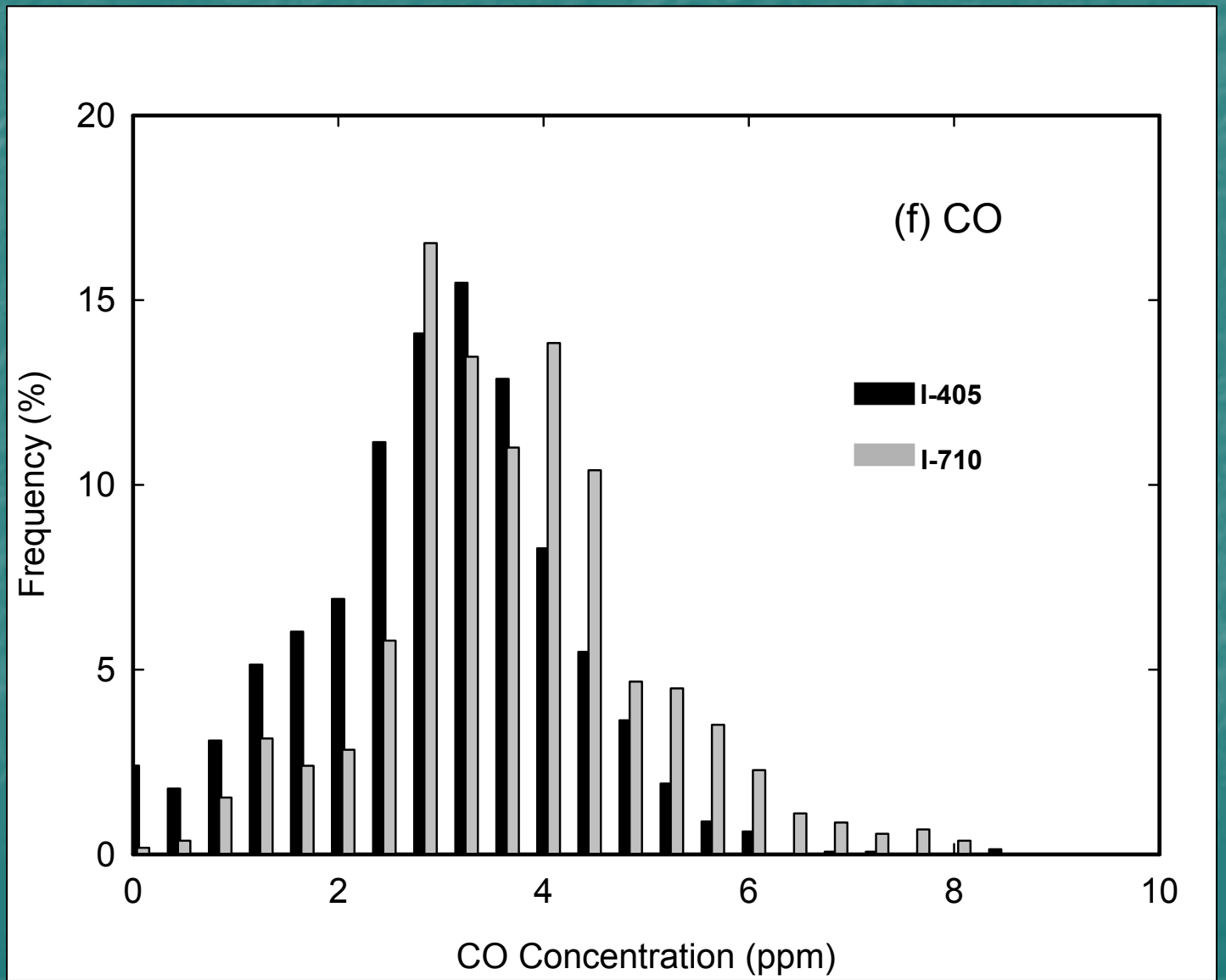


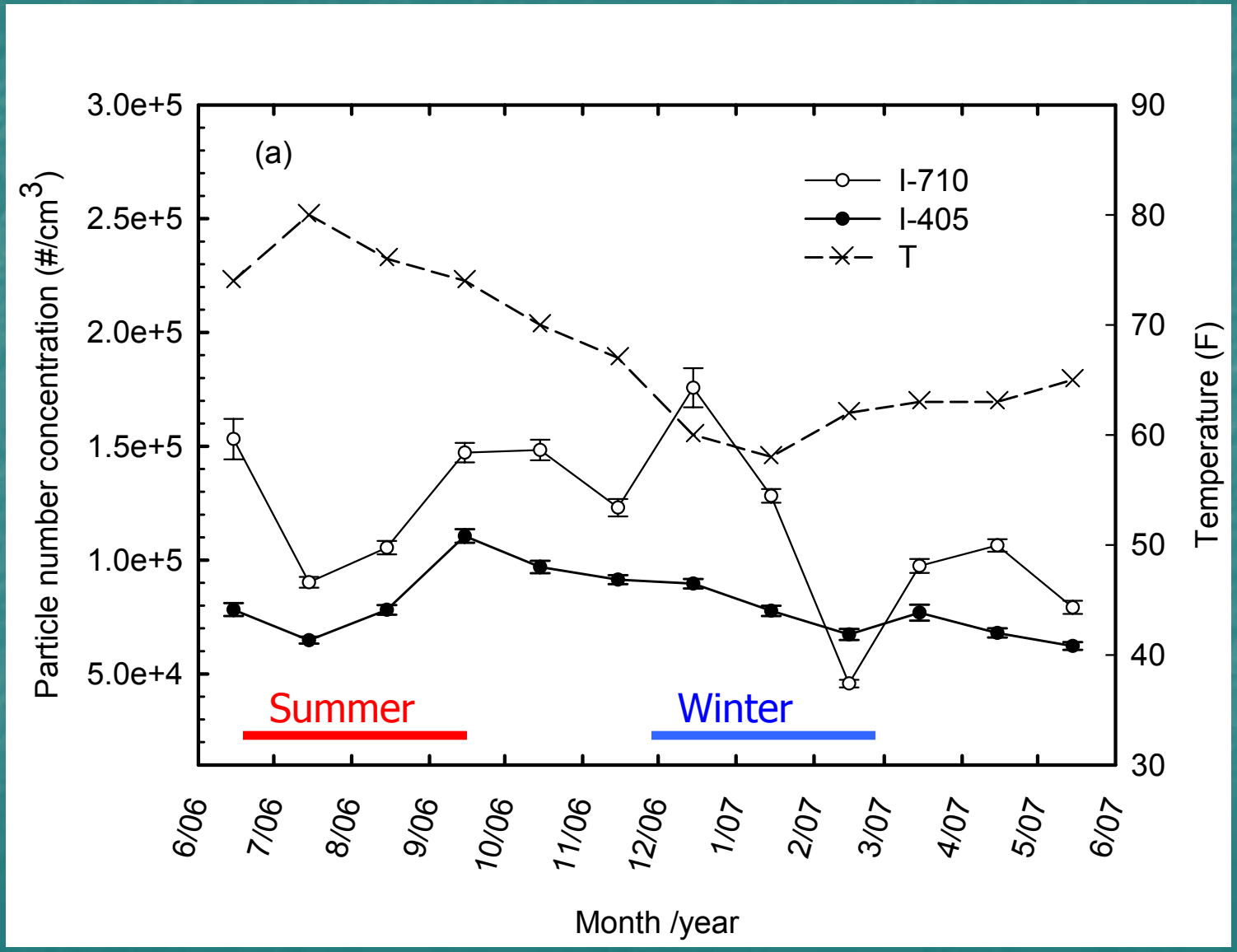
Distribution of Concentrations



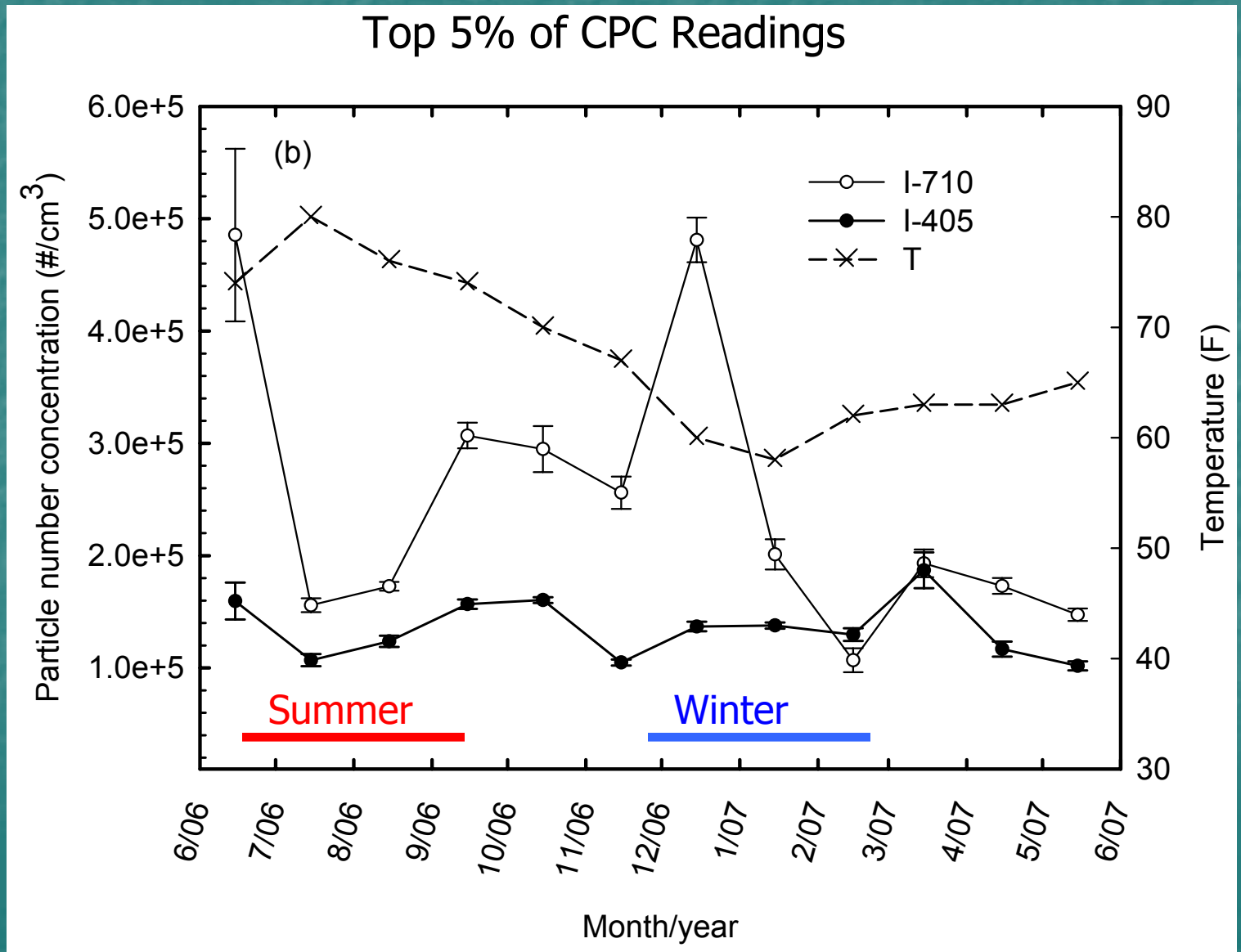
Distribution of Concentrations



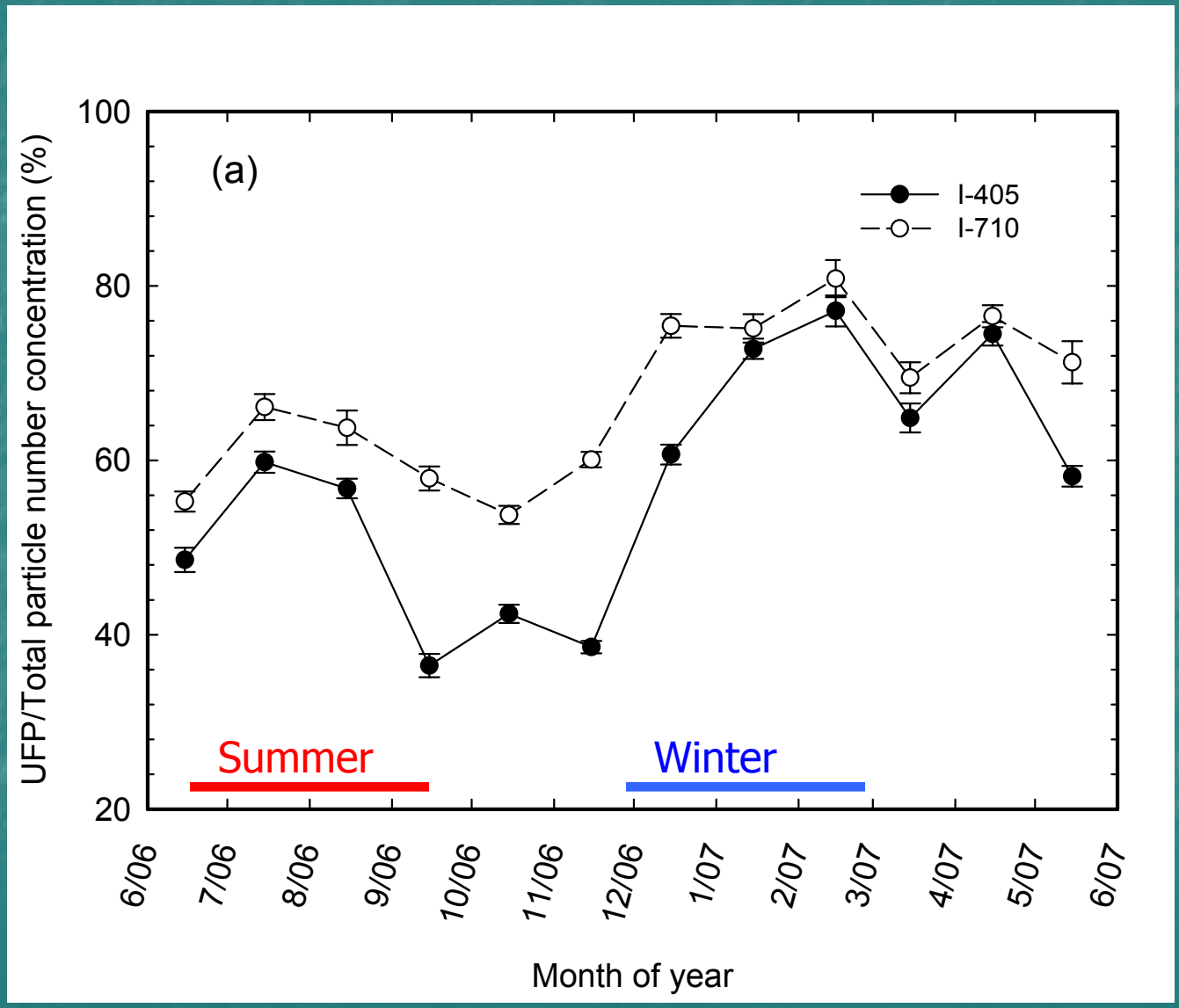
Seasonal Effects



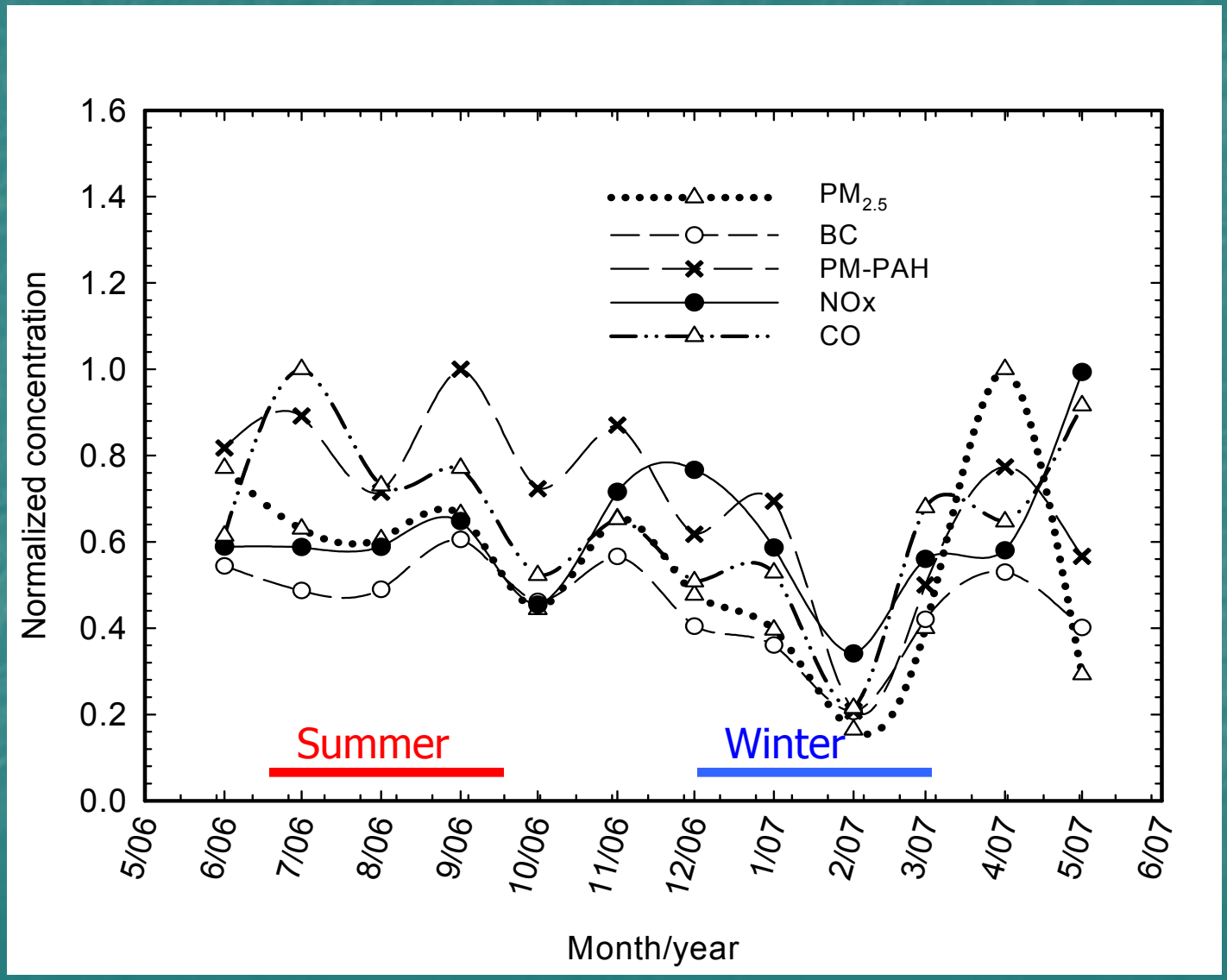
Seasonal Effects



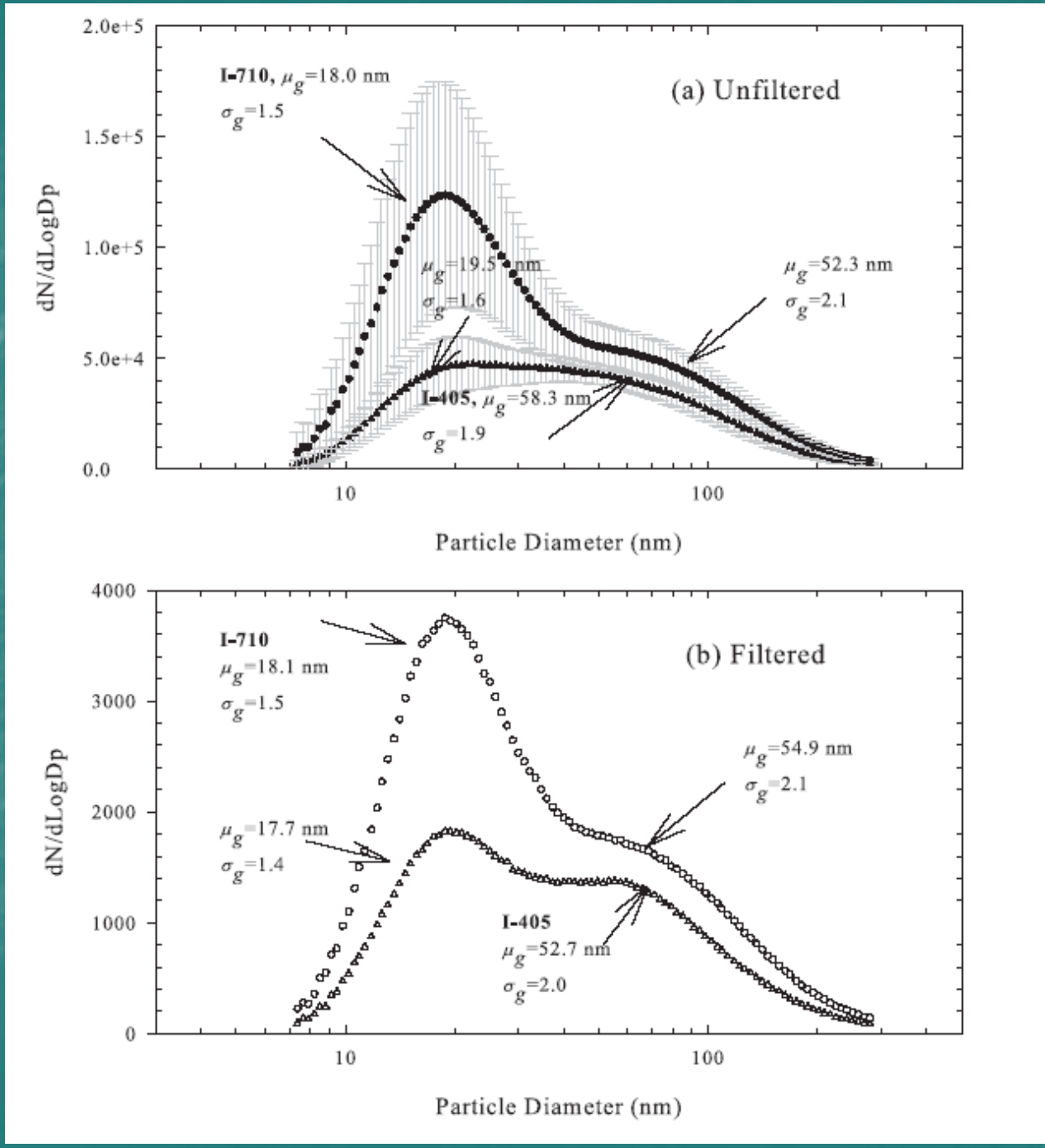
Seasonal Effects



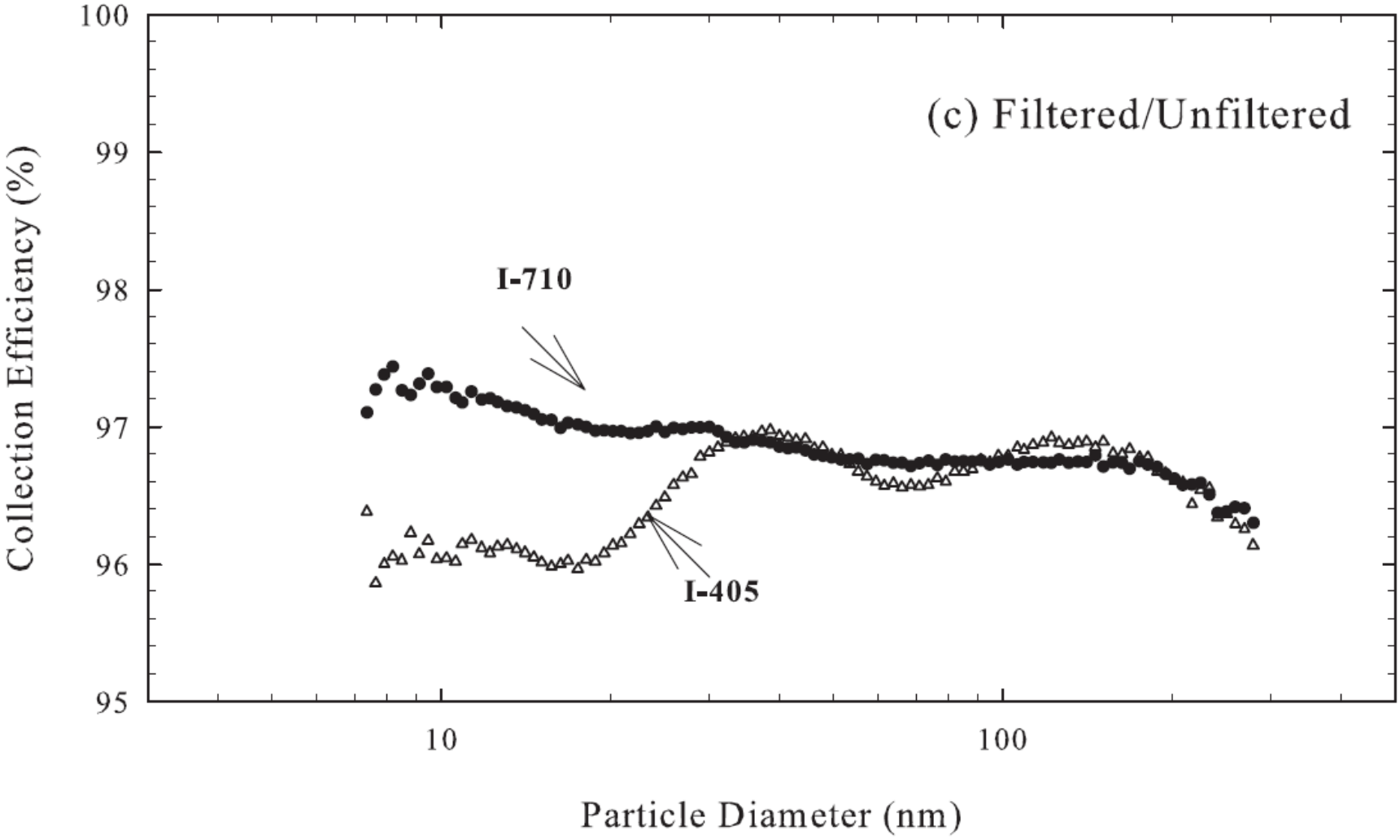
Seasonal Effects



Particle Size Distributions In Exposure Chamber

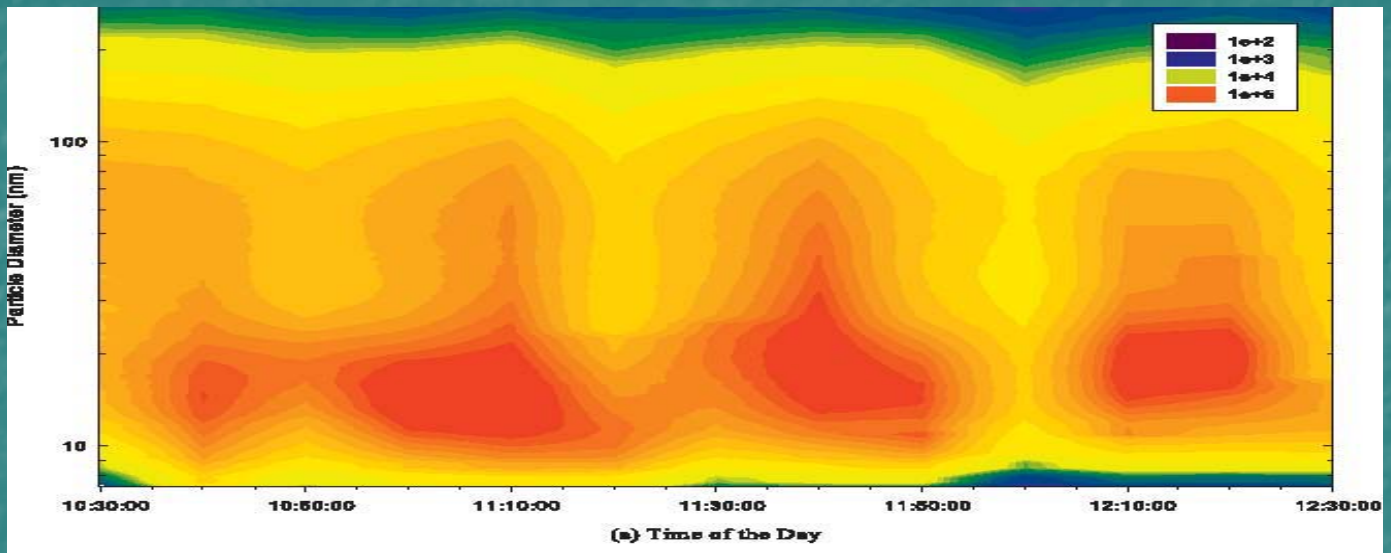


Size-Specific Filtration Efficiency

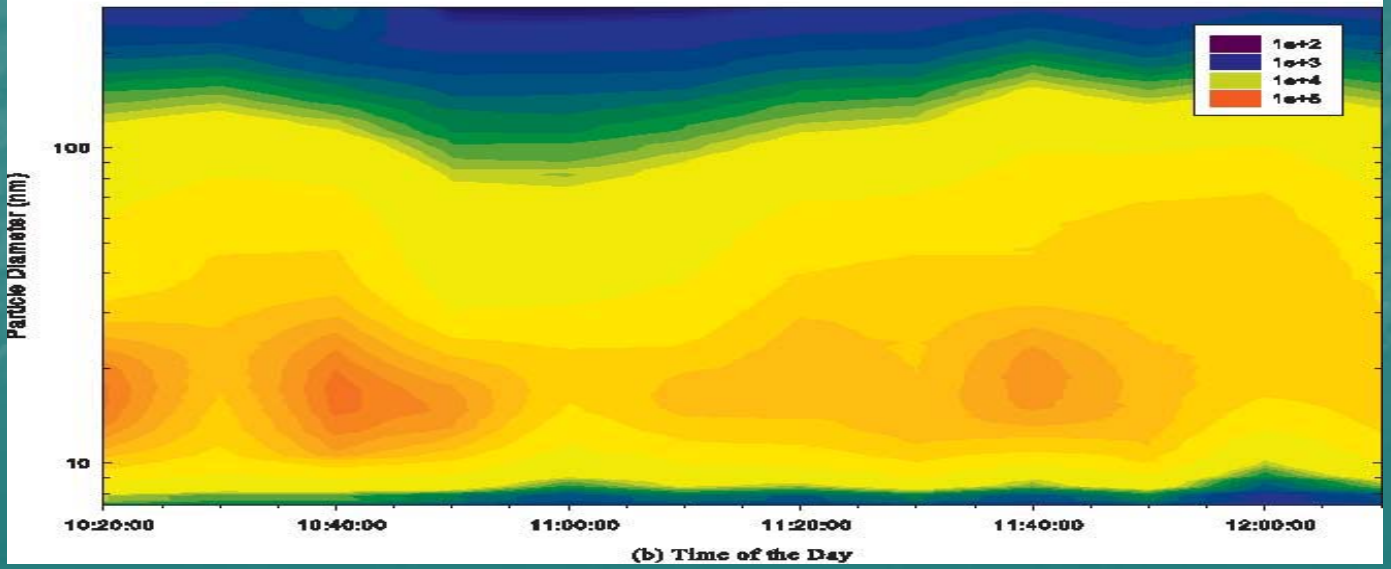


Contour Plots of UF Size Distributions v. time

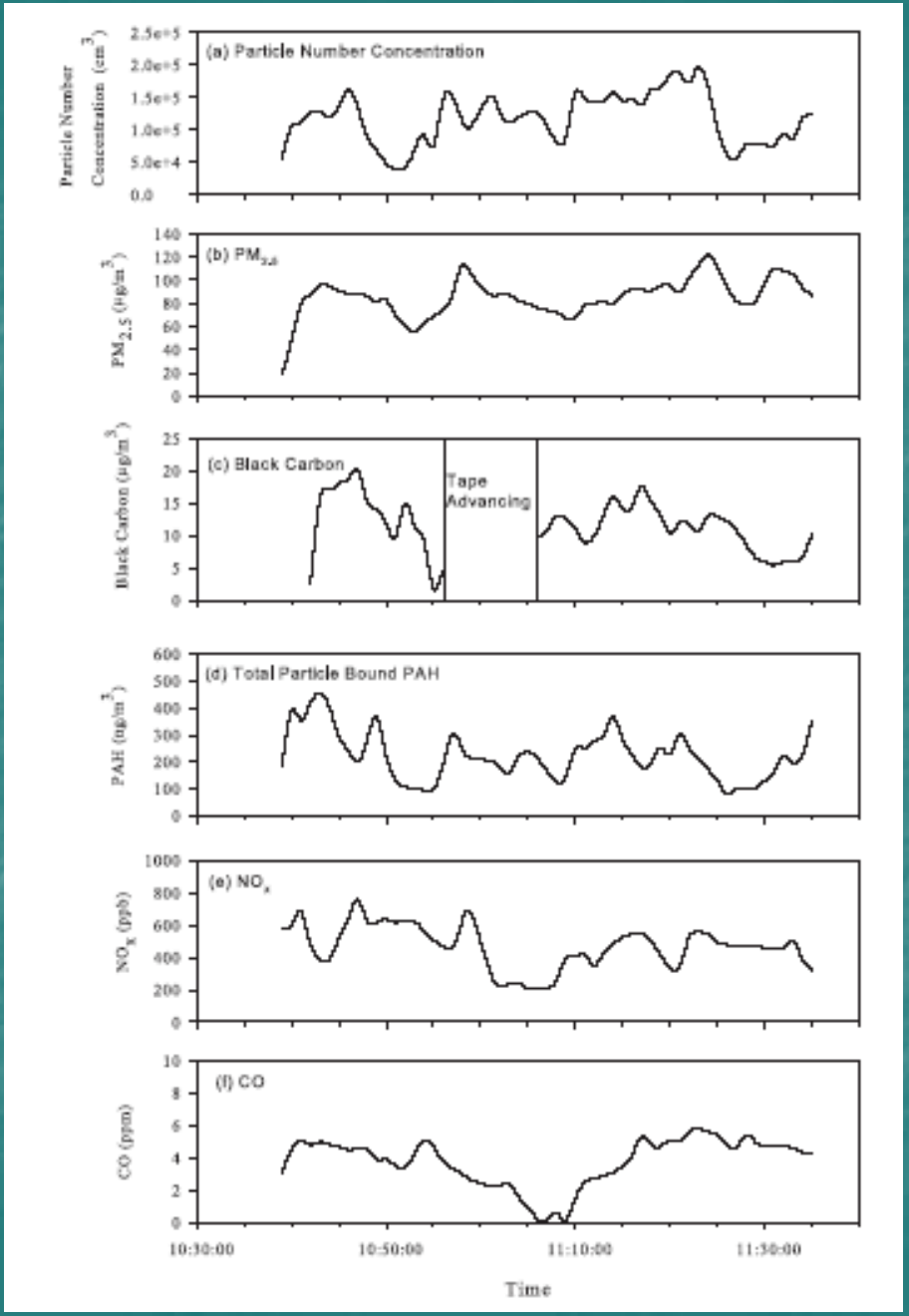
I-710



I-405



One-hour Time Series Plots of Chamber Concentrations on I-710.



Pearson correlation coefficients among measured pollutants inside the exposure chamber for unfiltered mode, for all subjects.

(a) I-405

	Total Particle Number	UF particles	PM-2.5	PM-10	BC	UVPM	PB-PAH	NO_x	CO	CO_2
Total Particle Number	1.000									
UF particles	-0.025 (0.920)	1.000								
PM-2.5	0.116 (0.706)	0.226 (0.457)	1.000							
PM-10	0.062 (0.841)	0.263 (0.385)	0.993 (<.0001)	1.000						
BC	0.277 (0.251)	0.485 (0.035)	0.570 (0.042)	0.603 (0.029)	1.000					
UVPM	0.279 (0.247)	0.453 (0.051)	0.569 (0.043)	0.587 (0.035)	0.943 (<.0001)	1.000				
PB-PAH	-0.245 (0.313)	0.323 (0.178)	0.242 (0.426)	0.297 (0.325)	-0.257 (0.288)	-0.208 (0.394)	1.000			
NO_x	-0.007 (0.977)	0.152 (0.534)	0.374 (0.208)	0.387 (0.191)	0.471 (0.042)	0.574 (0.010)	-0.212 (0.383)	1.000		
CO	0.302 (0.239)	-0.158 (0.546)	0.625 (0.022)	0.584 (0.036)	0.583 (0.014)	0.572 (0.016)	-0.737 (0.001)	0.511 (0.036)	1.000	
CO_2	-0.120 (0.647)	0.417 (0.096)	0.742 (0.004)	0.758 (0.003)	0.013 (0.960)	0.150 (0.567)	0.464 (0.061)	-0.087 (0.741)	-0.356 (0.161)	1.000

(b) I-710 freeway

	Total Particle Number	UF particles	PM-2.5	PM-10	BC	UVPM	PB-PAH	NO_x	CO
Total Particle Number	1.000								
UF particles	0.816 (<.0001)	1.000							
PM-2.5	0.280 (0.354)	0.145 (0.637)	1.000						
PM-10	0.278 (0.359)	0.119 (0.698)	0.997 (<.0001)	1.000					
BC	0.674 (0.002)	0.384 (0.105)	0.600 (0.030)	0.594 (0.032)	1.000				
UVPM	0.684 (0.001)	0.405 (0.086)	0.605 (0.028)	0.600 (0.030)	0.999 (<.0001)	1.000			
PB-PAH	0.328 (0.198)	0.246 (0.342)	0.336 (0.312)	0.315 (0.346)	0.305 (0.233)	0.287 (0.265)	1.000		
NO_x	0.192 (0.432)	0.272 (0.260)	-0.466 (0.108)	-0.496 (0.085)	0.297 (0.217)	0.291 (0.226)	0.556 (0.021)	1.000	
CO	0.114 (0.641)	-0.019 (0.940)	-0.178 (0.561)	-0.207 (0.498)	0.485 (0.035)	0.458 (0.049)	0.093 (0.722)	0.595 (0.007)	1.000
CO_2	-0.147 (0.550)	-0.175 (0.473)	-0.444 (0.128)	-0.419 (0.155)	-0.030 (0.904)	-0.050 (0.840)	-0.169 (0.516)	-0.033 (0.892)	0.318 (0.184)

*"Total particle number" refers to CPC readings, and "UF particles" refers to SMPS measurements.

(b) I-710 freeway

	Total Particle Number	UF particles	PM-2.5	PM-10	BC	UVPM	PB-PAH	NO_x	CO
Total Particle Number	1.000								
UF particles	0.816 (<.0001)	1.000							
PM-2.5	0.280 (0.354)	0.145 (0.637)	1.000						
PM-10	0.278 (0.359)	0.119 (0.698)	0.997 (<.0001)	1.000					
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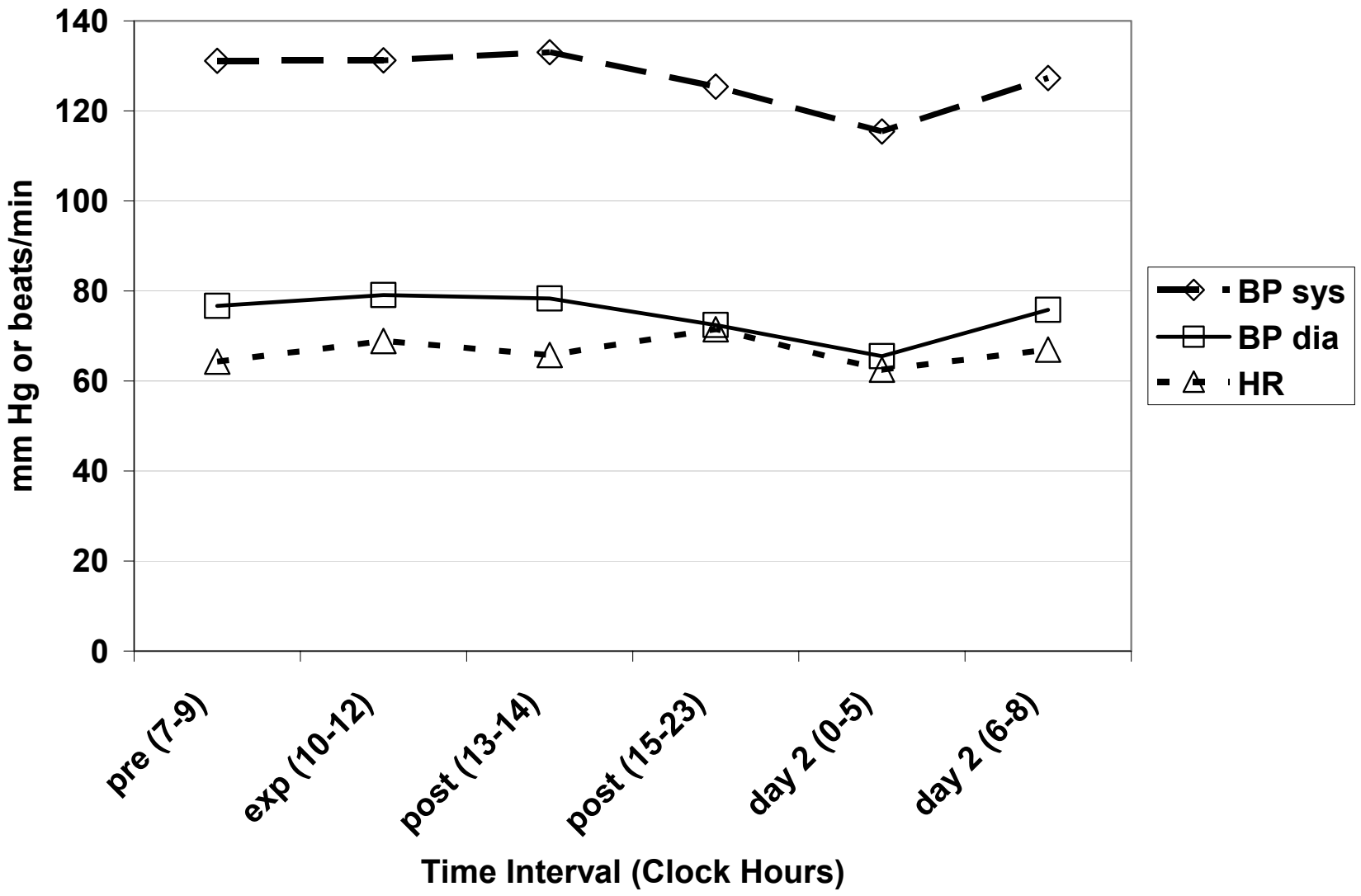
CO_2	-0.147 (0.550)	-0.175 (0.473)	-0.444 (0.128)	-0.419 (0.155)	-0.030 (0.904)	-0.050 (0.840)	-0.169 (0.516)	-0.033 (0.892)	0.318 (0.184)

significant Correlations for both freeways

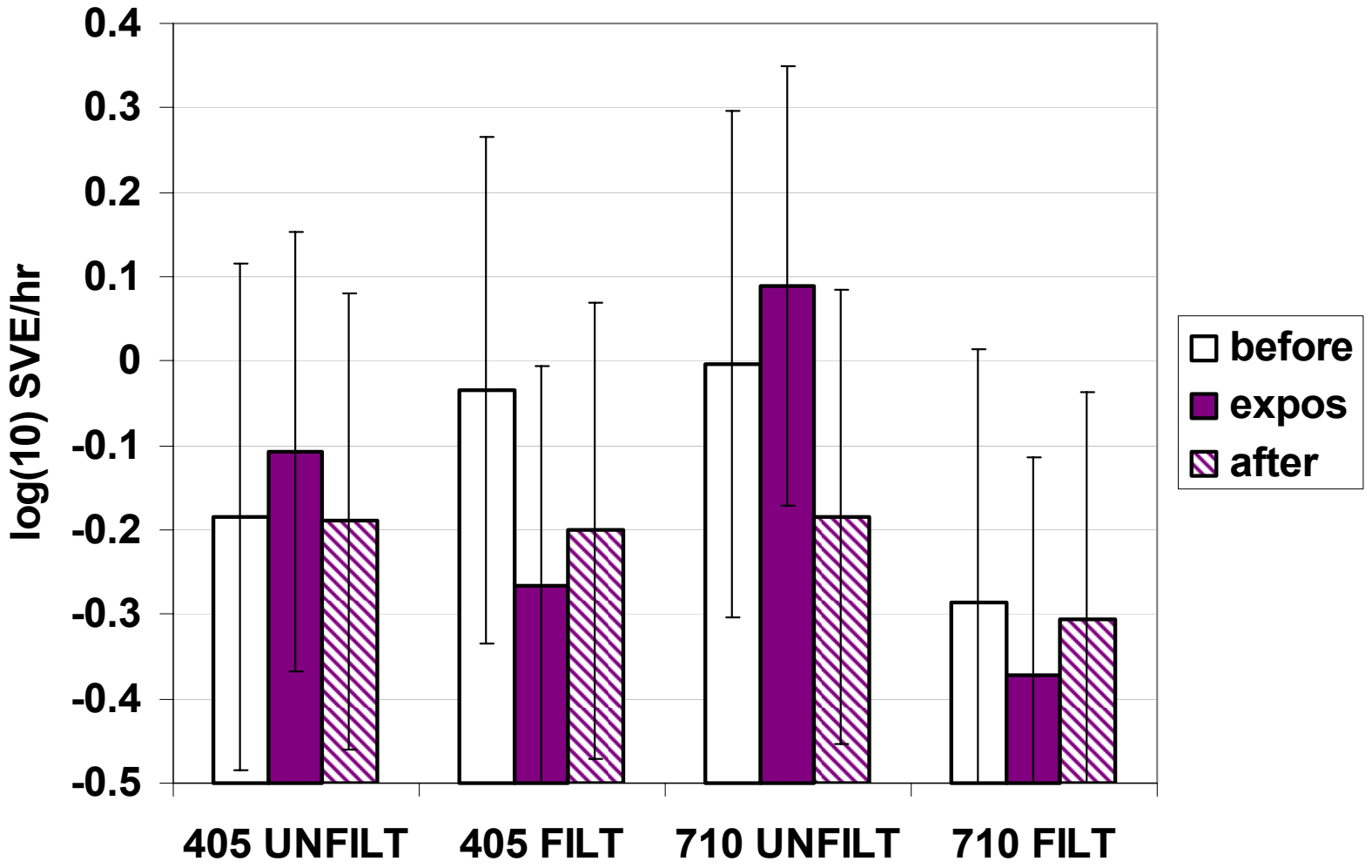
*"Total particle number" refers to CPC readings, and "UF particles" refers to SMPS measurements.

Physiological and C/V Results

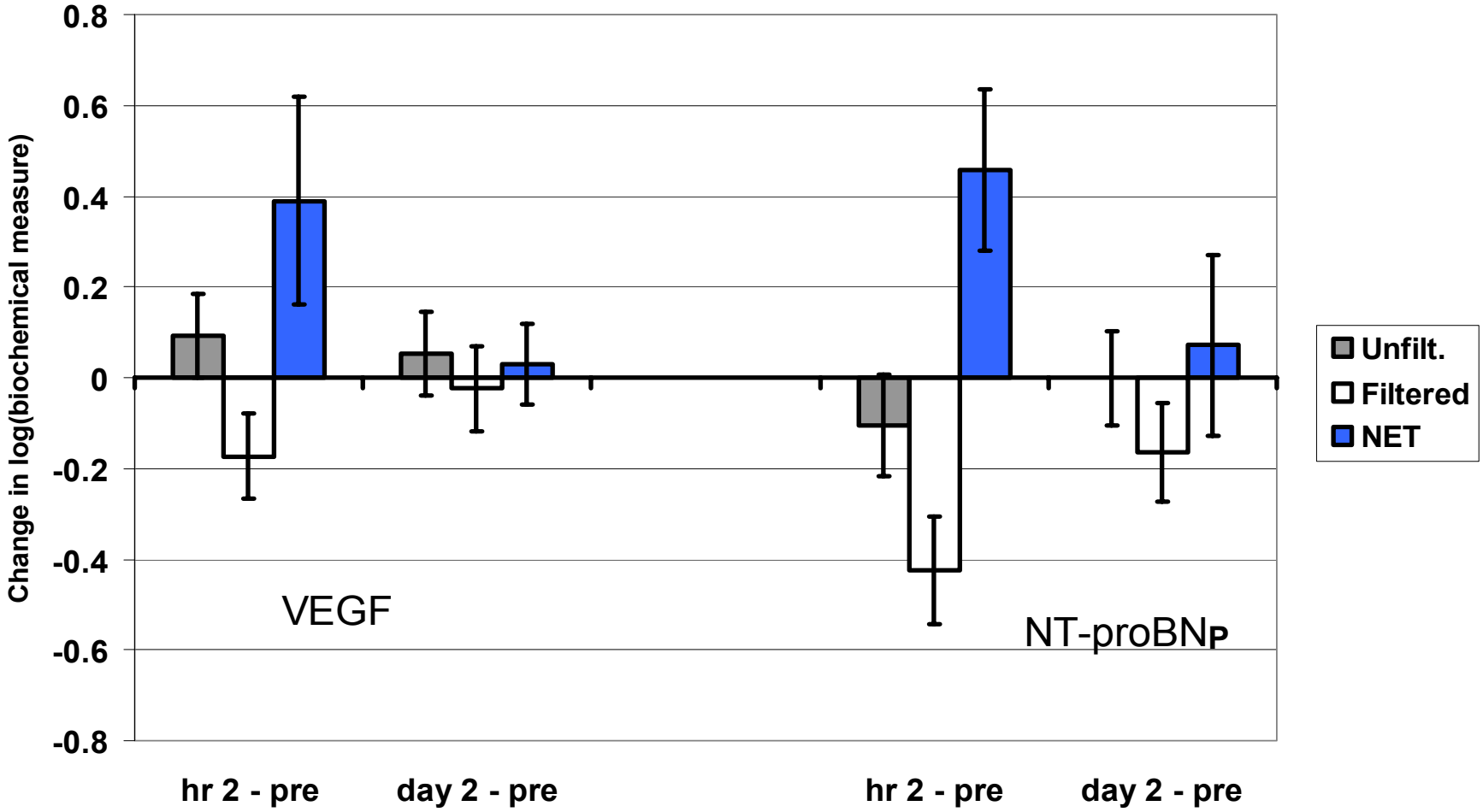
Blood Pressure and Heart Rate



Atrial Ectopic Beats



VEGF and NT-proBNP



Results of exposure-response analyses: Hourly incidence of supraventricular ectopic beats (from 24-hr recording) vs. exposure measures*

Exposure Measure	Effect Size	P Value
Particle number	+0.33% / 1000 particles	0.009
$PM_{2.5}$	+0.44% / ($\mu g/m^3$)	0.07
PM_{10}	+0.37% / ($\mu g/m^3$)	0.10
Black carbon	+2.2% / ($\mu g/m^3$)	0.04
PAH	+0.11% / (ng/m^3)	0.02
NOx	+0.014% / ppb	0.47
CO	+10% / ppm	0.10
Temperature	+0.83% / deg F	0.63
Prior 24 hr Ambient PM_{10}	-0.4% / ($\mu g/m^3$)	0.63
Prior 24 hr Ambient $PM_{2.5}$	-1.5% / ($\mu g/m^3$)	0.07

*Incidence is log-transformed for analysis, so effect-size estimates are expressed as percentages. See Table 2 for relevant exposure data.

CONCLUSION

Summary of Study Results

- Significant Results:
  - Unfiltered air compared to filtered air
    - Increased frequency atrial arrhythmias
      - +20% ectopic beats
      - Not significant for healthy individuals
      - Can trigger sustained arrhythmias in susceptible individuals
    - Increased concentration of NTproBNP
      - +38%
      - Marker for intra-atrial pressure
    - Increased concentration of VEGF
      - +30%
      - Marker for vascular response/injury

Summary of Study Results

- No significant differences in HRV
- No significant differences in respiratory response or blood pressure
- Suggests effect more strongly associated with ultrafine particles, P-PAH, and BC
  - p=0.01 for number concentration
  - p=0.02 for P-PAH
  - P=0.04 for BC
  - P=0.07 for mass concentration

Summary of Study Results

- For this study average concentrations greater on I-710 than I-405
  - Particle number +37%*
  - P-PAH +69%*
  - BC +89*
  - PM-2.5 +15%
  - NOx +84%*
  - CO +26%
  - * significant at p<=0.05

Summary of Study Results

- In-vehicle concentration of UFP high on heavily used freeways
- UFP fraction of total particulate higher on 710 than 405
- UFP not correlated with other pollutants
- UFP, BC, and P-PAH exposure can be reduced by:
  - Avoiding heavy-duty diesel trucks on freeways
  - Use of in-vehicle filtration

Acknowledgements

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  - California Air Resources Board
    (Contract # 04-324),
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  - USEPA Southern California Particle Center

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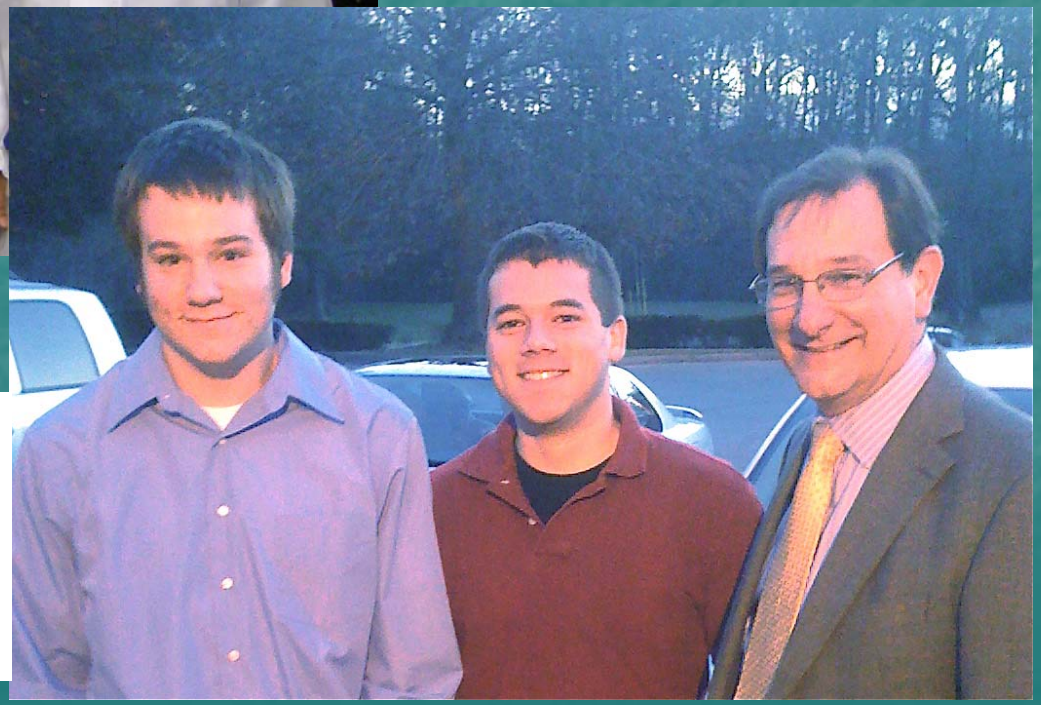

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Questions?