DISSERTATION

PERSONAL, SPATIOTEMPORAL EXPOSURE ASSESSMENT: METHOD DEVELOPMENT AND APPLICATION

Submitted by

Colby D. Adams

Department of Environmental and Radiological Health Sciences

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Doctoral Committee:

Advisor: John Volckens

Stephen Reynolds
Jennifer Peel
William Brazile
Melinda Laituri

ABSTRACT

PERSONAL, SPATIOTEMPORAL EXPOSURE ASSESSMENT:

METHOD DEVELOPMENT AND APPLICATION

Asthma is a common health disorder in children. Children's exposure to particulate matter (PM) air pollution has been implicated in asthma prevalence and severity. Individual exposure to PM depends on one's proximity to PM sources and on the immediate environment (i.e., the microenvironment) that surrounds the individual. Common PM sources include combustion by-products (gasoline and diesel engine exhaust, wood and cigarette smoke), other man-made particles (road dust and other fugitive emissions), and bioaerosols (pollen).

There is a paucity of studies that assess children's exposures to PM across space and time. Outdoor, community-based PM monitors (the current standard for regulatory monitoring of air pollution) do not adequately capture the spatial and temporal variability of ambient PM, nor can they capture the variability of personal exposure associated with movement through the community, e.g. vehicle transit, or movement into indoor microenvironments. Studies assessing personal exposures have been limited in scope, mainly because personal monitors are expensive and intrusive. Most studies of children's exposures have employed the method of time-averaged, filter-based sampling, where a sample is collected (integrated) over a 24-hour period. Time-integrated sampling tends to attenuate our ability to detect acute exposures, or peaks, which in turn may obscure our ability to detect relationships between exposure and adverse health outcomes. Recently, however, the advent of portable PM monitors,

capable of measuring concentrations every few seconds and suitable for wear, even for children, has enabled the assessment of children's exposure to PM across both space and time.

This work describes the development, evaluation, and application of a high-resolution, space and time-referenced sampling method for personal exposure assessment to airborne PM. This sampling methodology provides continuous measures of personal PM levels along with the corresponding location-activity, or microenvironment, of the subject. The exposure assessment method utilizes miniaturized monitoring equipment, including a handheld global positioning system (GPS) receiver, a miniature aerosol nephelometer, and an ambient temperature monitor. Collectively, these instruments estimate the location, time, and magnitude of personal exposure to particulate matter air pollution.

Method development consisted of laboratory and field evaluation of instrument performance (precision and accuracy testing), as well as development of a classification algorithm to apportion spatial data into pre-determined location-activity categories (i.e. work/school, home, transit). GPS units were more accurate than manufacturer's claims, providing outdoor locations within ~4 m and indoor locations within ~7 m. Dynamic thermal response of temperature monitors captured indoor/outdoor transitions ~20 seconds. The apportioning algorithm was very effective with an overall accuracy of 99.6%.

This novel sampling method was then applied to a panel of asthmatic school-children to examine their personal exposure to PM in four distinct microenvironments (home, school, morning and afternoon transit). In the school-based panel, 30 children

with physician-diagnosed asthma were monitored daily for four consecutive days (Mon-Thu) on two occasions during a school year. Personal PM exposures, asthma exacerbation markers, and data on personal behaviors were collected over a 5-month winter period (2008–2009) in Denver, Colorado.

This dataset provided over 950,000 personal exposure data points over 125 sampling days, as well as associated health outcome and personal behavior data. Relationships were evaluated between personal exposures measured in each microenvironment and concentrations measured by a community-based, outdoor monitor. Relationships were also evaluated between personal exposure to traffic-related particulate matter encountered during the morning commute to school and markers of asthma exacerbation (urinary leukotriene E4 levels). The data in both cases were analyzed using linear mixed models to control for the hierarchical nature as well as the repeated measures aspect of the data.

Analysis of microenvironment-based personal exposures showed that variation in personal exposures was primarily within-subject and space- and time-related. The highest to lowest mean personal concentrations per microenvironment were: home, morning transit, afternoon transit, and school ($p<0.01$ for differences between each microenvironment, except morning and afternoon transit). Concurrently measured *ambient* PM concentrations were not associated with personal exposures within microenvironments. Personal exposure in each microenvironment was associated with exposure in subsequent microenvironments (15-111% increase per 1 $\mu g/m^3$ increase in personal PM in preceding microenvironment, $p<0.01$).

For personal exposure to traffic-related particulate matter during the morning commute, an increase of an interquartile range in personal PM exposure was related to a 15.7% increase in urinary leukotriene E4 measured within 3-6 hours after exposure (95% CI, 7-46%; $p < 0.001$). This association was not discernible when measures of personal exposure were replaced with ambient concentrations measured by community-based monitors, or their statistical moments. Children's exposure to fine particles during morning commutes were lower, on average, than indoor exposures encountered at home and higher, on average, than exposures encountered at school.

Overall, we found that differences in personal PM exposures within urban-poor schoolchildren with asthma are microenvironment-driven; exposures are generally highest at home, followed by transit and then school. Personal home exposures are poorly predicted with community-based monitors, but are themselves strongly predictive of personal exposures in subsequent microenvironments. These data suggest a "personal cloud" effect that persists through different microenvironments and can only be measured with spatially and temporally precise personal monitoring. In addition, brief exposure to traffic-related particulate matter is associated with clinically significant increases in urinary leukotriene E4 levels among children with persistent asthma. This association was discernible from a relatively small sample size by measuring personal exposure segregated into specific microenvironments (i.e., the morning commute).

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DEDICATION

For Camden and Keaton, each equally my pride and joy.

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INTRODUCTION

Asthma prevalence among children has increased over the past three decades (Van Cleave, Gortmaker et al. 2010), sparking further interest in the role environmental factors play in asthma etiology and exacerbation. Ambient air pollution has long been associated with increased symptoms and decreased lung function among asthmatics (Peters 1997; NRC-NAS 1998; Yu 2000; EPA 2004; Pope and Dockery 2006). For children, asthma is the most common of chronic health problems and also one of the most common health complaints of the entire US population (IOM 2000).

Most epidemiological studies have not validated their estimates of individual exposure to PM, mainly because personal exposure monitoring can be obtrusive and also resource intensive. Community-based air pollution monitors, collecting 24-hour integrated samples, are often used to assign exposures to individuals, but these monitors cannot capture the spatial and temporal variability of ambient air pollution (Ott, Kumar et al. 2008), nor can they capture the variability of personal exposure associated with movement throughout the community, e.g. vehicle transit (Setton, Marshall et al. 2011; Brown, Sarnat et al. 2012), or movement into indoor microenvironments (Van Roosbroeck, Li et al. 2008). As a result, individual exposure estimates derived from ambient monitoring data are subject to exposure measurement error (Strand, Hopke et al. 2007; Hutcheon 2010).

In asthmatic children, increased symptoms and disease exacerbation occur with exposure to air pollution (Rabinovitch, Strand et al. 2006). In addition to chronic, long-term exposure, acute exposures to PM may also exacerbate asthma in children. This

exacerbation is most likely due to airway inflammation and hyper-responsiveness (Koenig 1999; Gauvreau, Parameswaran et al. 2001; Rabinovitch 2012). Recently, emphasis has been placed on the need for research regarding disease exacerbation associated with acute exposure to particulate matter (PM) from motor-vehicle traffic (HEI 2010).

Asthma exacerbation and the resultant changes in direct and indirect markers of disease, e.g. fractional nitric oxide in breath, serum eosinophil granulocytes, and increased urinary leukotriene E4, can occur within minutes or hours of an exposure (Rabinovitch, Strand et al. 2006; Rabinovitch, Reisdorph et al. 2011; Rabinovitch 2012). The resulting airway inflammation can be assessed with noninvasive markers, such as, exhaled gases, induced sputum, and urinary measurements. Exhaled nitric oxide (eNO), induced sputum eosinophils, and urinary cysteinyl leukotriene E_4 (LTE_4), and other markers have been assessed as non-invasive markers of airway inflammation. Urinary LTE4 is relatively insensitive to inhaled corticosteroid therapy (Rabinovitch 2007). This characteristic makes it attractive when attempting to assess health outcomes in a population using steroid-based therapies to control asthma symptoms.

Cysteinyl leukotrienes (LTC4, LTD4, LTE4), are highly potent mediators closely linked to the pathobiology of asthma (Drazen, Obrien et al. 1992; Bousquet, Jeffery et al. 2000; Kumlin 2000; Rabinovitch 2007; Sanak, Bochenek et al. 2010; Laidlaw and Boyce 2012; Rabinovitch 2012) . Cysteinyl leukotrienes are released by most cells involved in airway inflammation and facilitate several mechanisms that cause lung function decrement. Cysteinyl leukotrienes are potent bronchoconstrictors, directly binding to airway smooth muscle receptors (Bousquet, Jeffery et al. 2000). Cysteinyl

leukotrienes also mediate airway inflammatory response (Gauvreau, Parameswaran et al. 2001) and accelerate recruitment and proliferation of eosinophils (Braccioni, Dorman et al. 2002). They act as potent chemoattractants (Fregonese, Silvestri et al. 2002), leading to hyperresponsiveness of the inflammatory response to various stimuli (Gauvreau, Parameswaran et al. 2001).

Personal monitoring of exposure (i.e., sampling air from within a person's breathing zone) is an alternative to community-based monitoring; this form of exposure assessment is more precise but also more resource intensive, as each study subject must be fitted and monitored individually. Studies of personal PM exposure have shown that individual PM levels (i.e., personal samples) are often greater than estimates provided by stationary, area-based samples of indoor or outdoor environments (Weisel, Zhang et al. 2005; Wallace, Williams et al. 2006). This phenomenon has been termed the "personal cloud" effect. These increased personal exposure estimates are attributed to either a "proximity effect" (i.e. being closer to a source than an area monitor, or a "pigpen effect" (i.e. particles released from clothing or re-suspended due to subject movement) (Wallace, Williams et al. 2006).

To date, studies assessing personal exposures have been limited in scope and have mainly used measurement methods that average, or integrate, over a 24-hour period. Such personal sampling methods typically draw a known volume of air through a filter over time, followed by gravimetric or chemical analyses (Ozkaynak 1996; Williams, Suggs et al. 2000; Adgate, Ramachandran et al. 2002). Filter-based sampling is more accurate and precise than modeling an individual's exposure using a community-based monitor (Rodes, Lawless et al. 2001; Adgate, Ramachandran et al. 2003; Strand, Hopke

et al. 2007; Rodes, Lawless et al. 2010). However, gravimetric filter methods require time-integration (typically across 8 or 24 hours) to achieve sufficient PM mass for detection; such time averaging cannot capture changes in personal exposure that occur across space and time. For example, Quintana et al. reported that personal PM concentrations collected over 15 minute intervals were up to 10 times greater than the 24-hour mean measured during the same period (Quintana, Valenzia et al. 2001).

When considering the transient nature of exposure to environmental contaminants, knowing whether or not a person is in a particular microenvironment is an important step toward determining if exposure may occur (Klepeis, Nelson et al. 2001; McCurdy and Graham 2003). Time-location, which is defined as a person's location at a certain time, has been measured using self-report diary instruments for many years (Wallace, Pellizzari et al. 1987; Robinson 1988; Freeman, Lioy et al. 1999). The National Human Exposure Assessment Survey (NHEXAS) and EPA's Consolidated Human Activity Database (CHAD) are examples of self-report diaries. The CHAD self-report diaries were used to collect extremely detailed and regionally specific time-location data (EPA 2001). The CHAD-type diary is problematic for most exposure assessments as it requires extreme vigilance on the part of the respondent. This problem is even greater when a parent must report time-location for a child.

The use of 24-hr averaging periods for exposure assessment may attenuate the perceived relationship between exposure and adverse health outcomes, especially when a causal exposure is acute, lasting only minutes (Quintana, Valenzia et al. 2001). Thus, although personal sampling may be considered more representative (compared to area monitoring), the use of filter-based gravimetric analysis and activity logs for

personal sampling has limited our ability to determine when and where exposures to increased PM concentrations occur.

Identifying the magnitude, timing, and location of acute exposures are important aspects of symptom prevention and disease management. For example, combining patterns of exposure with clinically-relevant outcome measures may help to elucidate our understanding of environmental sources that act as triggers for this complex disease. A personal, spatiotemporal exposure assessment using miniaturized sensors, such as handheld real-time aerosol monitors and global positioning system receivers, allows for resolving temporal and spatial data related to personal exposures at levels down to seconds and meters. GPS-derived time-location data is the best available "gold standard" to use in testing the accuracy of self-reported time-location data. GPS-derived time-location information has several advantages over diary reported time-location. First, most compliance issues are avoided, second, human recall bias is avoided, as the continuous operation eliminates the need for "best guesses", and finally, the highly-resolved continuous time-location data allow researchers to pinpoint where subjects are in relation to contaminants. In a study of child time-location, Elgethun (2007) found that concurrent parent-reported diaries based on the NHEXAS format misclassified child time-location approximately 48% of the time when compared to GPS-derived time-location data. One important limitation of location monitors, however, is that they can only define location-time; estimating a subject's location-activity (i.e., what a person is doing at a given time and in a given location) is difficult.

The goal of this work was to develop a highly-resolved, space- and time-referenced method to improve personal exposure assessment for PM health hazards.

This method apportioned personal exposures based on highly resolved measurements (10-second intervals) of personal PM levels and location. Historically, such data has been difficult to collect and interpret. However, we developed a computer-based algorithm to transform this large amount of exposure data into useable information by interpreting the temporal and spatial information together. The assessment of the raw data resulted in a location-activity classification (i.e., at home, at school, in transit) being assigned to each exposure measurement. This project had two specific aims:

Specific Aim 1: Develop and validate method to assess personal exposure to particulate matter air pollution at high resolution across both space and time (i.e., personal, spatiotemporal exposure assessment). We hypothesized that time and space referenced data could be used to classify personal exposure into at least three different microenvironments: home, school, and transit.

The approach was to create a lightweight, low-profile sampling apparatus from off-the-shelf components. We tested the individual components of the apparatus against known standards and /or existing equipment to ensure adequate performance. In addition, we developed a space- and time-based algorithm to apportion exposure data into pre-determined location-activity, or microenvironment, categories (e.g., home, work/school, transit). Each data point was assigned a specific location-activity classification (home, work/school, morning transit, afternoon transit) using geographic proximity analyses of the spatial data, supplemented by time-based rules. We assessed the accuracy of the method in a controlled pilot study. The method development and assessment of the algorithm accuracy is presented in Chapter 1

(Adams, Riggs et al. 2009) which is reproduced by permission of The Royal Society of Chemistry.

Specific Aim 2: Apply the personal, spatiotemporal sampling method to investigate the timing and locale of peak PM exposures for asthmatic children and contrast these measurements with classical sampling techniques (e.g. time-integrated personal and time-integrated area-wide samples). Evaluate potential associations between daily activities and increased exposure to $PM_{2.5}$.

We monitored personal PM exposures of thirty schoolchildren over a 5 month period during a school year. Ethical and scientific approval for the study was obtained from the National Jewish Health's Institutional Review Board. The school-based panel was composed of inner city urban, mostly poor children with physician-diagnosed asthma. Microenvironment-based (i.e. home, school, morning transit, and afternoon transit) personal PM exposures were derived using the aforementioned sampling method. The microenvironment-apportioned personal exposure data was compared and contrasted with exposure data collected by stationary, community-based monitors. The application of the personal, spatiotemporal exposure method using a panel of asthmatic children is presented in Chapter 2. This chapter is version of a manuscript entitled, "Spatiotemporal Profiles of Particulate Matter Exposure Among Asthmatic Children," that has been prepared for submission for publication.

In addition to assessing the overall PM exposures of the panel, we examined the relationship between exposure to traffic-related air pollution during morning commutes and personal markers of asthma exacerbation (urinary cysteinyl leukotriene E_4). Personal PM exposures were segregated into three categories: at home (morning),

morning commute to school, and at school. Urinary biomarkers were collected from the children during the school day. Asthma worsening following the morning commute, based on the urinary cysteinyl leukotriene E_4 levels, was evaluated relative to each personal exposure category (home, commute, school) and also to ambient PM levels measured by a fixed, community-based monitor. This study is presented in Chapter 3. This chapter is version of a manuscript entitled, "Commute-related Particulate Matter Exposure Is Associated with Acute Asthma Worsening in Children," that has been prepared for submission for publication.

CHAPTER 1

"Development of a Method for Personal, Spatiotemporal Exposure Assessment"[1]

1.1. Summary

This work describes the development and evaluation of a high resolution, space and time-referenced sampling method for personal exposure assessment to airborne particulate matter (PM). This method integrates continuous measures of personal PM levels with the corresponding location-activity (i.e. work/school, home, transit) of the subject. Monitoring equipment include a small, portable global positioning system (GPS) receiver, a miniature aerosol nephelometer, and an ambient temperature monitor to estimate the location, time, and magnitude of personal exposure to particulate matter air pollution. Precision and accuracy of each component, as well as the integrated method performance were tested in a combination of laboratory and field tests. Spatial data was apportioned into pre-determined location-activity categories (i.e. work/school, home, transit) with a simple, space- and time-based algorithm. The apportioning algorithm was extremely effective with an overall accuracy of 99.6%. This method allows examination of an individual's estimated exposure through space and time, which may provide new insights into exposure-activity relationships not possible with traditional exposure assessment techniques (i.e., time-integrated, filter-based measurements). Furthermore, the method is applicable to any contaminant or stressor that can be measured on an individual with a direct-reading sensor.

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[1]Adams, C., P. Riggs, et al. (2009). "Development of a method for personal, spatiotemporal exposure assessment." Journal Of Environmental Monitoring **11**(7): 1331-1339. - Reproduced by permission of The Royal Society of Chemistry (RSC)

1.2. Introduction

The current state-of-the-art for estimating human exposures to occupational and environmental stressors involves the use of time-integrated, personal sampling. Personal sampling refers to individual-level exposure assessment (as compared to area sampling for one or more individuals). Traditionally, such samples are time-integrated for the collection of sufficient material for subsequent quantification. In workplace atmospheres, for example, time-integrated personal sampling involves placing a miniature sampler (or sampling inlet) within the worker's breathing zone and passing a pre-determined volume of air through a filter (or other collection media) over a period of several hours. The filter is then weighed or chemically analyzed to give an indication of the individual's time-averaged exposure for the period in question. Similar techniques are used to estimate individual exposures in the home or community (Lachenmyer and Hidy 2000). Time-integrated, personal sampling provides important information regarding an individual's average exposure, albeit with some drawbacks. First, the temporal variability in exposure throughout the sampling period is unknown (sampling periods typically span several hours). As a result, acute exposure events (i.e., concentration peaks), are often attenuated by corresponding periods of low exposure. The collection of short-term samples, which usually average about 15 minutes each, can be used to identify acute exposure trends. However, the repeated collection of short, consecutive samples is particularly labor and resource intensive. A second drawback is that the spatial variability of exposure is unknown, so that particular activities or locations cannot be directly ascribed to high exposure events. Third, the

results from laboratory analyses of collected samples may not be available for days to weeks.

These shortcomings hinder our ability to recognize and control potentially hazardous exposures, which is distressing in light of a growing body of evidence that associates acute exposures with adverse health effects (Salvi, Blomberg et al. 1999; Michaels and Kleinman 2000; Delfino and McLaren 2002; Oudyk, Hatnes et al. 2003; Henneberger, Olin et al. 2005; Kanwal, Kullman et al. 2006). Knowing when and where exposures occur is crucial for understanding the causality of exposure-related disease. The space and time resolution of exposure can also inform the design of effective intervention and control techniques. Consequently, there is a need for alternative, more informative, exposure assessment methodologies.

Several alternatives to traditional, time-integrated personal sampling have been proposed or attempted. Personal activity logs identify factors that may contribute to the integrated exposure metric (Lachenmyer and Hidy 2000). Activity logs specify the time and location of an individual when (pre-determined) activities occur. The logs are recorded by hand or voice and detail events such as leaving, or arriving, at home or work (Quintana, Valenzia et al. 2001; Williams, Suggs et al. 2003). However, these logs do not identify the time, location, or magnitude of exposure and are often affected by reporting bias (Elgethun, Yost et al. 2007).

To address the temporal facets of exposure, methods for direct-reading data collection were developed (Cohen 2001). Historically, direct-reading sampling methods have been both labor intensive and cost-prohibitive. Recently, however, the development of inexpensive, miniaturized personal monitors capable of collecting data

at second-to-minute resolution has afforded direct-reading methods wider use. The increased resolution of direct-reading instruments allows for the identification of short-term or peak exposures (Chakrabarti, Fine et al. 2004). However, without additional spatially-referenced information, the location and the activity associated with exposure remains undefined.

Combining direct-reading exposure assessment with personal, direct-reading location assessment may help identify activity patterns at the time of exposure, whether at home, work, or during transit between locations. This is important, as contaminant sources, strengths, and exposures can vary throughout the day as individuals move through different microenvironments. Understanding travel patterns may also be beneficial as recent research suggests there are increased health effects from exposure to traffic-generated pollution (Janssen, Brunekreef et al. 2003; McCreanor, Cullinan et al. 2007; Roosbroeck 2008). Integrating stationary ambient sampling information with the location of the subject may also assist in improving intervention and control of disease (Hsueh-Ting, Chir-Chang et al. 2006). Accurate assessment of instantaneous peak personal exposure would allow researchers to investigate associations between personal microenvironmental exposures and ambient, community-wide exposures.

To this end we have developed a highly-resolved, space and time-referenced sampling method for personal exposure assessment. Data collected with this method is transformed with a space- and time-based algorithm to apportion the exposure data into pre-determined location-activity profiles (described below). Although we present this method in the context of particulate matter air pollution, it can be adapted to any contaminant or stressor that may be monitored using miniature, direct-reading sensors.

1.3. Methods

The space- and time-based personal sampling method employs an aerosol nephelometer to measure fine particulate matter (PM) concentrations, a global positioning system (GPS) receiver to record geographic position data, and a thermocouple sensor to record the ambient temperature. These monitors are housed in a small backpack with a total weight of approximately 3.2 kg (7 lbs); each monitor is programmed to record data at 10 second intervals. We evaluated aspects of accuracy and precision for each instrument separately. We then conducted controlled field tests, where we evaluated the ability of the method to differentiate PM exposure as a function of activity (i.e., location and time).

The personal DataRAM 1200, or pDR, (Thermo Fisher Scientific Inc., Waltham, MA) is a light-scattering, direct-reading nephelometer that measures aerosol mass concentration. The pDR was programmed to collect an integrated sample every 10 seconds. The pDR was operated in conjunction with a pump (6.8 L/min flow, Omni Personal Pump, BGI Inc., Waltham MA) and cyclone (1.6 μm cut point, Model GK2.05, BGI Inc., Waltham MA) so that fine particulate matter was actively sampled and subsequently collected on a downstream filter (Teflo 37mm, Pall Inc. East Hills, NY). The 1.6 μm cut point resulted from a volumetric flowrate that was required to meet the gravimetric limit of detection for the downstream filter. The available equipment was configured to allow the best approximation of the fine particulate aerosol fraction. Other sampling train configurations would allow for a different cut point. The pDR inlet was positioned 2 inches above the top surface of the backpack, slightly to the rear of the wearer's left shoulder (Fig 1). The projected use of the backpack sampler constrained

the placement of the sampling train as minimal protrusion of equipment outside the physical boundaries of the backpack was required. Therefore the inlet location was chosen to best approximate the breathing zone, defined as the envelope around the head which is considered to have the same concentration of pollutant as the air breathed in by the person. The pDR has been used extensively in assessing personal exposure to PM (Reed 2000; Quintana, Valenzia et al. 2001; Fischer 2007) and can provide an estimate of aerosol mass concentration over very short time periods. Chakrabarti (Chakrabarti, Fine et al. 2004) found the pDR to be precise and in good agreement with other continuous monitors. However, the pDR has two major limitations. First, instrument response (i.e., the degree of scattered light) is positively biased when relative humidity exceeds 60% (Chakrabarti, Fine et al. 2004; Wu, Delfino et al. 2005). Second, the instrument response varies depending on the size, shape, and composition of sampled aerosol (Chakrabarti, Fine et al. 2004). To compensate for these biases, a filter sampler is used to normalize the direct-reading nephelometer measurements (Kim 2004; Benton-Vitz and Volckens 2008) during data processing. The filter was located immediately downstream of the sensing zone and was analyzed by standard gravimetric or chemical analysis. Because the accuracy and precision of the pDR (and similar devices) have been studied extensively, we did not conduct additional laboratory evaluation of this device. However, following the guidelines of Chakrabarti and Benton-Vitz, we operated the instrument in low-humidity environments and used a filter sampler to normalize the direct-reading measurements.

A consumer-grade GPS receiver (GPSMap 60Cx, Garmin Inc. Olathe KS) located inside the backpack and connected to an external, low-profile antenna (GA25

MCX, Garmin Inc. Olathe KS) recorded latitude and longitude every 10 seconds. The receiver included a high-sensitivity GPS microcontroller (SirfStar III, SiRF Technology, San Jose, CA) and was operated using the wide area augmentation system (WAAS), a form of differential GPS (DGPS) giving enhanced position accuracy. WAAS was developed primarily for aeronautical navigation but is available to other users (Bolstad, Jenks et al. 2005).

Positioning capability of the GPS units were evaluated both indoors and outdoors against reference standards, such as, geographic benchmarks (Floyd 1978). On three different days, four GPS receivers with antennae were placed upon the benchmark and positioning accuracy was recorded during morning and afternoon periods. Unit accuracy and precision was determined by comparing measured longitude and latitude positions with the National Geodetic Survey benchmark location. The average 2DRMS (twice distance root mean square) was calculated for each unit. The 2DRMS represents the 98th percentile for error between the monitor-reported position and known benchmark position.

Estimating the accuracy of the GPS receivers when indoors was less straightforward, as geographic benchmarks are only located outdoors. Therefore, we generated six indoor reference positions, three within a single-story, wood-framed, residence and three within a concrete masonry, single-story converted warehouse. These positions were established with data from a high-resolution, survey-grade GPS receiver (Geo XT, Trimble, Sunnyvale, CA) located on the roof of the structure. The positions within the residence were located in the living room, dining room, and bedroom. The offset distances and directions from the indoor reference positions were

accounted for by the GPS receiver and the reference position data was differentially corrected during post-processing to produce indoor reference positions with a horizontal accuracy within 50 cm.

Three locations were evaluated within the converted warehouse, including a glass-walled lobby, an office (with exterior windows), and an interior office (no windows). Indoor reference positions in the workplace were established as described above.

A miniature ambient temperature monitor (Thermo Record TR-52, T and D Inc., Saratoga Springs, NY) was used to determine whether the subject is indoors or outdoors by comparing recorded temperatures with known ambient conditions. In Colorado, average wintertime highs rarely exceed 15 °C (NOAA-NWS 2008). The reported accuracy of this unit is ±0.3°C with a thermal time constant of 15 sec. The thermal time constant is the time required for the monitor to register 63.2% of temperature differential following a sudden temperature change. Monitor accuracy was tested in the laboratory by comparison to a NIST-traceable reference standard across a range of temperatures (0-25°C). Additionally, we measured the dynamic thermal response of the monitors by moving the sampling apparatus between indoor and outdoor environments (~ 11°C span). The dynamic response is defined as the amount of change recorded by the thermistor within a certain time. A faster dynamic response reduces the likelihood of misclassification between indoor and outdoor environments.

After sampling, data from the pDR, GPS receiver, and temperature monitor were collated into a database by matching the associated timestamps from each instrument,

thereby integrating the data into a common array. The collated data is then available for post-processing and analysis.

We developed a simple temporal spatial algorithm to apportion exposure data into pre-determined location-activity categories (e.g., home, work, transit). Each data point is assigned a specific location-activity category (home, work/school, morning transit, afternoon transit) using geographic proximity analyses supported by time-based rules. The geographic proximity analysis determines if a recorded point lies within a predefined, two-dimensional area (i.e., a home boundary). The time-based rules further support the proximity analysis by establishing expected times for the individual to be in the home or work/school area. For example, if the recorded position of a sample is within a certain radius of the work/school position (e.g., 50 m) during expected work/school hours then the exposure is assigned to the work/school category. Similarly, the home category is assigned if the recorded position of the sample is within the defined home area during expected home hours. If the recorded position of the sample is neither at home or work/school, the sample is considered in-transit. To further categorize transit as morning or afternoon, the timestamp of the recorded location is evaluated. For each day, a timestamp before noon is considered morning transit, and a timestamp after noon is considered afternoon transit. More complicated location-activity schemes are easily derived, however, we chose to develop the method initially with a simple home/transit/work-school paradigm.

When a recorded sample interval lacked positional data (i.e., loss of satellite signal to the GPS), a time-based rule was applied. If the sample was recorded during one of the expected home or work/school time periods, the home or work position was

assigned to the sampling interval. The sample would then be apportioned to work/school. If the sample interval occurred outside the expected home or work/school time periods it was assigned the location-activity code as in the preceding sample.

Finally, an indoor or outdoor status is assigned to the sample. The status is only assigned when the recorded sample has been categorized as work/school or home. As the method is designed specifically for use during winter months, the sample is assigned an indoor status when the ambient temperature at the time of the aerosol sample is above 15.55°C (60°F). Otherwise, the status is assigned as outdoor.

We conducted an integrated field test to evaluate the effectiveness of the method for collecting and apportioning exposures during a normal workday. For this exercise, the sampling apparatus was worn by an individual for four workdays while an independent log of location-activities was recorded. The individual varied departure and arrival times and routes of transit to and from work. For evaluating the field data the expected time to be at the work/school location was from 9 AM to 3 PM and the expected time to be at the home location was from 8 PM to 6AM.

To prepare the sampling apparatus the following steps were performed: 1) A pre-weighed filter was placed downstream of the pDR sensor chamber, 2) Pump flowrate was calibrated, 3) A GPS receiver was allowed to acquire signal lock on at least four satellites, 4) The internal clocks of the pDR and TR-52 were synchronized to the clock of the GPS Receiver, 5) The data-logging memory of each monitor was reset, 6) The monitoring equipment and pump were secured to a custom frame (Figure 1.1), 7) Sampling hoses were connected and sampling equipment was placed in backpack, 8)

Monitors were activated (i.e., data-logging was initiated) and the sampling pump was turned on.

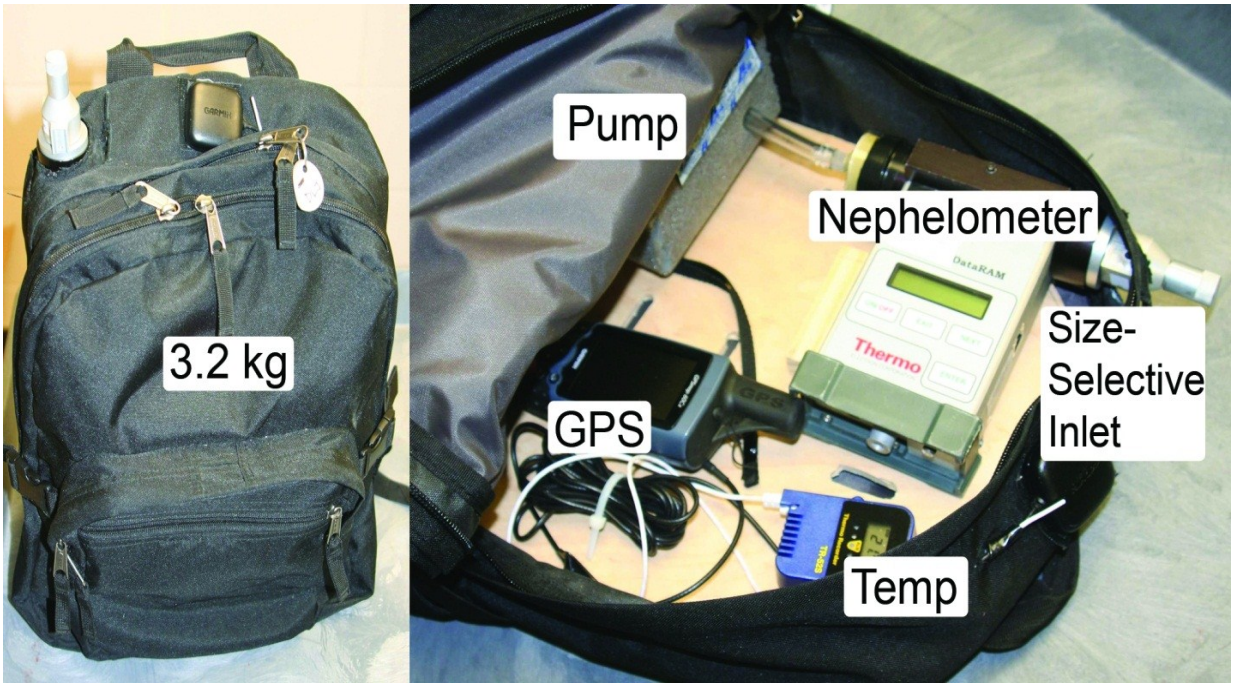

Figure 1.1. Apparatus for spatiotemporally-referenced sampling

During the integrated field testing the sampling apparatus was worn by the test subject over both shoulders like a normal backpack. A NIST-traceable timepiece was used to log ingress/egress of the residence, the workplace, and transportation vehicles to the nearest second. When the test subject was sitting or lying the backpack was placed upright on the floor nearby. Following the sampling period the pump flowrate was verified and the filter was removed for gravimetric analysis. The logged data from the monitors were downloaded to a personal computer.

We investigated two methods of defining the work/school or home boundaries. One method defines the home or work/school area by the physical footprint of the structure, taken from geo-referenced satellite imagery. The other method defines the

home or work/school area with a circular buffer region. In this case, the buffer denotes the area within a radial distance from the center of a defined point of interest (i.e., a home).

The accuracy of the apportionment algorithm was assessed by comparing the algorithm classification of the collected exposure data with the independent log of the location-activity categories recorded during the field test. The overall percent accuracy was calculated using the total number of samples that were correctly classified vs. the total number of recorded samples.

1.4. Results

1.4.a. GPS Positioning

The GPS receiver provided greater positional accuracy when outdoors versus indoors, as expected (Table 1.1). The 2DRMS distances for the four units when tested outdoors ranged from 3.1- 4.6 m (average, μ, was 3.8 m, standard deviation, σ, was 0.6). This accuracy was much greater than the manufacturer stated accuracy of the unit (<15 meters 95% of time). No signal losses were detected outdoors.

During the outdoor benchmark testing periods, the positional precision of the individual GPS receivers ranged from a 2DRMS distance of 0.65m to 6.6m (Table 1.2). Neither the GPS Receiver ($p>0.4$) nor the testing day ($p>0.7$) was a significant factor in determining the 2DRMS values. The average 2DRMS and standard deviation of the individual receivers from low to high were 2.1±1.2 m, 2.3±0.9 m, 3.5±0.8 m, and 4.0±1.8 m.

Table 1.1. GPS position accuracy (outdoors, in-residence and in-workplace)

Positioning Location	GPS Receiver $2D_{RMS}$(m)†			
	Min.	Max.	Avg.	Std. Dev.
Outdoor Benchmark	3.1	4.6	3.8	0.6
Home: Living Room	3.9	13.0	7.4	3.9
Home: Dining Room	6.3	12.9	8.4	3.0
Home: Bedroom	6.3	12.9	8.4	3.0
Work: Lobby	29.0	33.7	32.4	2.6
Work: Window Office	26.8	43.0	33.3	7.3

† $2D_{RMS}$ represents the 98^{th} percentile for error between the monitor-reported position and known benchmark position

When placed inside a typical wood-framed, single-story, residential structure the average 2DRMS of the GPS receiver increased by a factor of two. The range of the 2DRMS distances for the four units tested in the living room was 3.9 - 13 m (μ = 7.4 m, σ = 3.9), in the other two rooms the range was 6.3 - 12.9 m (μ = 8.4 m, σ = 3.0). The GPS receiver accuracy indoors was also greater than the manufacturer stated accuracy of the unit (<15 meters 95% of time). No signal losses were detected indoors.

In the concrete masonry building the average 2DRMS of the GPS receiver increased over the outside results by nearly a factor of 9 to approximately 33 m when in an office or lobby with exterior windows. In rooms with exterior windows the units recorded a position during more than 99.9% of the sampling intervals. When placed in an interior, windowless room the GPS receiver was not able to maintain signal reception and recorded a position during less than 1% of the sampling intervals. However, the

receiver regained the satellite signal nearly instantaneously and began recording positions when moved to a room with exterior windows or outdoors.

Table 1.2. GPS position accuracy (GPS receiver units over multiple periods)

	2DRMS(m) by Period				
Unit	1	2	3	Avg	Std Dev
1	3.52	4.44	2.43	3.47	0.82
2	2.15	3.52	0.65	2.11	1.17
3	2.60	2.83	6.60	4.01	1.83
4	1.52	3.46	1.87	2.29	0.85

1.4.b. Temperature Monitors

The ambient temperature monitors were tested for accuracy across a range of temperatures (0°C - 25°C). Over that range the temperature monitors were never greater than ±1°C from the reference standard. The Pearson's correlation coefficient (r2) between the reference standard and each of the temperature monitors over the same range was greater than 0.99. The dynamic thermal response of the sampling apparatus when moved from an indoor (~21°C) environment to an outdoor (~10°C) environment is shown at Figure 1.2. An exponential curve was fit to the data, T = 10.34e-0.059t, where T = temperature (°C) and t = time (sec). This model results in a thermal time constant of 16.9 seconds. Following this model, 44.6% of the temperature span between the two environments was recorded within 10 seconds of changing environments. Similarly, 69.3% of the change has been recorded within 20 seconds,

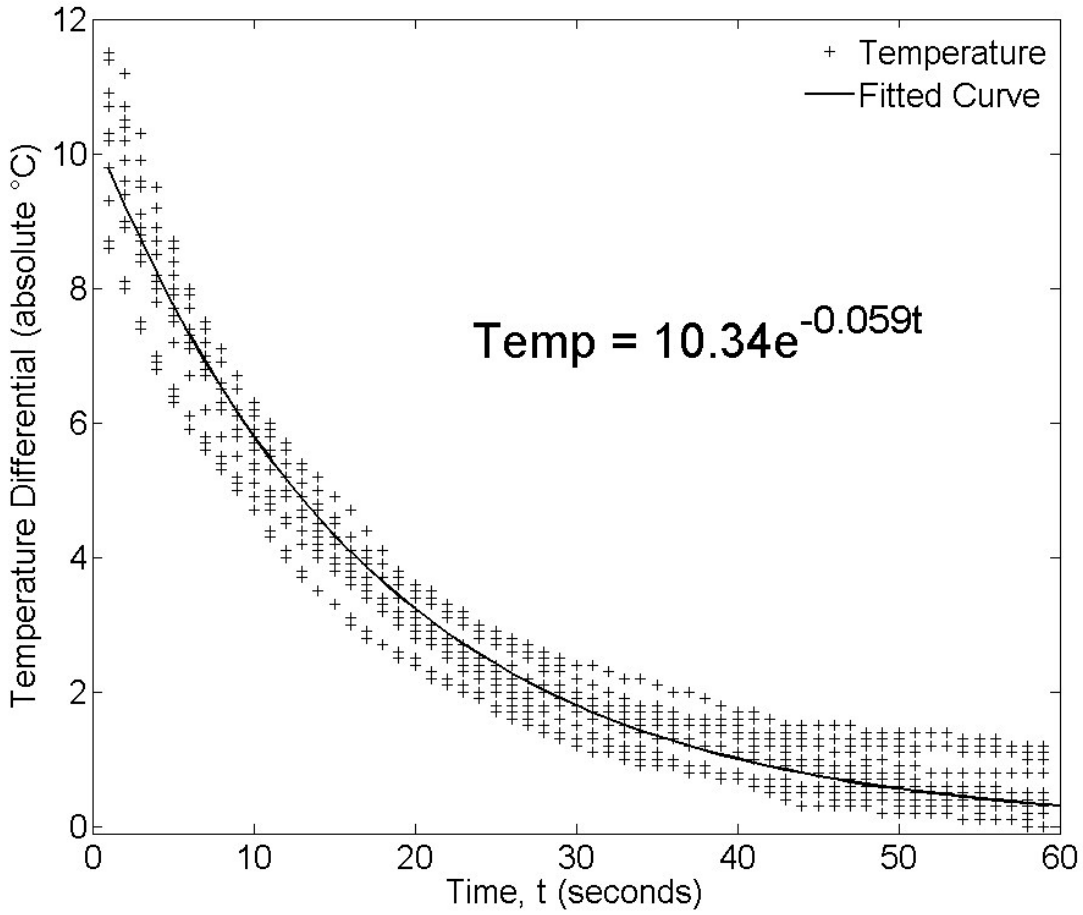

Figure 1.2. Thermal dynamic response of ambient temperature monitors

and 83.0% has been recorded within 30 seconds. The dynamic thermal response of the monitor was slightly faster when moving from an outdoor environment to an indoor environment.

1.4.c. Apportionment Algorithm

A geo-referenced aerial photograph of the residential structure used during the integrated field tests is shown at the upper left of Figure 1.3. At the upper right of Figure 1.3, the positions recorded while inside the residential structure are overlaid upon the physical footprint of the building. At the lower left of Figure 1.3, the results of a geospatial intersect operation between the recorded positions and the physical footprint

of the structure is displayed. Only 64.4% of the recorded positions are within the physical boundary of the structure. Using the physical footprint of the residence to define the home location resulted in 35.6% of the recorded position being misclassified as transit (shown in red). Therefore, we created 'buffer areas' to define the home and work locations that extended slightly beyond the physical boundaries of each building. At the lower right of Figure 1.3, circular buffers centered on the structure with radii of 20 m and 30 m are displayed. An intersection operation between the recorded positions and the 20 m radius buffer area captured 98% of the points. Using a circular buffer with a 30 m radius captured over 99.9% of the recorded positions, substantially reducing the amount of misclassification due to scattered GPS signals.

The accuracy assessment of the location-activity category classifications is shown at Table 1.3. The accuracy of the classification algorithm was determined by comparing the algorithm classifications with the user-defined classifications. The accuracy is a measure of the proportion of logged space- and time-referenced samples correctly assigned by the algorithm. The accuracy of the classification into the individual location-activity categories ranged from 93.9% to 99.9%.

For the home location-activity, 99.9% of the samples were classified correctly. There were 7 (0.03%) of the 21271 recorded samples misclassified as afternoon transit. This was due to scattering of the GPS-recorded signal, which resulted in a measured position outside the area delineating the home location.

For the work/school location-activity, 98.5% of the samples were classified correctly. There were 57 (1.47%) of the 3865 recorded samples misclassified as morning or afternoon transit. Once again this misclassification was due to signal scatter

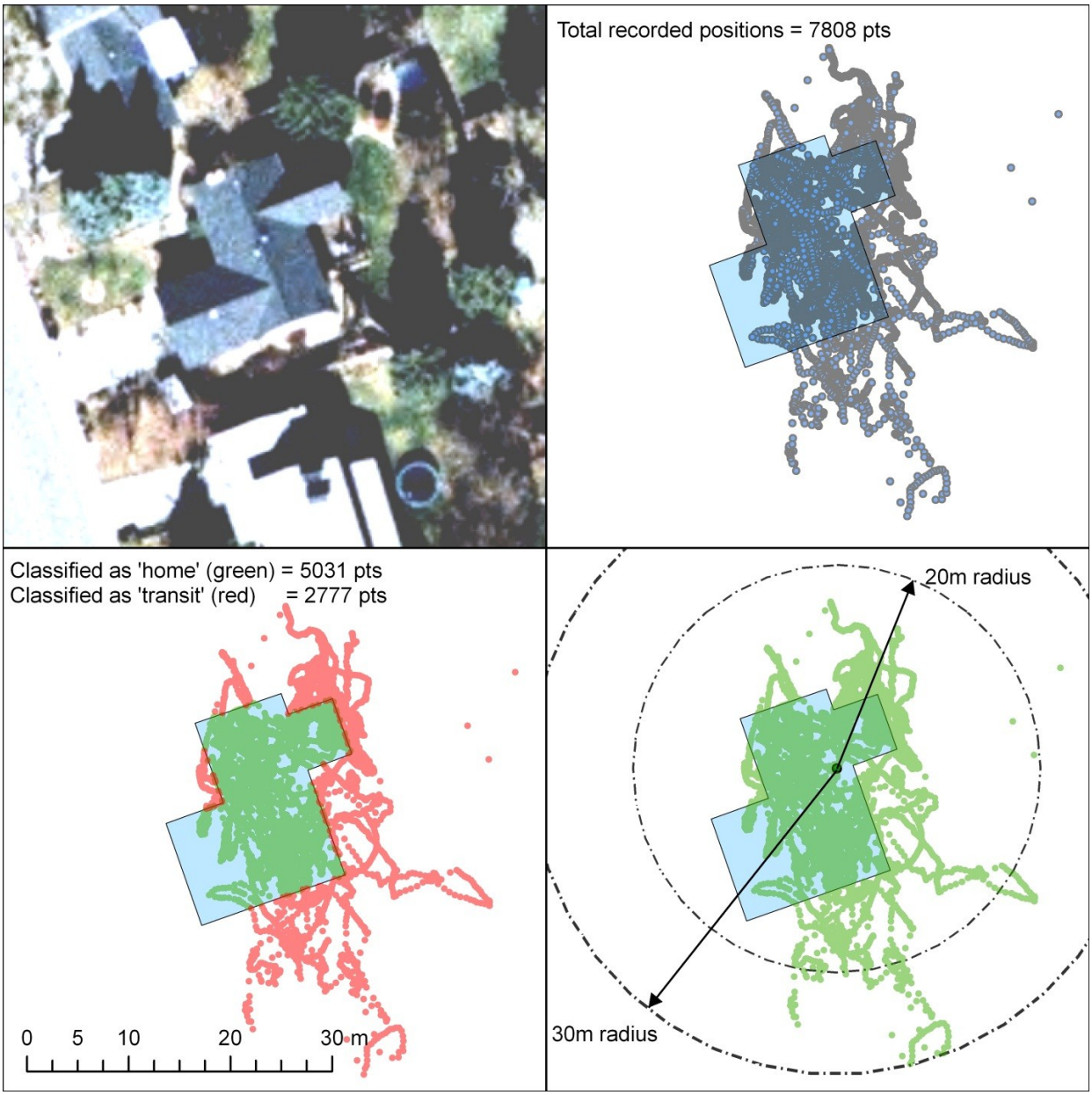

Figure 1.3. Location-activity classification using different geographical proximity analyses. Each circle represents a coordinate location recorded by the GPS receiver when sampling inside the residence. The green circles in the lower left indicate recorded positions encompassed by the physical footprint of the structure and classified as the Home location-activity. Using a circular buffer (lower right) substantially increases the proportion of samples correctly classified.

Table 1.3. Assessment table for the spatiotemporally-based algorithm classifications

		True Classification of Sample				
		Home	School	AM Transit	PM Transit	Num of Classified Samples
Algorithm Classification of Sample	Home	21264		37	28	21329
	School		3808	9	17	3834
	AM Transit		15	654		669
	PM Transit	7	42		1196	1245
	Number of Recorded Samples	21271	3865	700	1241	27077
	Accuracy (%)	99.9	98.5	93.4	96.3	

outside the buffer area around the workplace. The combination of the concrete/brick construction and small windows of the workplace resulted in a larger amount of scatter than at the home, however, the proportion of misclassification was considered acceptable. Enlarging the buffer would capture more of the recorded locations, however this would impinge on the classification of morning and afternoon transit. Amending the algorithm to reduce the number of these misclassifications would have eliminated the ability to capture transit periods away from the workplace between the hours of 9 AM and 3 PM.

For the morning transit location-activity, 93.4% of the samples were classified correctly. There were 46 (6.57%) of the 700 recorded samples misclassified as home

or work/school. As before, this misclassification was due to the size of the buffer area around the physical locations of the home and workplace. The subject independently recorded ingress and egress times when crossing the threshold of the structure's doorway, as this threshold was considered more intuitive and easier to identify than an invisible boundary line (i.e., the buffer zone). However, this choice did introduce error into the classification of the morning and afternoon transit activities. This percentage of misclassification was greater than with the home or work/school misclassification due to a smaller amount of time spent in transit. The misclassification of morning transit to the home or work/school amounted to less than 2 minutes per day.

For the afternoon transit location-activity, 96.3% of the samples were classified correctly. There were 45 (3.6%) of 1241 recorded samples misclassified as home or work/school. The misclassification of afternoon transit was due to the same causes as the misclassification of morning transit. The number of misclassifications of this location-activity was similar to the morning transit location-activity, however the percentage was lower because of an increased amount of time in the afternoon transit category.

Overall, the algorithm was 99.6% accurate at classifying location-activities. Over the 75.2 hours of sampling, approximately 74.9 hours were classified correctly and approximately 26 minutes were misclassified. This misclassification amounted to less than 7 min per day. The majority of that daily misclassification, about 4.5 min, was due to the misclassification of transit activity samples as home or work/school when the samples were recorded within the buffer areas of the home and workplace. The

remainder of the time, just over 2 min was due to the scattering of the GPS-recorded positions when at home or work/school.

When the indoor/outdoor ambient temperature monitor data were assessed with the apportionment algorithm, the algorithm classification of indoor/outdoor changed in less than 8 seconds. The response of the ambient temperature monitors can be seen in Figure 1.4. In the Figure each circle represents a 10-second interval measurement of the ambient temperature at the subject's location. The change in temperature recorded at each sampling location while the sampler was moved from indoors to outdoors is represented with color scaling (red = warmer, blue = colder). Points 1 and 2 were indoors, the others outdoors. Recorded temperatures below 15.55°C were classified as outdoors. In this example only one sampling interval was misclassified as indoors.

The accuracy assessments for the classification of indoor vs. outdoor status while within the home buffer area and the school buffer area are shown at Table 1.4 and Table 1.5. The accuracy of the indoor/outdoor classification algorithm was determined by comparing the algorithm classifications of samples with the independently-logged classifications of samples. As before, the accuracy is a measure of how many of the logged indoor/outdoor locations were correctly classified by the algorithm. The accuracy of the individual apportionment categories ranged from 65.4% to 99.9%.

While the subject was within the home area buffer, 99.9% of the indoor samples were correctly classified. There were 21 (0.01%) of the 21225 recorded indoor samples misclassified as outdoor. This misclassification was due to the dynamic thermal response of the ambient temperature monitor. Additionally, 65.4% of the outdoor samples were correctly classified. There were 36 (34.6%) of the 104 outdoor samples

misclassified as indoors. This was due mostly to driving into the home buffer area in a warm vehicle during the afternoon transit.

While the subject was within the work/school area buffer, 99.8% of the outdoor samples were correctly classified. There were 6 (0.16%) of the 3808 recorded samples

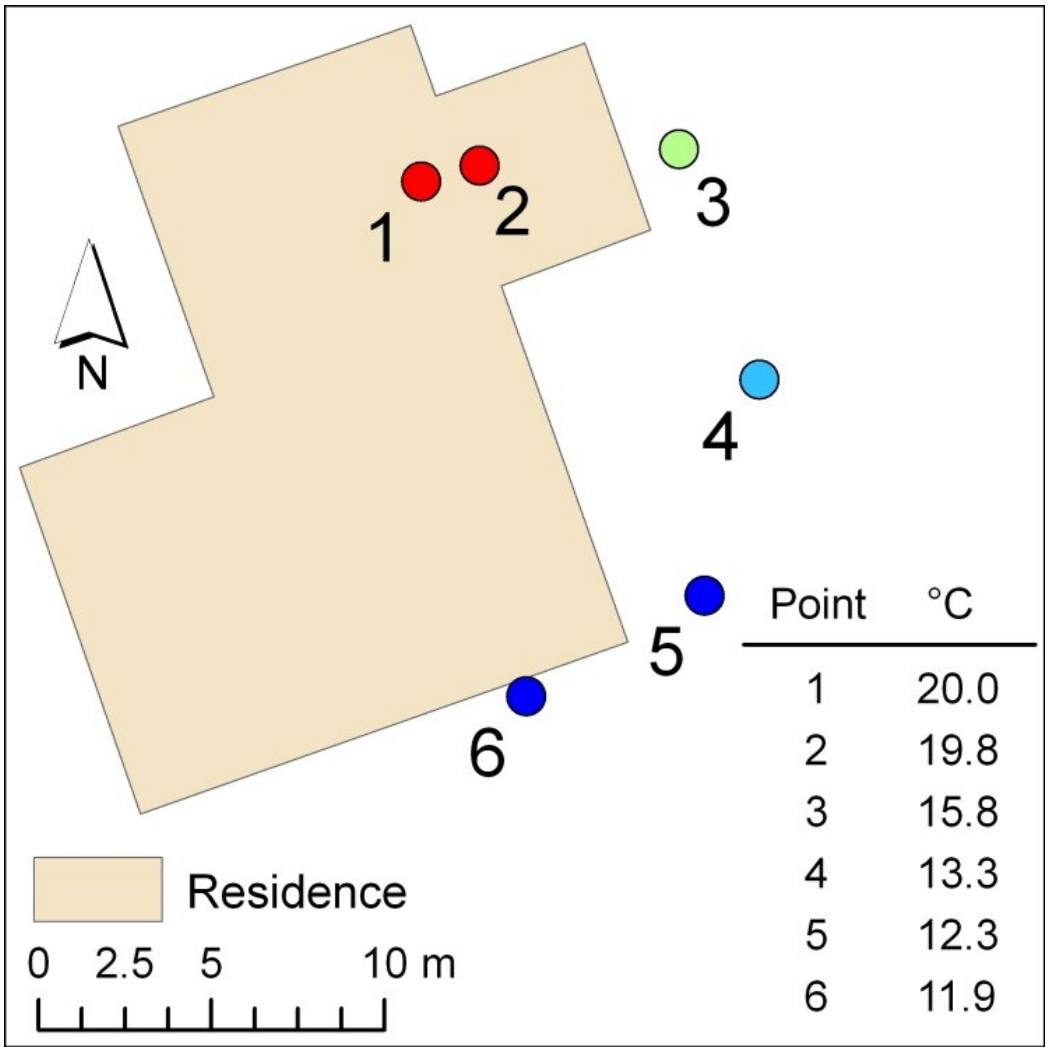

Figure 1.4. Ambient temperature monitoring analysis. Each circle represents a 10-second interval measurement of the ambient temperature at the subject's location. Circle color indicates the relative temperature at the location. Points 1 and 2 were indoors, the others outdoors. Temperatures below 15.55°C were classified as outdoors. In this example only one sampling interval, #3, was misclassified as indoors.

Table 1.4. Temperature-based classification algorithm accuracy assessment table (home location-activity category)

		True Classification of Sample		
		Indoor	Outdoor	Num of Classified Samples
Algorithm Classification of Sample	Indoor	21204	36	21225
	Outdoor	21	68	104
	Number of Recorded Samples	21225	104	21329
	Accuracy (%)	99.9	65.4	

misclassified as outdoor. Once again this misclassification was due to the dynamic thermal response of the ambient temperature monitor. Additionally, 84.6% of the outdoor samples were correctly classified. There were 4 (15%) of the 26 outdoor samples misclassified as indoors. This was also due to the dynamic thermal response of the ambient temperature monitor.

Overall, the accuracy of the indoor/outdoor classification portion of the algorithm was 99.7% accurate. The algorithm was 99.7% accurate at the home and school locations. The classification results from the simple 60° F were surprisingly good.

Table 1.5. Temperature-based classification algorithm accuracy assessment table (work/school location-activity category)

		True Classification of Sample		
		Indoor	Outdoor	Num of Classified Samples
Algorithm Classification of Sample	Indoor	3802	4	3806
	Outdoor	6	22	28
	Number of Recorded Samples	3808	26	3834
	Accuracy (%)	99.8	84.6	

However, a more complex algorithm that classified samples relative to the outdoor temperature could improve the accuracy by reducing the effect of the monitor's thermal dynamic response.

A 24-hour portion of the integrated field test data is represented with an emphasis on spatial characteristics in Figure 1.5. Here, location-activity categories are differentiated by color (green = home, blue = school, orange = morning transit, purple = afternoon transit) while relative personal PM exposure levels are represented by the size of each data point (larger circles represent higher concentrations). With this representation, the viewer may appreciate the subject's movements throughout the day

while still gaining a sense of the timing and magnitude of measured personal PM levels. In Figure 1.5, the viewer can see that during the morning commute, measured personal PM levels while traveling on major roadways (8:19AM and 8:25 AM) were relatively larger than measured personal PM levels while traveling on side streets (8:15 AM).

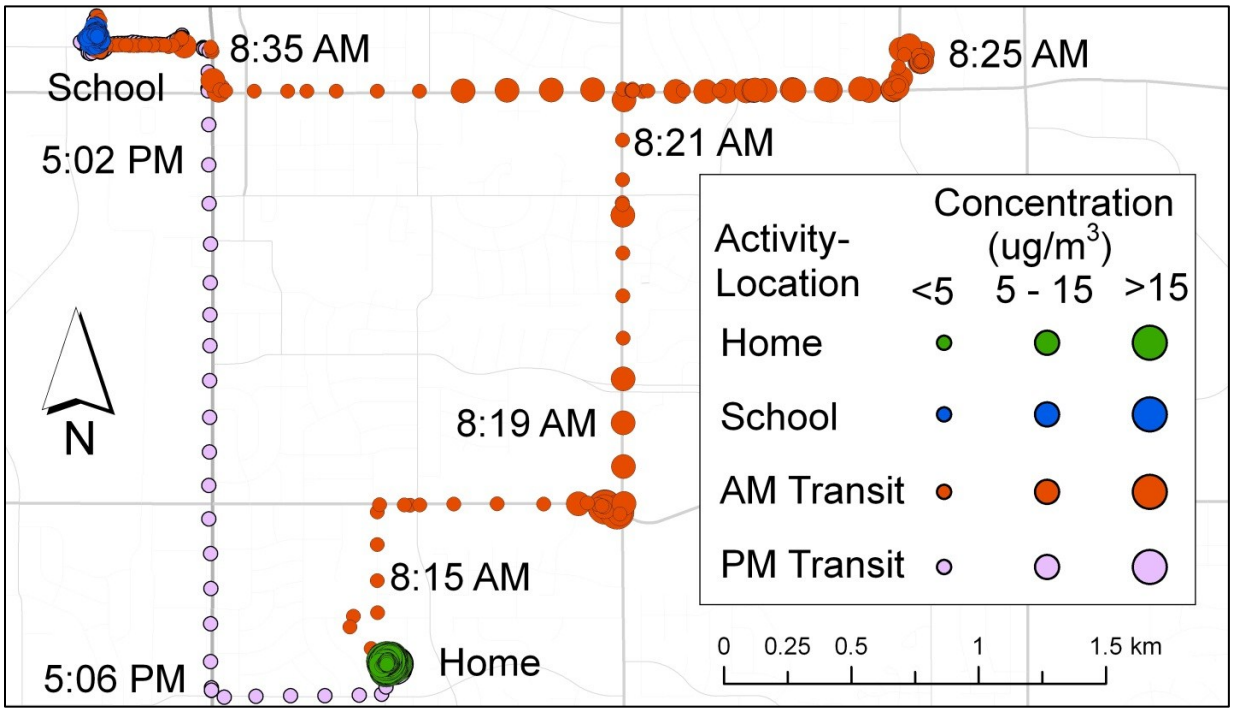

Figure 1.5. Street-map overlay for personal PM levels. Each circle represents a 10-second average exposure of at the subject's location throughout a single day. Circle color indicates the location-activity of exposure and circle size indicates the relative *magnitude* of measured PM_{Fine} levels.

The advantage of associating time-activity data with exposure monitoring is further depicted in Figure 1.6, with an emphasis on temporal effects. Here, the algorithm- derived location-activity categories are represented by coloring of the recorded personal PM level. In Figure 1.6 the viewer can appreciate the temporal attributes of the exposure assessment. At home, PM concentrations increase after 7:30 AM as the subject prepares for work/school and food is prepared. During the morning transit period (8:15 AM – 8:40 AM) the PM levels are relatively less than at home.

However, one large peak during the morning commute is evident and coincides with the crossing of a major traffic intersection. This phenomenon is annotated in Figure 1.5 at 8:19 am.

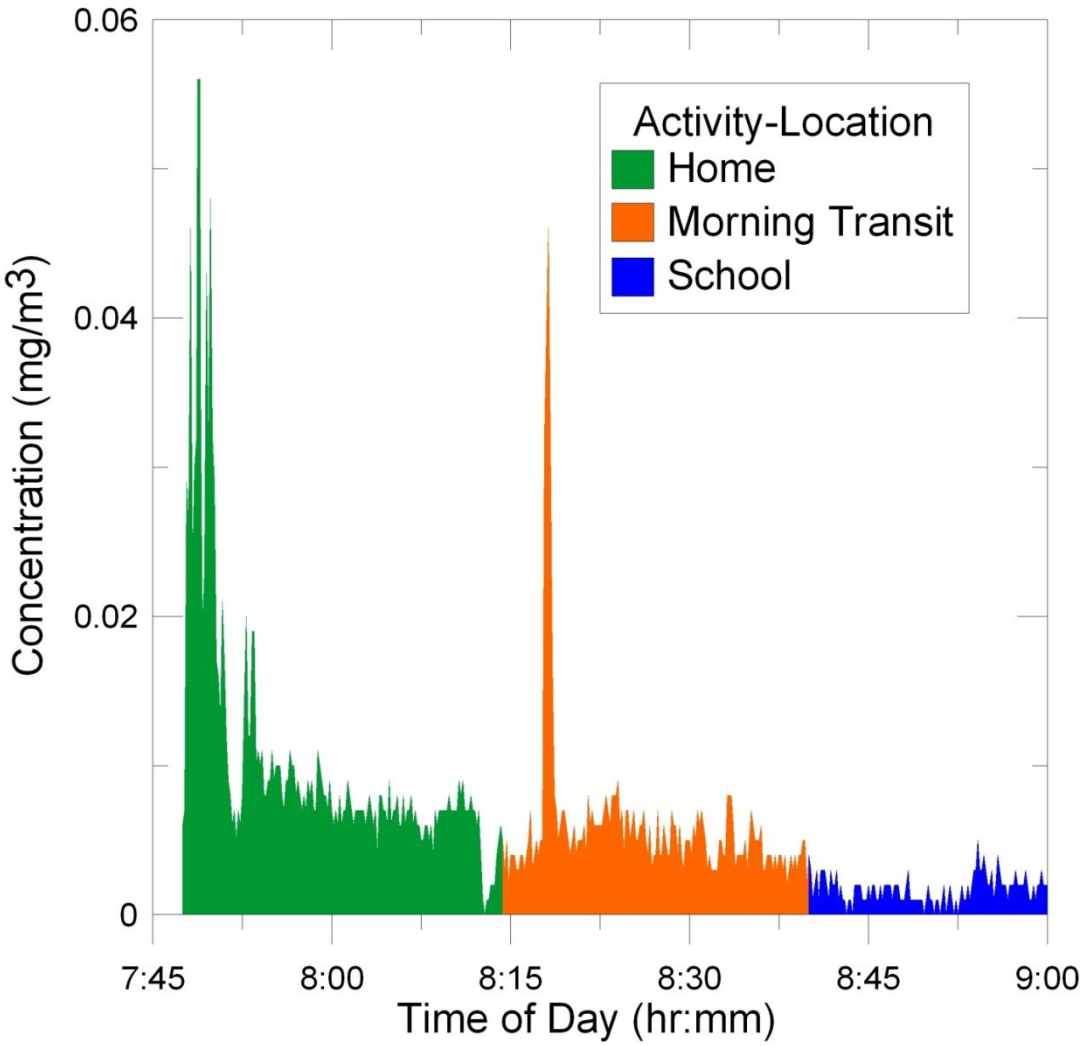

Figure 1.6. Time-series of a subject's personal PM levels apportioned into location-activity categories. Data is color-coded based on output from the spatiotemporally-based algorithm.

1.5. Discussion

The GPS receivers were more accurate than expected. The outdoor capability was more than adequate; inside residential structures, the receivers performed surprising well. This performance was most likely due to the use of a high-sensitivity

GPS microcontroller in the GPS receiver. Even with a high-sensitivity GPS receiver, indoor positioning accuracy will likely vary based on the construction materials (e.g., brick, metal) or on the construction design (e.g., multiple stories, apartment buildings). The performance of the units in the workplace was also better than expected. There was a larger amount of scatter, however, the units recorded a position whenever within an area with an exterior window. Although positions were not recorded when the sampler was in an interior room of a concrete building, the receiver regained the satellite signal nearly instantaneously when moved to a room with exterior windows or to the outdoors, as evinced by the data in Tables 1.4 and 1.5.

Newer handheld, consumer-grade GPS receivers have greatly improved the ability to receive satellite signals when indoors. This improved capability is most likely due to the higher sensitivity GPS controllers that have recently been introduced into these product lines. However, additional sensitivity for these instruments may not be available in the near term. Therefore, alternatives may be needed to improve to the positioning portion of the method when a subject is inside a building. This is especially important in industrial settings where large exposure gradients can occur over a small distance. A GPS signal repeater could be used inside larger indoor spaces to mimic satellite signals. Another technology that may prove useful is radiofrequency-identification (RFID). RFID readers used in conjunction with RFID tags could provide a means to track the subject's movement where GPS signal reception is difficult.

The temperature monitors appeared to be very sensitive to changes in the ambient temperature. Our results indicated that they were slightly less accurate than the manufacturer's claim. However, the accuracy was adequate for our sampling

method. The dynamic thermal response of the monitor when used in the sampling apparatus was also adequate. In practice, the results from the monitor allowed correct classification of the indoor/outdoor status within a 10 second interval.

Using temperature as an indicator of the indoor/outdoor status of the sampler will likely work best when there is a large temperature gradient between the indoor and outdoor environments. However, this technique would be limited in more temperate climates. Alternative, or additional, indicators of indoor/outdoor status include ambient light (Quintana, Valenzia et al. 2001) or logging the strength of the satellite signals received by the GPS receiver.

Most personal sampling methods, including this one, cannot ensure that the subject is wearing the sampler at all times. Adding a lightweight accelerometer to log movement of the sampler would assist in confirming that subjects were wearing the sampler during non-sleeping periods.

When assessing which geographic proximity analysis method to use to determine if a recorded location was classified as home or work/school, a geographic intersection operation between the recorded points and the physical footprint of the structure was considered inadequate to support the apportionment classification algorithm. Therefore, the classification algorithm used a geographic proximity analysis with a buffer region (circular area centered on the structure) to capture a greater portion of the recorded positions. The required size of the buffer varied based on the construction characteristics of the structures involved. Determination of an adequate buffer radius was obtained by visually evaluating the recorded positions in a GIS software program. This allowed an optimum size buffer for each structure as using one

larger sized buffer for all structures would capture more of the recorded locations, however this would also impinge on the classification of morning and afternoon transit.

The classification error inherent in using a geographical buffer larger than the physical footprint of the building could be reduced with additional, more complex signal analysis of the ambient temperature. The analysis of temperature changes near the time of transition between stationary locations (work, school, or home) and commuting period could be used to “fine tune” the algorithm and reduce the amount of misclassification at the beginning and end of transit periods caused by the proximity analyses with geographical buffers.

1.6. Conclusion

The resultant location/activity-exposure database provides a powerful means to assess personal exposure through multiple methods of analysis and visualization. The spatial and temporal aspects of the exposure can be represented in complementary figures. Figures 1.5 and 1.6 allow one to view the *when* and *where* of exposure with a high degree of spatial and temporal resolution. For example in Figure 1.5, the viewer can see that during the morning commute measured personal PM levels while traveling on major roadways (8:19AM and 8:25 AM) were relatively larger than measured personal PM levels while traveling on side streets (8:15 AM). During the morning commute there were several low-level peaks and one larger peak during the morning commute. The larger peak coincides with the transit of a major traffic intersection. This type of representation is especially useful when analyzing spatial and temporal attributes. For instance, the personal PM levels occurring during the commute to and from work/school can be compared to traffic densities on the corresponding roadways.

Also the locations where a majority of time is spent can be related to other spatially-referenced data (e.g. traffic density, industrial areas, etc.) to model the influence of potential environmental exposure sources.

This ability to temporally-delineate personal PM levels along short time intervals allows visualization of peak PM levels that occur throughout the day. The timing and magnitude of peak signals can then be analyzed for association with other events (e.g. asthma exacerbation, symptoms, perceptions). This method could be used to supplement traditional time-integrated personal monitoring techniques (i.e., a filter-pump sampling method) (used in compliance monitoring of personal exposures) that reduce these thousands of exposure phenomena to a single, averaged data point.

This method can collect and apportion over 8600 personal exposure data points per day with both high resolution and accuracy. The method provides greater resolution of personal PM levels in the home, work/school, and transit micro-environments and allows preparation of a more detailed 'exposure budget' for each subject. The production of highly-resolved, space- and time-referenced exposure data allows for rigorous exposure assessment of mobile cohorts in the workforce or community. These personal exposure estimates can then be compared to estimates of personal exposure derived from ambient air pollution monitors to evaluate the correlation between the two. Exposure models may be further developed by incorporating additional environmental information, such as traffic density, ambient temperature, atmospheric mixing height, and wind velocity relative to the exposure of interest.

CHAPTER 2

"Spatiotemporal Profiles of Particulate Matter Exposure Among Asthmatic Children"[2]

2.1. Summary

Background: Children's exposure to particulate matter (PM) air pollution has been implicated in asthma prevalence and severity. There are a paucity of studies that assess children's exposures to PM air pollution across space and time.

Objectives: Examine children's personal exposure to PM in four distinct microenvironments (home, school, morning and afternoon transit). Evaluate relationships between personal exposures measured in each microenvironment and those measured by a community-based, outdoor monitor.

Methods: We monitored thirty schoolchildren for four consecutive days (Mon-Thu) on two occasions during the school year. Microenvironment-based personal PM data were derived from personal, space- and time-referenced exposure assessment by integrating data from direct-reading, personal exposure PM monitors with global positioning receivers. Data were analyzed using linear mixed models.

Results: Variation in personal exposures was primarily within-subject and space- and time- related. Highest to lowest mean personal concentrations per microenvironment: home, morning transit, afternoon transit, and school ($p<0.01$ for differences between each microenvironment except morning and afternoon transit). Concurrently measured ambient PM concentrations were not associated with personal exposures during microenvironments. Personal exposure in each microenvironment

[2] Adams, C., N. Rabinovitch et al. (2013). "Spatiotemporal Profiles of Particulate Matter Exposure Among Asthmatic Children." Unpublished manuscript.

was associated with exposure in subsequent microenvironments (15-111% increase per 1 μg/m^3 increase in personal PM in preceding microenvironment, $p<0.01$).

Conclusion: Differences in personal PM exposures in urban-poor schoolchildren with asthma are microenvironment-driven; exposures are generally highest at home, followed by transit and then school. Personal home exposures are poorly predicted with community-based monitors, but are themselves strongly predictive of personal exposures in subsequent microenvironments. These data suggest a "personal cloud" effect that persists through different microenvironments and can only be measured with spatially and temporally precise personal monitoring.

2.2. Introduction

Asthma is a complex disease whose development is influenced by inherited genes and environmental exposures (Arrandale, Brauer et al. 2011) . Asthma prevalence among children has increased over the past three decades (Van Cleave, Gortmaker et al. 2010), sparking further interest in the role environmental exposure plays in asthma etiology and exacerbation. In particular, asthmatic children appear to have an increased risk of adverse health effects from airborne pollutant exposures due to airway inflammation and hyper-responsiveness (Rabinovitch, Strand et al. 2006; Rabinovitch, Silveira et al. 2011).

Epidemiologists have typically used outdoor, fixed-site monitors, and questionnaire data to predict personal exposure and investigate potential associations with health effects (Dockery, Pope et al. 1993; Samet, Dominici et al. 2000; Pope 2004). Community-based exposure assessment has long been associated with increased symptoms and decreased lung function among asthmatics (Peters 1997; NRC-NAS

1998; Yu 2000). However, fixed-site monitors rarely capture spatial and temporal variability of air pollution (Strand, Hopke et al. 2007; Ott, Kumar et al. 2008; Setton, Marshall et al. 2011), leading to exposure misclassification when such data are used to assign exposure levels to individuals (Hutcheon 2010). Recently, more complex land-use regression models have been developed to improve estimates of personal exposure (Weis, Balshaw et al. 2005; Hoek, Beelen et al. 2008). However, such models have met with only limited success, given that individual exposures to air pollutants are highly variable through time and space and indoor sources dominate personal exposures (Ozkaynak 1996). Additionally, the majority of a child's time is typically spent indoors in various microenvironments (e.g., at home or school) (Hoek, Brunekreef et al. 2002). Models for indoor exposures based on ambient concentrations have been developed (Wilson and Brauer 2006; Hystad, Setton et al. 2009), but these models often do not account for indoor sources of air pollution and are limited in their ability to account for penetration of ambient air pollutants indoors (Thornburg, Ensor et al. 2001; Qing Yu, Turpin et al. 2005). Subject reporting bias is also an issue when a parent is asked to recall where and when a child spent their day (Elgethun, Yost et al. 2007). For these reasons, children's personal exposures to PM remain poorly understood.

As an alternative to community-based sampling, individual exposures to PM can also be estimated by sampling air directly within an individual's breathing zone. Such *personal* sampling methods typically draw a known volume of air through a filter over time, followed by gravimetric or chemical analyses (Ozkaynak 1996; Williams, Suggs et al. 2000; Adgate, Ramachandran et al. 2002). Filter-based sampling is more accurate

and precise than modeling an individual's exposure using a community-based monitor (Rodes, Lawless et al. 2001; Adgate, Ramachandran et al. 2003; Strand, Hopke et al. 2007; Rodes, Lawless et al. 2010). However, personal sampling is also resource intensive and thus, limited in scope. A second disadvantage to filter-based methods is that they are time-integrated (typically across 8 or 24 hours); such time averaging cannot capture changes in personal exposure that occur across space and time. For example, Quintana et al. reported that personal PM concentrations collected over 15 minute intervals were up to 10 times greater than the 24-hour mean measured during the same period (Quintana, Valenzia et al. 2001). Bi-modal personal exposure profiles (morning and evening concentration peaks) have been reported (LaRosa 2002; Zhu, Aikawa et al. 2005) in various populations. Because asthma exacerbation can occur within minutes or hours of an exposure (Delfino, Staimer et al. 2006; Rabinovitch, Strand et al. 2006), knowing when and where exposures are greatest would likely improve our understanding of environmental triggers of this complex disease.

Recently, methods have been developed to resolve personal exposure across both space and time (Elgethun, Fenske et al. 2003; Gulliver and Briggs 2007). For example, miniature direct-reading, or real-time, instruments have been developed to measure PM concentrations at fine temporal scales (i.e., seconds to minutes) (Chakrabarti, Fine et al. 2004; Benton-Vitz and Volckens 2008; Dons, Int Panis et al. 2011). Personal tracking methods have also been developed; these methods typically use global positioning system (GPS) receivers to follow an individual as they move between microenvironments (Phillips 2001; Elgethun, Fenske et al. 2003; Wu, Jiang et al. 2011). Compared to personal log entries, GPS-derived location information was

considered the best available solution or “gold standard” for determining time-location of a subject (Elgethun, Yost et al. 2007; Shoval 2008). The combination of miniature direct-reading instruments with personal tracking technology allowed the advent of new methods for personal spatiotemporal exposure assessment (Adams, Riggs et al. 2009).

This work examined children’s exposure to PM as a function of time, location, and activity for a panel of asthmatic children living in Denver, Colorado during wintertime in 2008. The primary objective was to evaluate the relationship between a child’s microenvironment (home, school, or in-transit) and their exposure to PM. A secondary objective was to compare these micro-environmental exposures to each other and to contrast them with community-based, ambient PM concentrations measured by a fixed outdoor monitor (located at their school).

2.3. Methods

2.3.a. Study Panel, Design and Methods

The study panel consisted of 32 children (6–14 years of age), with physician-diagnosed asthma, attending the Kunsberg School on the campus of National Jewish Health in Denver, Colorado. Panel subjects at the Kunsberg School were predominately African American (43%), followed by multiracial (36%), Hispanic (16%) and White (5%). All suffered from asthma with diagnoses of mild (41%), moderate (45%), or severe (14%). The majority of students were urban poor living in the Denver area (Rabinovitch, Strand et al. 2008). Over a 5-month period, (Dec 2007- Apr 2008) personal PM exposures were measured continuously on a daily basis (~ 21 hrs per day) using a recently developed method for personal spatiotemporal exposure assessment (Adams, Riggs et al. 2009). Ethical and scientific approval for the study was obtained from the National

Jewish Health's Institutional Review Board. The study design called for each child to be followed across two non-consecutive weeks and for four consecutive days each week (8 days total) during the school year, mid-day Monday through mid-day Friday. Subjects were asked to carry backpacks containing an aerosol nephelometer to measure fine PM concentrations, a global positioning system (GPS) receiver (GPSMap 60Cx, Garmin Inc. Olathe KS) to record geographic position data, and a temperature sensor to record personal microenvironment temperature; a separate section of each backpack was available to carry books and school supplies. Each monitor recorded data at 10-second intervals. Personal PM levels were actively sampled with a Personal DataRAM 1200, or pDR, (Thermo Fisher Scientific Inc., Waltham, MA) in conjunction with a pump (6.8 L/min flow, Omni Personal Pump, BGI Inc., Waltham MA) and cyclone (1.6 μm size cut, Model GK2.05, BGI Inc., Waltham MA). The 1.6 μm aerodynamic size cut resulted from a volumetric flow necessary to meet method quantification limits for gravimetric analysis of a filter sampler (Teflo 37mm, Pall Inc. East Hills, NY) located immediately downstream of the pDR.

The pDR has been used extensively to assess personal PM exposure (Reed 2000; Quintana, Valenzia et al. 2001; Fischer 2007) and has been found to be precise and in good agreement with other continuous monitors (Chakrabarti, Fine et al. 2004). However, the pDR has limitations; instrument response (i.e., degree of scattered light) is positively biased when relative humidity exceeds 60% (Chakrabarti, Fine et al. 2004; Wu, Delfino et al. 2005) and instrument response also varies depending on the size, shape, and composition of sampled aerosol (Benton-Vitz and Volckens 2008). This study was conducted during wintertime in Denver, when average ambient relative

humidity was below 60%. To correct for instrument bias due to PM light scattering properties, data from the pDR were normalized to personal filter data (Kim 2004; Benton-Vitz and Volckens 2008) during data processing. The normalization factor was calculated from the ratio of the daily personal filter data (integrated over 21 hr) to the corresponding daily pDR average; this correction was specific to each child's daily exposure. Hereafter, levels of $PM_{1.6}$ measured in this fashion are referenced as *personal PM;* levels of ambient $PM_{2.5}$ measured using outdoor federal reference methods will be referred to as *ambient* $PM_{2.5}$. The pDR inlet was positioned 2 inches above the top surface of the backpack, near the wearer's left shoulder, so as to sample air from within the child's breathing zone.

Backpacks were issued to subjects with instructions to wear them as much as possible throughout the day and to place the backpack upright on the floor nearby when sitting or lying. Subjects were also surveyed on activities, behaviors, and potential household exposures during the sampling period. Data from the pDR, GPS receiver, and temperature sensor were collated into a database by matching timestamps associated with each instrument's data. Collated data were then processed algorithmically to classify each 10-second sample into a predetermined microenvironment.

The microenvironment classification algorithm has been described in detail previously (Adams, Riggs et al. 2009). Briefly, geographical areas, or buffer regions, were developed to define an area surrounding each child's home and the common Kunsberg school using geographical information system software (ArcGIS 9.1, ESRI Inc.). Size and shape of the buffer regions were optimized to minimize misclassification

error, especially during times of transit between home and school. Using customized home and school buffer regions in conjunction with time-based rules, a space- and time-based algorithm classified exposures into four pre-determined microenvironments: at home, at school, morning transit (i.e., commuting from home to school), and afternoon transit (after school-hours and not at home). Accuracy of the classification for home and school using this method during a pilot study was greater than 98% (Adams, Riggs et al. 2009). Additional quality assurance of post-processed data was performed to ensure that the subject was carrying the backpack during the sampling period. Data were excluded with geospatial information indicating the backpack was left at school overnight or backpack temperature data indicating the backpack was left in a car overnight.

Additional data collection included ambient PM and weather data, and survey data regarding potential exposures (e.g. smoking, fried food preparation, and fireplaces). Ambient $PM_{2.5}$ concentrations at the Kunsberg School were measured with a Tapered Element Oscillating Microbalance averaged over one-hour time periods located on National Jewish Health (NJH) Campus (East Colfax Ave and Colorado Boulevard), approximately 2.5 miles south east of the urban center of Denver.

2.3.b. Statistical Analysis

This novel dataset presented several challenges for statistical analyses. For example, the continuous, 10-second levels of personal PM taken throughout the day tended to be non-normally distributed and auto-correlated in time. These issues (hierarchical, or nested data structure, temporal autocorrelation, and repeated measures) were addressed by using linear mixed models with a nested structure and a

covariance matrix to account for repeated measures. Model results and descriptive statistics were obtained using log-transformed personal PM data, associated ambient data, and additional covariates, described below.

To include 10-sec personal PM readings that were assigned zero values by the instrument (i.e., values lower than the instrument detection limit of 1 μg/m^3); an imputed value was substituted for the zero reading. This substitution was performed prior to (and necessary for) log-transformation of the data set. Imputed values were created first by stratifying the dataset by subject. Next, zero values for each subject were replaced with a heuristic value equal to one half of the smallest concentration recorded by the pDR (0.5 μg/m^3). Geometric means and geometric standard deviations of the log-transformed stratified data subsets were then calculated. These distribution parameters were used to impute values for the original zero readings via a probability integral transform (Casella 2002). The imputed, or modeled, values were substituted for the original zero readings.

The basic linear mixed model is represented in Equation 2.1:

$$Y_{ij} = \ln(X_{ij}) = \mu_Y + \sum_{m=1}^{p} \beta_m C_{mij} + b_i + \varepsilon_{ij} \quad \text{(Equation 2.1)}$$

for i = 1, 2,…, k individuals

for j = 1, 2,…, n_i measurements of the *i*th individual, and

for m = 1, 2,…, p covariates

where X_{ij} represents measurements at the j^{th} time interval for child i, and Y_{ij} is the natural log-transformed value of X_{ij}. Y_{ij} represents the sum of the effects of: μ_Y, representing the overall intercept; the product of the regression coefficients $\beta_1, \beta_2,\ldots, \beta_p$ (the fixed effects) and the observed values of their corresponding covariates $C_{1ij}, C_{2ij},\ldots,$

C_{pij}; b_i representing the random effect for the *i*th individual; and ε_{ij} representing the residual error for j^{th} observation on the i^{th} individual. Random variables b_i and ε_{ij} were assumed to be independent and normally distributed with means of 0 and variances of σ_b^2 and σ_w^2 (representing the between- and within-subject components of variance, respectively).

Several, more complex, models were also developed as described below to evaluate different aspects of the dataset (model structure and output are described in detail in Appendix 1). These models included additional covariates such as: ambient $PM_{2.5}$ concentration, pDR instrument used, sampling date, and microenvironment temperature. Models were also adjusted for the autoregressive aspect of repeated samples. All data analyses were conducted using SAS (version 9.2; SAS Institute Inc., Cary, NC) with an alpha level of 0.05 to evaluate statistical significance.

2.3.c. Personal PM (Panel-level)

Summary statistics were generated for personal and ambient PM levels and for personal and ambient temperatures on a daily and hourly basis. Additional analysis included estimating within-subject and between-subject variance components of PM exposure. The variance components were evaluated with an unconstrained model (*sup Model 3*). This model controlled for hierarchical effects of different samples (first level) within individual subjects (second level).

2.3.d. Personal PM (Microenvironment)

Summary statistics were generated for each microenvironment on daily and hourly bases: personal and ambient PM levels, personal and ambient recorded temperatures, and cumulative personal PM exposures. The effects of different microenvironments on personal PM exposure (using 10-sec data) was also explored (Appendix 1, *model 1*). This model controlled for hierarchical effects of 10-sec samples within different sample periods (first level) and for different sample periods within individual subjects (second level). Additionally, a relative exposure measure, or mass/time ratio, was calculated for each microenvironment. The mass/time ratio was calculated by dividing the percentage of time spent (on a daily basis) in a given microenvironment into the percentage of cumulative PM exposure (based on the total exposure from all microenvironments) experienced in that microenvironment The mass/time ratio provides a relative exposure metric to compare relationships between exposures experienced in the subjects' microenvironments.

2.3.e. Ambient PM as a Predictor of Personal Exposure

The ability of the fixed-site ambient $PM_{2.5}$ monitor to predict personal exposure in and across microenvironments was evaluated with a model (*Appendix 1, model 2*) that included additional covariates of: ambient $PM_{2.5}$ concentration, pDR instrument, sampling date, and microenvironment temperature. Adjustment for the autoregressive aspect of the repeated samples was also considered. Several different variations of covariates and covariance matrix structures were evaluated and a final model was chosen based on Akaike information criterion (AIC) statistics. This model controlled for hierarchical effects in the same manner as previous models with the addition of the

ambient $PM_{2.5}$ data as a covariate and an exponential spatial covariance matrix structure. The model used 5 minute averaging intervals (based on original 10-second data) to reduce run-time due to computing requirements.

2.3.f. Personal Exposure between Microenvironments

The uniqueness of the exposure sampling methodology allowed us to investigate whether PM exposure in one microenvironment was related to a subsequent microenvironment. For example, we assessed the relationship between home and school exposures during morning hours (*Appendix 1, model 4*). As with the development of previous models, several different variations of covariates and covariance matrix structures were evaluated. Personal PM concentrations at school were related to levels measured earlier in the day (at home and during morning transit) while adjusting for ambient $PM_{2.5}$ levels measured during various time intervals by the fixed-site monitor (located adjacent to the school). This model contained an exponential spatial covariance matrix and controlled for hierarchical effects within different sample periods (first level) and for different sample periods within individual subjects (second level). Pairwise comparisons were then assessed between each microenvironment.

Relationships between other microenvironments were also assessed (*Apppendix 1, model 5*). For example personal PM concentrations at school were used to predict personal PM concentrations measured later that day during afternoon transit. As in the development of previous models several different variations of covariates and covariance matrix structures were evaluated. This model controlled for hierarchical effects within different sample periods (first level) and for different sample periods within individual subjects (second level).

2.4. Results

The sampling campaign successfully collected 137 daily samples from 30 different subjects, resulting in 1,036,422 measurements (10-second data). At the beginning of the sampling campaign a battery charging fault damaged the sampling pumps, causing the first 44 potential samples (15%) to be lost/uncollected; 40 additional samples (14%) were lost due to subject compliance issues (e.g., backpack left at home or absence from school due to illness), and 30 (14%) samples were lost due to miscellaneous equipment failures (e.g., tubing breakage, filter tears, etc.). Following exclusion due to the preceding causes, 5 of the remaining samples were excluded because of abnormally low readings from the direct-reading instruments. Additional sampling was not pursued after the scheduled sampling campaign to avoid seasonality effects between Winter and Spring/Summer.

Approximately 18% of the direct-reading measurements in the dataset (i.e., 186,556 of the 1,036,422 10-sec personal PM readings) were lower than the instrument detection limit of 1 $\mu g/m^3$ and were replaced with imputed values in order to allow log-transformation. A Box-Cox analysis of both gravimetric filter data (137 samples) and direct-reading pDR data (1.03M samples) indicated that personal PM concentrations collected during this study were log-normally distributed. Similar tests indicated that personal temperature, ambient temperature, and ambient $PM_{2.5}$ levels were normally distributed. Mean daily sample length was 21 hours; the remaining three-hour period (11 AM-2 PM each day) included time to download data, replace batteries, calibrate sampling equipment, and survey subjects.

2.4.a. Personal PM (Panel-level)

The geometric mean concentration of the daily filter-based personal PM samples (Table 2.1) was 10.4 μg/m^3, with a geometric standard deviation (GSD) of 2.5. The daily median for direct-reading personal PM concentration was 10.9 μg/m^3. After normalization with filter-based sampling data, geometric mean and median direct-reading personal PM concentrations (10-second pDR samples) were 4.3 μg/m^3 (GSD = 5.2) and 4.5 μg/m^3, respectively. Histograms based on the 10-second personal PM data for each child (across all days and microenvironments) are shown in Figure 2.1.

Personal PM exposure variance within subjects was 8 times larger than the PM exposure variance between subjects. Within-subject variability of personal PM dominated throughout each of the microenvironments. Although within-subject variance was dominant, variations between-subject were also noted, as shown in Figure 2.1. The unconstrained model estimate for the intercept (representing the overall mean concentration from pDRs) indicated a geometric mean personal PM concentration for subjects at 4.6 μg/m^3; approximately 7% greater than the study subject's direct-reading measured geometric mean.

Table 2.1. Summary Statistics for Daily (21-hr average) Personal PM Levels

Statistic	pDR	Filter
Geometric Mean (GSD), μg/m^3	4.3 (5.2)	10.4 (2.5)
Median, μg/m^3	4.5	10.9
5^{th} percentile, μg/m^3	0.3	2.6
95^{th} percentile, μg/m^3	64.6	45.5

Average times spent in each microenvironment were (Table 2.2): 14.4 hours for home (59.9% of the day), 7.5 hours (31.4%) for school, 0.6 hours (2.4%) for morning transit, and 1.5 hours (6.3%) for afternoon transit. Afternoon transit included all travel between school and home, including errands, afterschool care, etc.. Geometric means of personal PM concentrations for each of the microenvironments were: 5.8 $\mu g/m^3$ (GSD =5.3) for home, 2.0 $\mu g/m^3$ (GSD = 3.8) for school, 3.4 $\mu g/m^3$ (GSD = 4.7) for morning transit and 2.7 $\mu g/m^3$ (GSD = 5.2) for afternoon transit. Pairwise comparison (*Appendix 1, model 3*, averaged in 5-min increments) indicated each mean microenvironmental personal PM concentration (home, school, afternoon transit, and morning transit) was significantly different from the others ($p<0.01$) except when comparing afternoon and morning transit ($p=0.7$).

Median personal PM concentrations measured in the home were approximately three times larger than concentrations measured in school (Figure 2.2); this ratio increased slightly with increasing cumulative exposure. Home exposures were approximately five times higher than school at the 90^{th} percentile and seven times higher at the 99^{th} percentile. Median personal PM concentrations measured during morning transit were approximately 30% higher than concentrations measured during afternoon transit. However, this relationship was reversed at the 90^{th} percentile where PM concentrations during afternoon transit were greater than morning transit.

Cumulative distributions of personal PM concentrations by microenvironment (direct-reading data averaged across all subjects and days) appeared log-normally distributed (Figure 2.2). Gravimetric filter data were also log-normally distributed, however, the integrated daily filter data had a larger median value and a narrower

distribution compared to the direct-reading data. Personal PM (10-sec data) averaged daily (analogous to the gravimetric filter) appeared log-linear with a slightly larger variance than the daily filter data.

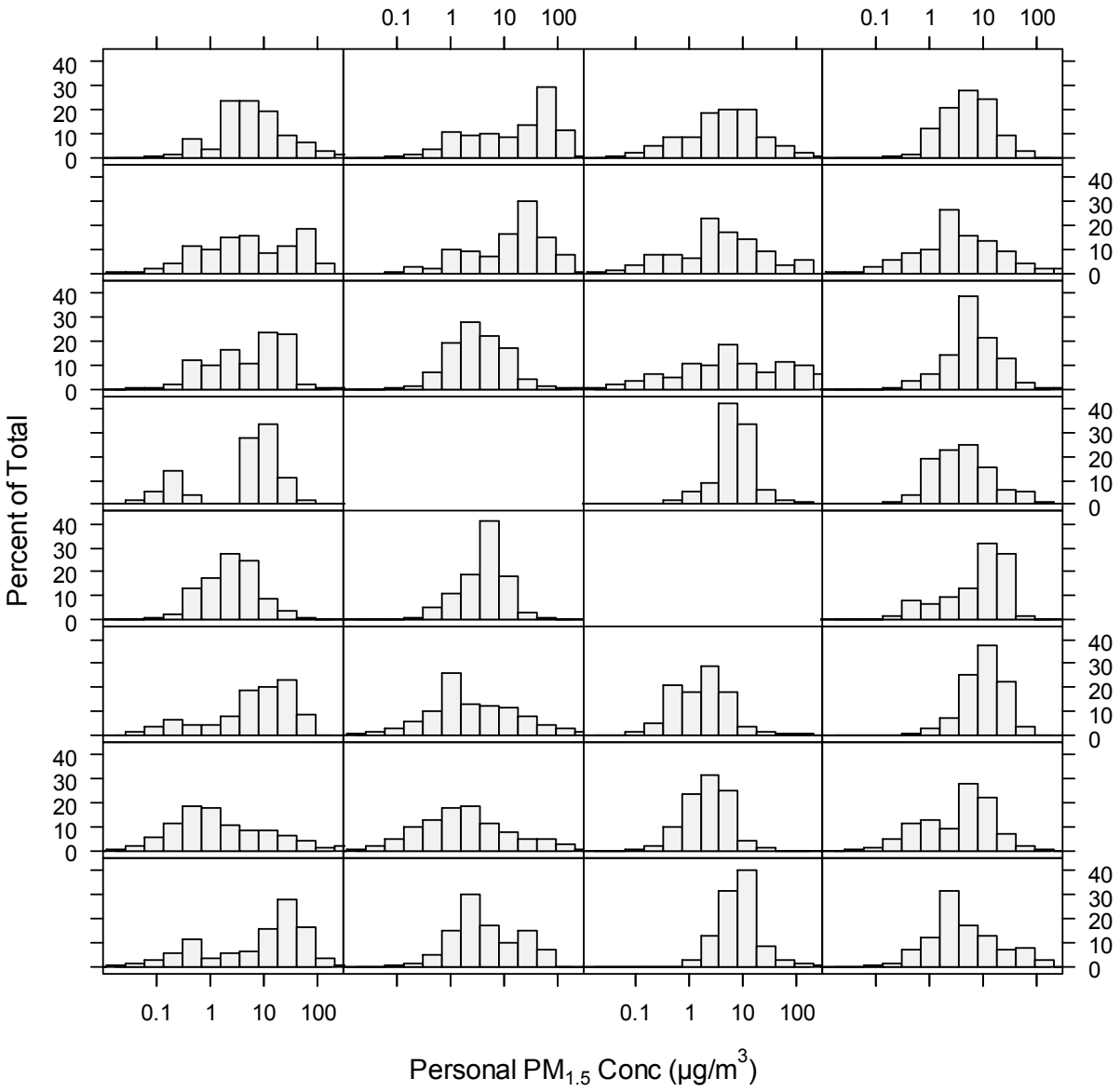

Figure 2.1. Personal PM Distributions by Subject (averaged across all sampling days). Personal PM (Microenvironment)

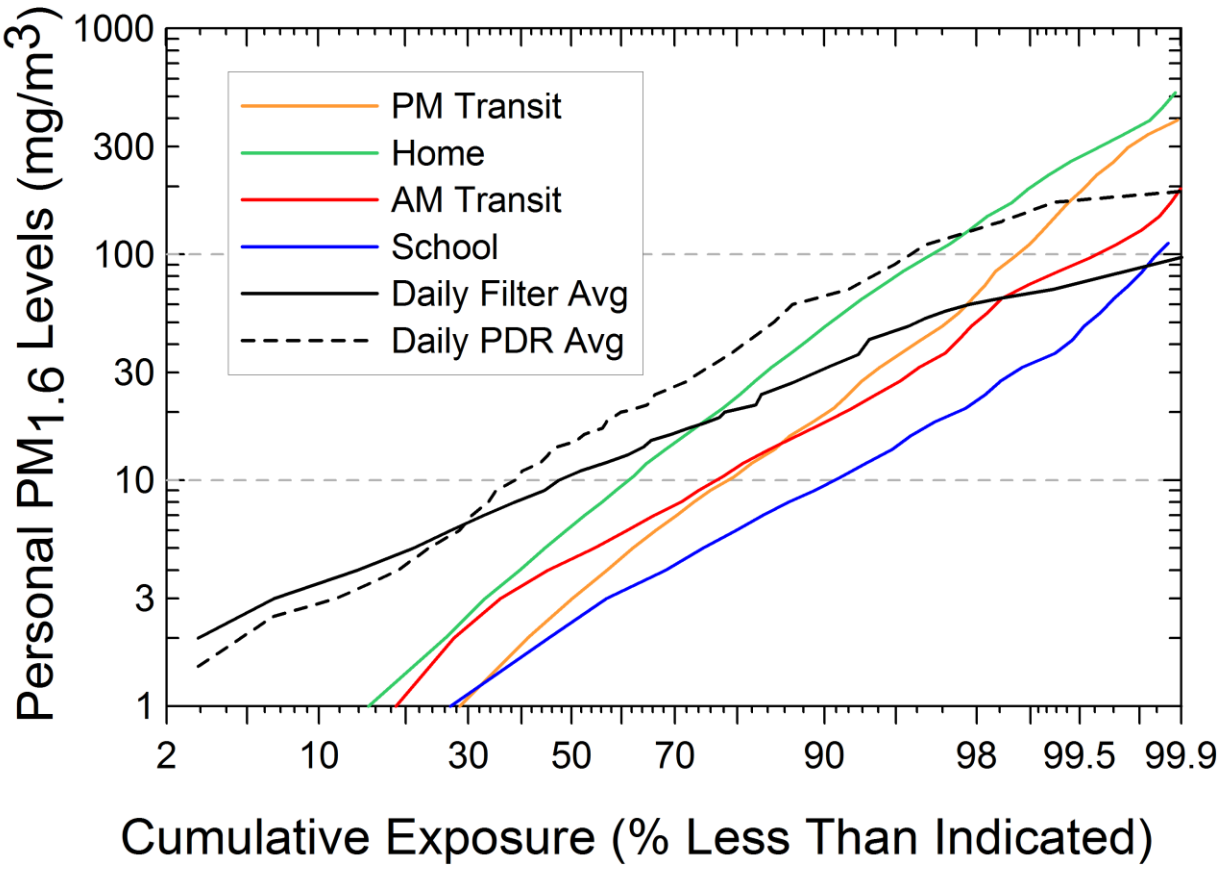

Figure 2.2. Cumulative Personal PM Levels (entire panel) by Microenvironment

Mass/time ratios were calculated to evaluate the relative contribution of a given microenvironment to an individual's daily PM exposure. Mass/time ratios larger than unity indicated a higher contribution of the particular microenvironment to the total exposure. For example, mass/time ratios indicated that an hour spent at home contributed three times more to personal PM exposure compared to an hour spent at school (Table 2.2, Figure 2.3). The home environment represented the largest relative personal PM exposure per time spent of all microenvironments (Figure 2.3). Mean (median) values of mass/time ratios ranged from 1.18 (1.28) for the home environment to 0.43 (0.22) for the School environment; the transit ratios fell near the middle of the range, Afternoon at 0.82 (0.61), and morning at 0.72 (0.50).

Table 2.2. Personal and Ambient Sampling Statistics by Microenvironment

	School	PM Transit	Home	AM Transit
Number of 10-second Samples	224148	74844	708966	28464
Daily Time in Microenvironment, hrs (SD)	7.5 (0.7)	1.5 (1.6)	14.4 (1.7)	0.6 (0.5)
Percent Time	31.4	6.3	59.9	2.4
Mass/Time Ratio	0.43	0.82	1.19	0.72
Geometric Mean Personal PM, µg/m3 (GSD)	2.0 (3.8)	2.7 (5.2)	5.8 (5.3)	3.4 (4.7)
Median Personal PM, µg/m3	2.4	3.0	6.3	4.5
5th % PM, µg/m3	0.2	0.2	0.3	0.1
95th % PM, µg/m3	14.0	35.8	80.3	26.9
Ambient $PM_{2.5}$† Mean, µg/m3, (SD)†	8.4 (6.7)	5.8 (4.5)	6.7 (6.8)	7.0 (5.7)
Ambient $PM_{2.5}$† Median, µg/m3	6.3	4.9	5.1	5.1
Ambient $PM_{2.5}$† 5th %, µg/m3	1.1	0.8	0	1
Ambient $PM_{2.5}$† 95th %, µg/m3	22.9	15.3	18.7	18.3
Microenvironment Temp Mean, °C, (SD)	21.4 (2.3)	21.1 (6.1)	21.3 (2.5)	18.0 (6.8)
Microenvironment Temp Median, °C	21.5	21.8	21.5	19.5
5th % Microenvironment Temp, °C	18.5	9.6	17.4	1.9
95th % Microenvironment Temp, °C	24.2	29.5	24.9	25.4
Outdoor Temp, °C (SD)	4.0 (6.7)	6.8 (7.9)	1.1 (6.5)	-0.5 (6.3)
Outdoor Temp Median, °C	4.5	6.4	1.4	0.2
5th % Outdoor Temp, °C	-7.8	-5	-9.4	-12.7
95th % Outdoor Temp, °C	14.2	22.3	11.7	8.2

† Ambient $PM_{2.5}$ levels were measured within 100 m of the subject's school.

2.4.b. Ambient PM as predictor of Personal PM

Ambient $PM_{2.5}$ was not a significant predictor of personal PM at 5-min (p=0.8) or 15-minute (p=0.3) averaging intervals. Ambient $PM_{2.5}$ concentrations were significant predictors of personal PM at slightly longer intervals. For example, ambient $PM_{2.5}$ was significant (p<0.01) in predicting personal PM when data were averaged over several hours (*Appendix 1, model 2*). The magnitude of the relationship between ambient and personal PM, while statistically significant, was small; a unit increase (1 µg/m^3) in

ambient PM concentration explained only a 1% change in hourly personal exposure. During the 6 AM to 11 AM timeframe (morning waking hours), ambient $PM_{2.5}$ accounted for 6% of the relative variation in personal exposure (i.e., a 1 $\mu g/m^3$ increase in the ambient concentration resulted in a 0.06 $\mu g/m^3$ increase in personal PM levels). The daily (24-hr average) ambient $PM_{2.5}$ was not a significant predictor of personal PM concentrations experienced within microenvironments (home, school, and afternoon transit) during the same day. The exception was the morning transit period when children commuted to school (Table 2.3).

2.4.c. Relationships of Personal PM between Microenvironments

Mean personal PM concentrations (Table 2.4) from preceding microenvironments were significant in predicting personal PM concentrations in subsequent, or ensuing, microenvironments ($p<0.03$). This effect was relatively independent of how the personal PM data were averaged or aggregated. The relative effects (% change) on personal PM concentration during subsequent microenvironments (referenced relative to a 1.0 μg/m3 increase in preceding environment) were relatively large (20% to 111%). For example, a unit increase in personal exposure at school was associated with a 111% relative increase in personal PM exposures experienced during the afternoon transit. A unit increase in personal PM exposure at home during the morning hours was associated with a 77% increase in personal PM exposure during morning transit. Afternoon transit personal PM had the smallest relative increase effect on the personal PM at home (only 20%). Additionally, we found personal PM exposures at home were

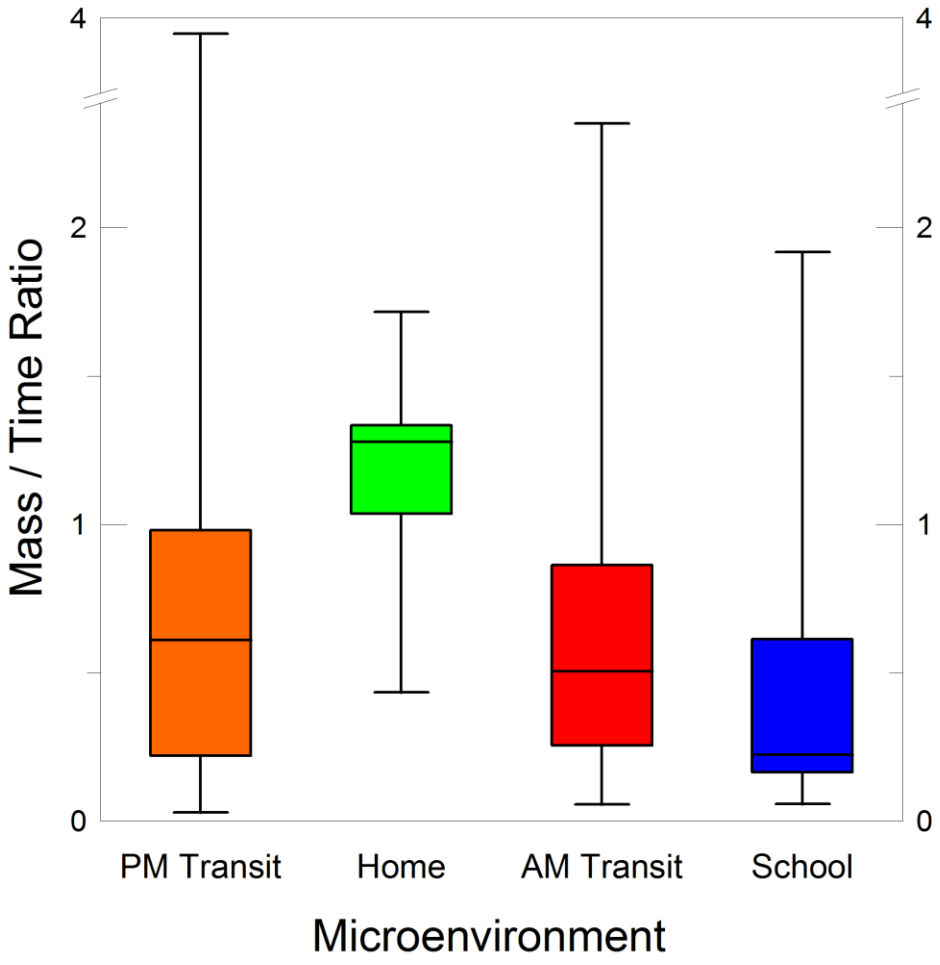

Figure 2.3. Mass / Time Ratio by Microenvironment (percent of cumulative personal PM from a microenvironment over percent of the daily time spent in that microenvironment)

predictive of school exposures later that day ($p<0.03$), with a relative increase effect of 38% regardless of exposures measured during transit (Table 2.3). A simple representation of this relationship in exposure between microenvironments is illustrated in Figure 2.4, where the relationship between mean personal PM levels from the home and school microenvironments are plotted (beginning at 6 AM until 11 AM). Effects of personal PM from home on the personal PM at school during different hours of the morning indicated a continued predictive ability. Personal PM from the home

Table 2.3. Percent Increase (and associated p-values) in Personal Exposure in a Given Microenvironment as Predicted by a Unit Increase in Ambient PM Levels (1 µg/m3) Measured by the Fixed Ambient Monitor over the same time period.

	PM School	PM Transit	Home	AM Transit	AM School
PM School Ambient	8 (<0.01)	8 (<0.01)			
PM Transit Ambient		10 (<0.01)	0 (0.85)		
Home Ambient			0 (0.84)	4 (.05)	
AM Transit Ambient				7.4 (<0.01)	6 (<0.01)
AM School Ambient					5.9 (<0.01)
Daily Ambient	3 (0.17)	3 (0.22)	0 (0.84)	6 (0.01)	2.7 (0.23)

microenvironment (6 to 7 AM) was predictive of personal PM at school during the 9 to10 AM and the 10 to 11 AM hours ($p<0.01$). The strength of these associations, however, tended to decrease as the duration between different microenvironmental exposures increased (i.e., there was a slight decrease in the slope estimate between home and school PM when home was compared to the 9-10 AM school exposure vs. the 10-11 AM time frame).

Table 2.4. Percent Increase (and associated p-values) in Personal Exposure in an Ensuing (later) Microenvironment as Predicted by a Unit Increase in Personal Exposure (1 µg/m^3) Measured in a preceding (earlier) Microenvironment

	Ensuing Microenvironment				
Preceding Microenvironment	PM School	PM Transit	Home	AM Transit	AM School
Afternoon School		111 (<0.01)	15 (0.03)		
Afternoon Transit			20 (<0.01)		
Home				77 (<0.01)	38 (<0.01)
Morning Transit					87 (<0.01)

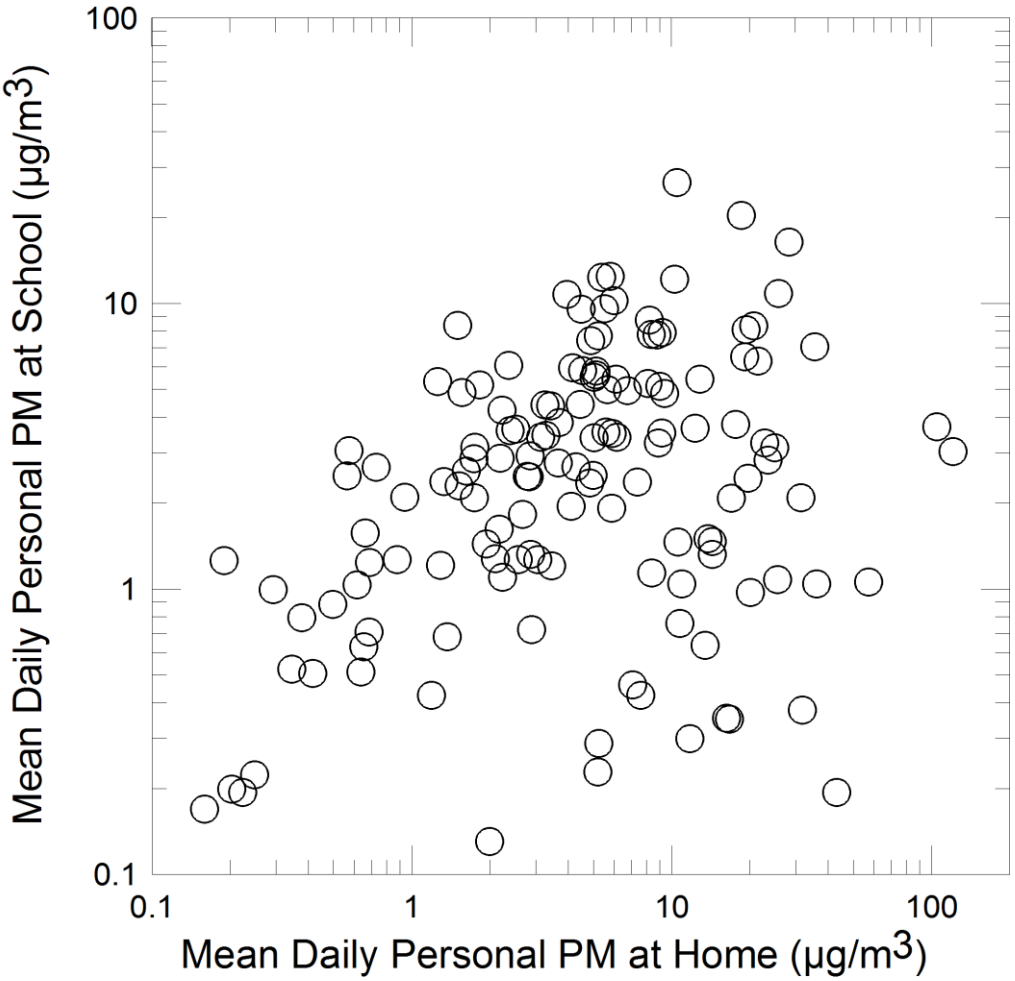

Figure 2.4. Personal PM at Home vs. School during 6-11 AM Timeframe (by Subject)

2.5. Discussion

2.5.a. Personal PM (Panel-level)

Asthmatic children living within metropolitan Denver experience PM exposures generally comparable with adults and children studied in other areas. The normalized direct-reading geometric mean (4.3 µg/m^3) was lower than exposure assessments of asthmatic children in Southern California, GM = 12.6 µg/m^3 (Wu, Delfino et al. 2005). The geometric mean filter-based personal concentration (10.4 µg/m^3) was lower than the geometric mean of 19 µg/m^3 reported in Minneapolis-St Paul (Adgate,

Ramachandran et al. 2002), and higher than the 2.3 μg/m^3 reported in Gothenburg, Sweden (Johannesson, Rappaport et al. 2011). Attempts to compare measured concentrations are difficult without considering a multitude of co-factors, e.g. sources of both personal PM vs. ambient $PM_{2.5}$, indoor penetration of ambient PM, human activity patterns, and meteorology. In addition, comparison of these results with studies focused on adults from the general population is problematic, as asthmatic children are not as likely to conduct the same PM producing tasks as adults, e.g. cooking (frying, grilling), household cleaning, or work-related. However, children are likely engaged in indoor play activities (e.g. on carpet or furniture) that can generate PM.

Although a normalization factor was used in the analysis, the difference in the geometric means between the direct-reading instrument (4.3 μg/m^3) and gravimetric filter sampler (10.4 μg/m^3) was relatively large. This was likely due to the overall greater number of direct-reading (pDR) samples and a greater proportion of direct-reading samples with low concentrations, skewing the central tendency of continuous (pDR) samples toward zero. This aspect of the central tendency was also represented by the much lower median value for direct-reading samples (4.5 μg/m^3) vs. the gravimetric filter sampler median (10.9 μg/m^3). The 95^{th} percentile value from direct-reading measurements in this study was 15 times higher than the geometric mean taken across all the data. The tendency for subjects' direct-reading samples to have lower mean levels when averaged over longer periods was described by Quintana et al (2001). They observed 15-min and 1-hour means up to 10 and 5 times higher than 24-hour means.

The 95th percentile value for the daily *filter-based* measures (45.5 μg/m^3) was larger than the value mandated by the National Ambient Air Quality Standards (NAAQS) 24-hour concentration (35 μg/m^3). The NAAQS standard is an outdoor ambient $PM_{2.5}$ compliance standard, which was established to protect the health of sensitive populations from outdoor air pollution. Although comparisons to this standard provide a reference point for personal exposure, it should be noted that the composition of personal vs. ambient PM are often quite different (Qing Yu, Turpin et al. 2005).

Within-subject variability in the daily personal PM concentrations dominated between-subject variability. Within-subject variation in exposure is likely driven by the dynamic nature of daily human activity; transit exposures, day-to-day differences in microenvironment sources (household cooking and cleaning), and daily differences in personal activities and behaviors (or other personal-cloud effects). Greater within-subject variability for personal PM concentrations has been reported in other studies of environmental exposure (Rappaport and Kupper 2004; Egeghy, Quackenboss et al. 2005; Sørensen, Loft et al. 2005; Lanki, Ahokas et al. 2007; Johannesson, Rappaport et al. 2011). Sørensen et al. (2005) reported that, surprisingly, nearly all variability among college students' exposures to $PM_{2.5}$ in Copenhagen was due to the within-subject component. Lanki reported within-subject variability accounted for 8 times the between-subject variation of $PM_{2.5}$ exposure in elderly subjects in Amsterdam and Helsinki. Johannesson found equal within-subject and between-subject variances for $PM_{2.5}$. Rappaport and Johannesson also reported that within-subject variance was dominant for other environmental contaminants, e.g. black smoke, trace elements, and VOCs.

Between-subject variation in personal PM exposure was likely due to differences among residences, personal activities, household- and lifestyle- associated sources, etc. Heterogeneity both between and within subjects was clearly visible in the subjects' distributions (Figure 2.1). Generally, the distributions of personal PM concentrations among panel subjects were unimodal and symmetric, however, variations were observed from subject to subject (Figure 2.1). Personal PM concentration distribution peaks within the histograms centered on values spanning from 1 $\mu g/m^3$ to 100 $\mu g/m^3$. Some histograms indicated a skewed or bimodal tendency in the distribution, however, concentrations below 1 $\mu g/m^3$ (instrument limit of detection) have been imputed from the remainder of the data (above 1 $\mu g/m^3$). Imputed data tends to smooth the lower end of the exposure distributions but may indicate a more bimodal character than actually exists (Figure 2.1). Histograms of personal PM concentrations grouped by each of the microenvironments indicated that the distributions were generally symmetric for all microenvironments (data not shown).

2.5.b. Personal PM (Microenvironment)

Personal PM concentrations were highest at home, followed by concentrations from morning and afternoon transit; personal PM concentrations were lowest when subjects were at school (Table 2.1 and Figure 2.2). Study subjects also spent the largest amount of time in the home microenvironment, followed by school, afternoon transit and morning transit. Percent time recorded at home (59.9%) was slightly lower than reported for other studies, such as the DEARS study (Rodes, Lawless et al. 2010) and the National Human Activity Pattern Survey (Klepeis, Nelson et al. 2001), 77.4% and 68.7%, respectively. The DEARS study involved Detroit-area adults, only some of

which had employment outside the home, whereas all of the current study subjects attended school daily. The NHAPS studied a sample of US inhabitants (all ages, employment status, and geographic areas).

Personal PM levels at home were also more variable (GSD = 5.3) than the other microenvironments, as indicated in Table 2.2. The cumulative distribution (Figure 2.2) of the daily averages (filter and PDR) were "flatter" due to reduced variability from averaging over a longer (daily) sampling period.

The analysis of mass/time ratios indicated that an hour spent at home contributed nearly 3 times more to personal exposure than an hour spent at school (Table 2.2, Figure 2.3). The mass/time ratio is a measure of exposure intensity; it is calculated by normalizing relative PM levels from a given microenvironment (taken as a percentage of the daily cumulative exposure) by the percent of total time spent in that microenvironment. A mass/time ratio greater than unity indicated a greater exposure than would be expected based solely on the amount of time spent in that microenvironment. The difference between the school and home mass/time ratios was likely due to differing indoor sources in two microenvironments. Morning and afternoon transit periods had similar mass/time ratios, despite the afternoon transit period lasting 3 times longer. Rank order of the mass/time ratios roughly corresponded with rank order of the mean personal PM concentrations from each microenvironment, indicating that measured personal PM levels tend to drive cumulative exposures, as opposed to the total time spent in a given microenvironment.

Mass/time ratio for personal PM in the home microenvironment was much larger than unity (1.43) and also varied less than other microenvironments (Figure 2.3). The

lower variance was expected because children spent most of their day at home. A larger amount of time spent in a microenvironment (expressed in the denominator of the ratio) tends to attenuate effects of concentration swings (expressed in the numerator of the ratio). Mean mass/time ratios from the other microenvironments were less than unity but had greater variation. Afternoon transit mass/time ratios had the largest variability; one reason for the larger amount of variability could be exposure misclassification during afternoon transit, especially if subjects encounter various indoor environments (errands, daycare, etc.) after leaving school and before arriving home (Adams, Riggs et al. 2009). Mass/time ratios of the microenvironments in this study did not have an upper range as great as in a study by Branis (2010) in which a mass-time ratio greater than 20 was found in restaurant microenvironments (where smoking was allowed). However, there was some correspondence between mass/time ratios. In both studies transit and school microenvironments were less than unity. Mass/time ratios of the home microenvironments varied widely between the studies, most likely due to a greater percent of the samples in the other study being collected outdoors near the home. Branis (2010) described observing the highest mass/time ratios in highly-polluted indoor spaces, specifically, restaurants and buildings heated with wood-burning stoves.

Percent of subjects' time spent in microenvironments other than home was dominated by the school microenvironment (31.4%). Personal PM levels at school tended to be lower and less variable than other microenvironments. This was expected as the school was generally considered the “cleanest” of the microenvironments (without any obvious indoor sources of PM). The mass/time ratio was also lowest at

school, which emphasize the relative "cleanliness" of the school microenvironment. Branis (2010) also observed a school (college campus) microenvironment mass/time ratio less than unity.

Transit to and from school accounted for <10% of a subject's typical day. Mean morning transit time was 0.6 hours while afternoon transit was 1.5 hours. Personal PM levels measured during morning transit (4.5 μg/m^3) were second only to the home microenvironment (6.3 μg/m^3). Children's transit to school was concurrent with the general population's transit to work and occurred during the latter portion of the typical morning commute period. Compared to the subjects typical afternoon transit timeframe, the ambient atmosphere during the morning transit timeframe was more likely to have calm winds and a lower atmospheric mixing height; both of these phenomena would result in higher pollutant concentrations near roads (Adams, Nieuwenhuijsen et al. 2001; Patel, Chillrud et al. 2009). Vehicle traffic has been identified as a significant source of $PM_{2.5}$ (Kinney, Aggarwal et al. 2000) and several studies have reported higher in-vehicle exposures to $PM_{2.5}$ compared to central ambient monitors (Riediker, Williams et al. 2003; Brown, Sarnat et al. 2012). Emissions from combustion and non-combustion sources (HEI 2010) during commutes are of interest; more specific commuting-related analyses will be described in follow-up work.

Afternoon transit had the second lowest personal PM concentration (3.4 μg/m^3) of the four microenvironments. Subject's spent over twice as much time in afternoon transit than morning transit. The afternoon transit microenvironment encompassed all travel away from school or home in the afternoon. Therefore, other activities such as, errands, visiting friends/relatives homes, afterschool care, etc. were classified as

afternoon transit. Children's afternoon transit periods typically began before peak commuting window for Denver (4-6 PM). Also, afternoon transit was more likely to occur during periods with greater atmospheric mixing heights due to afternoon winds typical for the Front Range of Colorado. These conditions would likely minimize traffic-related PM exposure. However, the largest 10% of recorded concentrations during the PM transit period were larger than those of the AM Transit (Figure 2.2). This may be due to traffic-related exposures or could be from subjects visiting "dirtier" indoor microenvironments away from home in the afternoon/evening timeframe.

2.5.c. Ambient PM as predictor of Personal PM

Ambient $PM_{2.5}$ levels were a significant but not a strong predictor of personal PM levels. At hour-long time periods a unit increase (1 $\mu g/m^3$) in ambient $PM_{2.5}$ concentration was associated with only a 0.02 $\mu g/m^3$ increase in the average personal PM levels, a relative increase of <1%. A growing body of research has described the geographic (spatial) and temporal variability of ambient PM (Delfino, Zeiger et al. 1998; Henderson, Beckerman et al. 2007; Jerrett, Arain et al. 2007; Ott, Kumar et al. 2008), suggesting that central ambient monitors are not an important predictor of the personal PM exposure within various microenvironments. The relationship between ambient and personal PM was not significant at shorter (15 min) and longer (daily) averaging periods.

The ability of the ambient $PM_{2.5}$ monitor to predict personal exposure was strongest during morning and afternoon transit periods (Table 2.3; $p < 0.01$). The relative effect size, however, was small: a unit change in ambient $PM_{2.5}$ accounted for less than a 10% change in personal PM. The same relationship (and effect size) was

also true at the school microenvironment, which is somewhat surprising since the ambient $PM_{2.5}$ monitor was located adjacent to the children's school. The ambient $PM_{2.5}$ concentration during the home microenvironment was not significant when predicting personal PM concentrations ($p = 0.8$), which is understandable, since most subjects lived several miles from the school.

2.5.d. Relationships of Personal PM Exposures between Microenvironments

Personal PM exposures were correlated from one microenvironment to the next (Table 2.3, *Appendix 1, model 5*), even when the two microenvironments were separated by distances of several miles (i.e., home to school). The findings that personal PM levels from one microenvironment were not only significant predictors but also had relatively large effects on subsequent microenvironments was somewhat surprising. For example, personal exposure at home had a strong predictive effect on school exposures, even though these two microenvironments were interceded by morning transit. The strength of this association is shown graphically in Figure 2.4. This result suggests a strong 'personal cloud' effect within the panel, such that the child either continually generated or carried with them a 'cloud' of PM throughout the day. This 'personal cloud' effect was more pervasive and stronger at predicting personal PM exposure compared to ambient $PM_{2.5}$ levels measured by a central, outdoor monitor.

Several potential confounders for this relationship (e.g. sampling day and sampling instrument ID) were investigated and did not reduce the strength or significance of this association. Further assessment of the effect indicated that the prediction capability of the home personal PM concentration did not decrease as the morning progressed at the 'clean' school microenvironment. This finding suggests that

the 'personal cloud' is a subject-specific phenomenon that depends more on the person generating the cloud than the microenvironment where the cloud is being generated.

The largest personal cloud effects occurred between the afternoon school and afternoon transit microenvironments (a 111% relative effect) and between the home and morning transit microenvironments (a 77% relative effect, Table 2.3). These relatively large effects occurred on the two shortest duration microenvironments. Since these two microenvironments were relatively short, any misclassification errors that occurred while subjects were transitioning from/to a buffer area (e.g. sitting in a car or standing at a bus stop while still physically within the designated school buffer zone) would have had a larger influence. The afternoon transit had the lowest relative effect on the home microenvironment, only a 20% increase on the home personal PM concentration. This could be expected as the home environment was likely to provide the strongest and most variable sources of PM exposure. However, the 38% relative increase observed during school due to the personal PM concentrations from the home microenvironment would not be greatly affected by misclassification as the larger amount of time spent in these microenvironments would minimize any misclassification effects created during transition from one microenvironment to another.

2.5.e. Study Limitations and Avenues for Continued Research

Previous studies have shown that seasonality can affect air pollutant concentrations (Rodes, Lawless et al. 2010). Our sampling campaign did not allow assessment during both a winter and a summer season (the school- based panel curtailed possibility for summer sampling). Our sampling occurred only in the winter, when most of the day was spent indoors. With a younger panel there is a possibility

that substantially more time could be spent outside during the summer. Therefore, future work should examine children's exposures during fall and spring school seasons.

Our sampling was limited to weekdays, given that instrument battery life was limited to 30 hours and that all interactions with subjects took place at school. Thus, weekend exposures were not studied. During week-days, a larger amount of time spent in a relatively "clean" microenvironment may have biased the daily personal PM exposure. The data from the weekdays indicated that personal PM concentrations in the home environment were substantially larger than other microenvironments. Subjects spending larger portions of the weekend days at home would likely experience increased daily personal PM concentrations.

As in other studies, various technological problems (e.g. battery failures, tube connections, etc.) reduced the overall number of samples that could be collected within the available timeframe. Panel compliance was also an issue; approximately 14% of available sample days were lost because sampling backpacks were left at school or at home. Compliance may have also been an issue when outside of the school environment. Subjects were educated on proper handling of the backpack and interacted with the study coordinators on a daily basis, however we cannot be certain how long the samplers were worn at home (although GPS data confirmed locations during home, transit, and school periods).

The particle cut size of our personal sampling equipment was not standardized to more common measures such as $PM_{2.5}$, PM_{10}, or respirable PM. However, based on common urban aerosol particle distributions (Seinfeld 1998) the cut size was large enough to capture greater than 90% of the likely urban $PM_{2.5}$ size distribution. Aerosol

monitoring with a nephelometer has limitations that are inherent to most light-scattering instruments. However, we attempted to account for aerosol specific biases by normalizing our data each day (and for each child) to a gravimetric filter measurement made immediately downstream of the pDR.

The panel investigated in this study may have only represented a subfraction of the population of young asthmatics. The majority of the children in this panel suffered from moderate to severe asthma. Also, some of the children in this panel were attending the Kunsberg school because they were at higher risk due to poor disease management. These panel background factors indicate that the panel would not adequately represent the likely population of all asthma sufferers.

2.6. Conclusions

A key goal of this study was to enhance the understanding of children's exposures to fine particulate matter. Our research demonstrated that children's personal exposures vary substantially between different places (microenvironments) visited throughout the day. The exposures can be more fully characterized using mobile-monitoring protocols and time- and space-based rules.

Centrally-located ambient monitors were, at best, only marginally predictive of medium-term (hour-length) personal exposures and only when individuals are proximate to that monitor, which suggests that ambient PM measurements represent only a small fraction of an individual's daily intake. Ambient monitor concentrations were not correlated with personal exposure in the home microenvironment where subjects were exposed to the highest PM levels. Alternatively, an individual's microenvironment had significant impact on measured personal exposures. Furthermore, personal exposures

in one microenvironment were strongly correlated with levels in ensuing microenvironments later in the day. This finding supports a 'personal cloud' effect that is subject-specific and indicates that subjects may create a 'personal cloud' effect as they travel from one microenvironment to the next.

Spatiotemporal exposure assessment is a powerful new technique that can provide substantial insight into an individual's daily intake of PM. Such data may eventually be used to develop a personalized approach to prevention, or treatment, of asthma exacerbation based on multiple personal environmental risk factors, not simply the measured ambient concentration of particulate matter "near" someone's home.

CHAPTER 3

"Commute-related Particulate Matter Exposure Is Associated with Acute Asthma Worsening in Children" [3]

3.1. Summary

Rationale: Traffic-related particulate matter (PM) concentrations have been associated with adverse effects in children with asthma but the relationship between personal PM exposures while commuting and asthma severity has not been studied.

Objectives: To determine whether personal exposures apportioned to home, school and morning commute are associated with increases in urinary leukotriene E4 ($uLTE_4$); an asthma-related biological mediator in children with asthma.

Methods and Measurements: In an elementary school-based panel, 30 children with physician-diagnosed asthma were monitored over a 5-month winter period (2008–2009) in Denver, Colorado. Real-time personal exposure monitoring integrated with a geographical position sensor was performed daily (n = 125 sample-days) and measures of asthma severity were collected. Mixed linear models assessed the association between home, school and transit-related personal and ambient PM exposures and same-day $uLTE_4$ levels.

Results: Transit related PM exposures were lower, on average, than home and higher than school-related exposures. In models controlling for second hand smoke exposure and upper respiratory infection symptoms, an interquartile range increase in personal transit-related PM exposure was associated with a 15.7 % increase in $uLTE_4$

[3] Adams, C., J Volckens et al.; "Commute-related Particulate Matter Exposure Is Associated with Acute Asthma Worsening in Children." Unpublished manuscript.

measured within 3-6 hours after exposure (95th CI, 7, 46%; $p < 0.001$). Weaker relationships were observed between $uLTE_4$ and personal PM exposures at home (13.9% increase per IQR, 95th CI 2, 58, ($p=0.03$) and school (8.6% per IQR, 95th CI, -4, 31, $p=0.15$). Similar associations were not observed with PM concentrations measured concurrently by outdoor, area-wide monitors ($p \geq 0.7$).

Conclusions: Brief localized exposure to traffic-related PM is associated with increased $uLTE_4$ levels in children with asthma.

3.2. Introduction

Asthma prevalence among children has increased over the past three decades (Van Cleave, Gortmaker et al. 2010), sparking further interest in the role environmental factors play in asthma etiology and severity. In asthmatic children, increased biological and physiological markers of asthma severity are associated with fine particulate matter (PM) concentrations measured by area-wide monitors during the morning commute to school (Rabinovitch, Strand et al. 2006). Proximity to busy roadways has also been associated with pediatric asthma prevalence and severity in multiple studies (HEI 2010). Almost all such studies employ surrogate measurements to estimate actual exposures, mainly because personal exposure monitoring can be obtrusive and also resource intensive. Community-based air pollution monitors are often used to assign exposures to individuals, but these monitors cannot fully capture the spatial and temporal variability of ambient air pollution (Ott, Kumar et al. 2008), nor can they capture the variability of personal exposures associated with movement throughout the community, e.g. vehicle transit (Setton, Marshall et al. 2011; Brown, Sarnat et al. 2012), or movement into indoor microenvironments (Van Roosbroeck, Li et al. 2008). As a result, individual

exposure estimates derived from ambient monitoring data are subject to exposure misclassification and error (Strand, Hopke et al. 2007; Hutcheon 2010). Exposure assignment based on home and/or school proximity to busy roadways may be confounded by correlation with important asthma related factors prevalent in low socioeconomic status households such as poor medication compliance and increased exposure to second hand smoke (SHS) (Green, Smorodinsky et al. 2004).

Personal monitoring of exposure (i.e., sampling air from within a person's breathing zone by virtue of a miniaturized sampler) is an alternative to these surrogate exposure measurements; this form of exposure assessment can capture localized exposures that cannot be measured with community monitors, but is also more resource intensive, as each study subject must be fitted and monitored individually. To date, studies assessing personal exposures have been limited in scope and have mainly used personal PM exposure samples that were averaged, or integrated, over a 24-hour period. Unfortunately, the use of 24-hr averaging periods for exposure assessment can attenuate the perceived relationship between exposure and adverse health outcomes, especially when a causal exposure is brief, lasting only minutes (Quintana, Valenzia et al. 2001).

In earlier studies (Rabinovitch, Zhang et al. 2004; Rabinovitch, Zhang et al. 2006), we reported changes in urinary leukotriene E4 ($uLTE_4$), a mediator of airway inflammation and bronchospasm. Increased $uLTE_4$ occurred within minutes to hours after ambient outdoor PM concentrations spiked during the morning rush-hour (Rabinovitch, Strand et al. 2006; Rabinovitch, Reisdorph et al. 2011; Rabinovitch 2012). However, we could not precisely identify the magnitude, timing, and location of localized

traffic exposures which presumably were responsible for this response and could not discern individual exposure patterns with health outcomes until now.

In the present study, we utilized a personal monitoring system that could integrate real-time monitoring with a geographic information system (GIS) platform. By using this novel approach, we were able to apportion PM exposures to home, school and transit microenvironments and assess the relationship between these microenvironmental exposures and increased $uLTE_4$ in a well-defined group of mostly urban-poor schoolchildren. In this way, we were able to determine the magnitude, location and timing of personal PM exposures and their relationship with asthma-related inflammation while also comparing these health effects to PM concentrations measured by an area-wide monitor.

3.3. Methods

3.3.a. Study Subjects

Elementary-aged children, who attended the Kunsberg School at the National Jewish Medical and Research Center (Denver, CO) and who had physician-diagnosed asthma, were studied over a 5-month winter period. Ethical and scientific approval for the study was obtained from the National Jewish Health's Institutional Review Board. Personal PM exposures were measured continuously on a daily basis (~ 21 hrs) using a recently developed method for personal spatiotemporal exposure assessment (Adams, Riggs et al. 2009). In addition, ambient PM and personal asthma exacerbation data were collected on school days from the 30-child panel from December 2008 to April 2009. Each child was to be followed across two non-consecutive weeks and for four consecutive days each week (8 days total) during the school year, mid-day Monday

through mid-day Friday. Ethical and scientific approval was obtained from the National Jewish Center's Institutional Review Board.

3.3.b. Personal PM and Exposure Survey

Personal PM monitoring backpacks, including a nephelometer, air pump, PM sample filter, GPS recorder, and temperature monitor were worn by students with instructions to wear them as much as possible throughout the day and to place them by their bed at night. The methodology has been published (Adams, Riggs et al. 2009), however, a brief description follows.

Monitoring backpacks contained an aerosol nephelometer to measure fine PM concentrations, a global positioning system (GPS) receiver (GPSMap 60Cx, Garmin Inc. Olathe KS) to record geographic position data, and a temperature sensor to record ambient temperature within the breathing zone. These monitors were housed in a small backpack with a total weight of approximately 3.2 kg (7 lbs); a separate section of each backpack was available to carry books and school supplies. The monitors recorded data at 10-second intervals. Personal PM levels were actively sampled with a Personal DataRAM 1200, or pDR, (Thermo Fisher Scientific Inc., Waltham, MA) in conjunction with a pump (6.8 L/min flow, Omni Personal Pump, BGI Inc., Waltham MA) and cyclone (1.6 μm size cut, Model GK2.05, BGI Inc., Waltham MA). The samplers collected data on PM concentration, temperature, and location every 10 seconds. Daily, the 10-second readings of PM, location, and temperature were downloaded and PM sample filters collected for gravimetric analysis. Data from the pDR, GPS receiver, and temperature monitor were collated into a database by matching the associated timestamps from each instrument, thereby integrating the data into a common array.

Time- and location- based algorithms were used to categorize and assign direct-reading exposure data with predetermined microenvironment classifications (at home, in transit, and at school). Personal temperature records were used to segregate indoor vs. outdoor periods. Subjects were surveyed about behaviors (e.g. mode of transport during commute), and potential household exposure sources (cigarette smoke, cooking) each day.

3.3.c. Leukotriene E4 and Cotinine

On days when personal monitoring was performed, urine was collected at approximately the same time each day (11:00 AM to 1:00 PM), spun down and frozen at minus 70 degrees Celsius after addition of protease inhibitors. Samples were subsequently batch assayed for $uLTE_4$ levels by mass spectrometry as previously described (Armstrong, Liu et al. 2009). Cotinine levels were determined by immunoassay (Muscat, Djordjevic et al. 2005). Urinary LTE_4 levels were reported in picograms (pg) per milliliter and standardized per milligram (mg) of creatinine (measured via Jaffe procedure) in order to control for urine volume. Urinary cotinine levels were reported in nanograms (ng) per milliliter and standardized per mg of creatinine.

3.3.d. Ambient $PM_{2.5}$ Monitoring

Ambient $PM_{2.5}$ concentrations were measured by a Tapered Element Oscillating Microbalance (TEOM; Rupprecht and Patashnick, East Greenbush, NY) located on the National Jewish Campus, adjacent to the elementary school and operated by the Colorado Department of Health Air Pollution Control Division. This monitor produced hourly mean concentrations on a continuous basis.

3.3.e. Analysis

We assessed whether personal PM experienced during the morning commute was associated with asthma exacerbation as indicated by $uLTE_4$ levels. The commute microenvironment comprised the outdoor portion of travel, from home to school. Additionally, ambient $PM_{2.5}$ data collected at the school was tested for a corresponding association with $uLTE_4$.

To include personal 10-sec PM readings that were lower than the instrument detection limit, an imputed value was substituted for the zero reading. This substitution was performed prior to (and necessary for) log-transformation of the data set. Imputed values were created first by stratifying the dataset by subject. Next, zero values for each subject were replaced with a heuristic value equal to one half of the smallest concentration recorded by the pDR (0.5 μg/m3). Geometric means and geometric standard deviations of the log-transformed stratified data subsets were then calculated. These distribution parameters were used to impute values for the original zero readings via a probability integral transform (Casella 2002). The imputed, or modeled, values were substituted for the original zero readings.

Levels of $uLTE_4$ were modeled as a function of home, school and morning transit-apportioned personal PM exposure and ambient morning maximum $PM_{2.5}$ using a linear mixed model with a hierarchical structure for multiple samples per panel member and a spatial exponential covariance structure to account for within-subject repeated daily measurements. Model results and descriptive statistics were obtained using log-transformed personal PM data, log-transformed $uLTE_4$ values, associated ambient data, and additional covariates, described below.

The basic linear mixed model is represented in Equation 3.1:

$$Y_{ij} = \ln(X_{ij}) = \mu_Y + \sum_{m=1}^{p} \beta_m C_{mij} + b_i + \varepsilon_{ij} \quad \text{(Equation 3.1)}$$

for i = 1, 2,…, k individuals

for j = 1, 2,…, n_i measurements of the *i*th individual, and

for m = 1, 2,…, p covariates

where X_{ij} represents measurements at the j^{th} time interval for child i, and Y_{ij} is the natural log-transformed value of X_{ij}. Y_{ij} represents the sum of the effects of: μ_Y, representing the overall intercept; the product of the regression coefficients $\beta_1, \beta_2,\ldots, \beta_p$ (the fixed effects) and the observed values of their corresponding covariates $C_{1ij}, C_{2ij},\ldots, C_{pij}$; b_i representing the random effect for the *i*th individual; and ε_{ij} representing the residual error for j^{th} observation on the i^{th} individual. Random variables b_i and ε_{ij} were assumed to be independent and normally distributed with means of 0 and variances of σ_b^2 and σ_w^2 (representing the between- and within-subject components of variance, respectively) (see Appendix 2 for detailed models).

Survey responses about health status (upper respiratory infection (URI), or cold) were included with a separate model containing concurrent ambient $PM_{2.5}$ concentrations and co-variates. Subject behavior, urinary cotinine, time-trend, meteorological conditions (temperature, pressure, humidity), subject physical characteristics (height, weight, and body mass index), and sampling instrument were tested in these models and found to be non-significant. A linear mixed model, with a spatial exponential covariance structure was used to account for within-subject repeated measures over time. All statistical analyses were conducted using SAS, PROC MIXED

(version 9.2). The interquartile range (IQR) (i.e 75th percentile minus the 25th percentile) was used to standardize pollutant slope estimates. Two-sided p-values are reported.

3.4. Results

3.4.a. Panel Data

Table 3.1 summarizes the demographics and physiological characteristics of the panel. These children were predominately African American (43%), followed by multiracial (36%), Hispanic (16%) and White (5%). One-third had been admitted into an intensive care unit for asthma at least once and nearly two-thirds had experienced an asthma exacerbation during the previous year. Based on the frequency of nighttime symptoms, approximately one-third were classified as mild, and 20% were severe based on National Asthma Education and Prevention Program (NAEPP) guidelines (Colice, Vanden Burgt et al. 1999). The mean uLTE4 value of the panel over the study period was 78.8 pg per mg creatinine. Relationships between measured PM levels and daily uLTE4, for both personal sampling and outdoor ambient sampling, are plotted in Figure 3.1.

3.4.b. PM Concentration Profiles

We segregated each child's personal exposure into home, transit, and school periods using data from the GPS and temperature sensors (Adams, Riggs et al. 2009). Time series of ambient and personal PM exposures (averaged across the entire panel) are plotted in Figure 3.2. Box-whisker plots overlaid on the Figure (3.2) indicate personal exposures for three different microenvironments (home, transit, and school).

Table 3.1. Subject demographics, asthma severity, urinary LTE_4 levels. Entries are number of children or mean value. Shown in parentheses are percentage values or minima/maxima, where indicated.

Subject Variable	Data
Panel size	30
Mild asthma*	11 (36.7%)
Moderate asthma*	13 (43.3%)
Severe asthma*	6 (20.0%)
African American	13 (43.3%)
Children with at least one ICU admission for asthma	10 (33.3%)
Children with at least one exacerbation within past year†	19 (63.3%)
Children using daily inhaled steroids	26 (86.7%)
Urinary LTE_4 (pg per mg creatinine)	78.8 (9.4, 445)
Urinary Cotinine (ng per mg creatinine)	23.5 (0.1,206)
Age	10 (7, 13)

Definition of abbreviation: ICU - intensive care unit.

Entries are number (percentage) of children or mean (minimum, maximum) unless otherwise indicated.

* Daily asthma severity categories per National Asthma Education and Prevention Program criteria.

† Exacerbations were defined as episodes requiring hospitalization, visits to emergency or urgent care departments, or prednisone bursts.

Much of the children's time during this wintertime study was spent indoors where they were exposed to PM sources that varied in source and concentration from the ambient outdoor $PM_{2.5}$ measured at the school. In the morning, during the 4 a.m. to 11

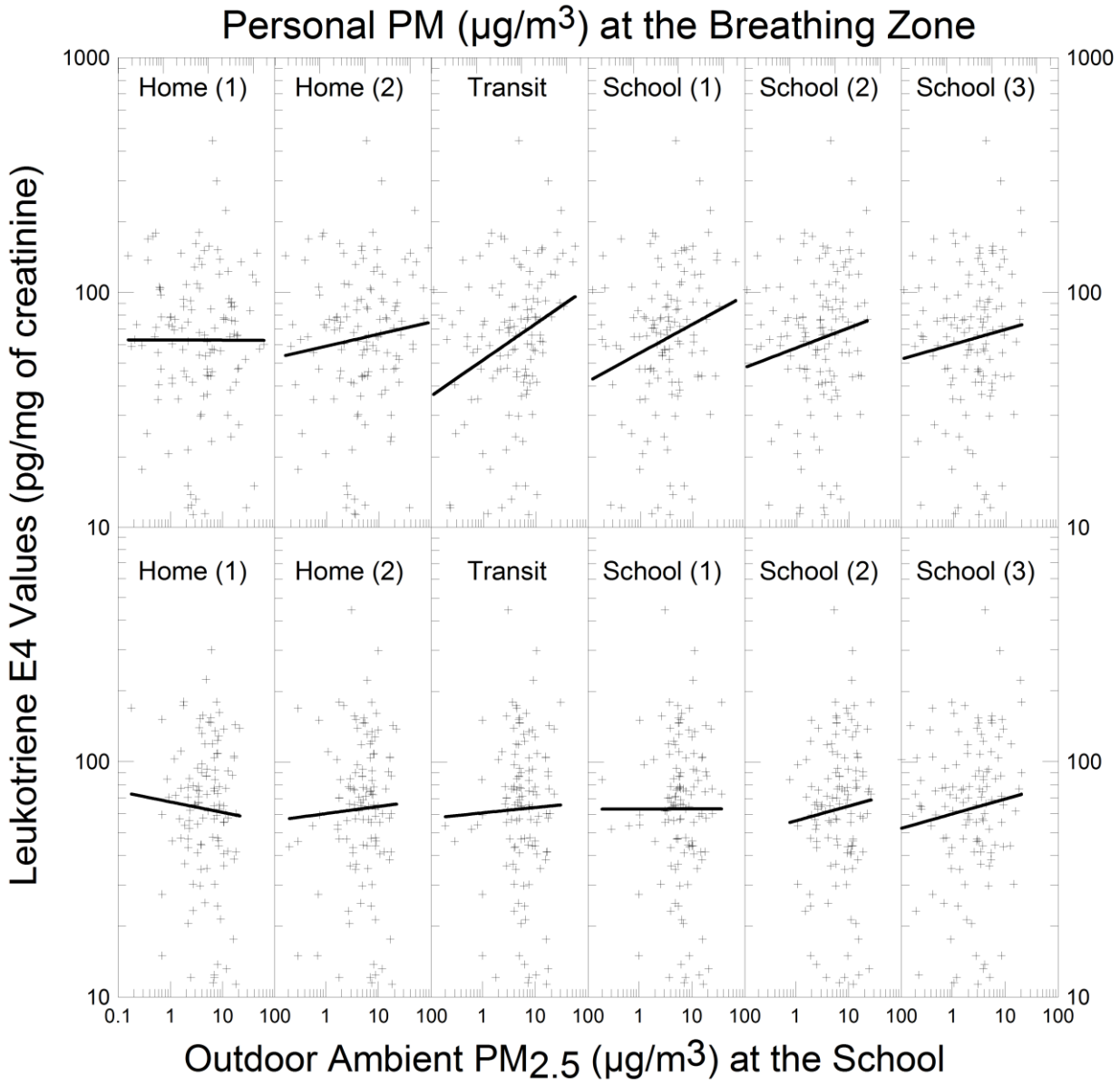

Figure 3.1. Relationships between PM levels and uLTE4. Top panels represent the relationship between uLTE4 and personal exposures; bottom panels represent uLTE4 and outdoor area-wide PM concentrations. Regression lines represent raw data associations, accounting for neither hierarchical data nor repeated measures. Panels for Home (1 & 2) represent 30 min time periods preceding transit between home and school. Panels for School (1, 2 & 3) represent 30 min time periods subsequent to the transit period.

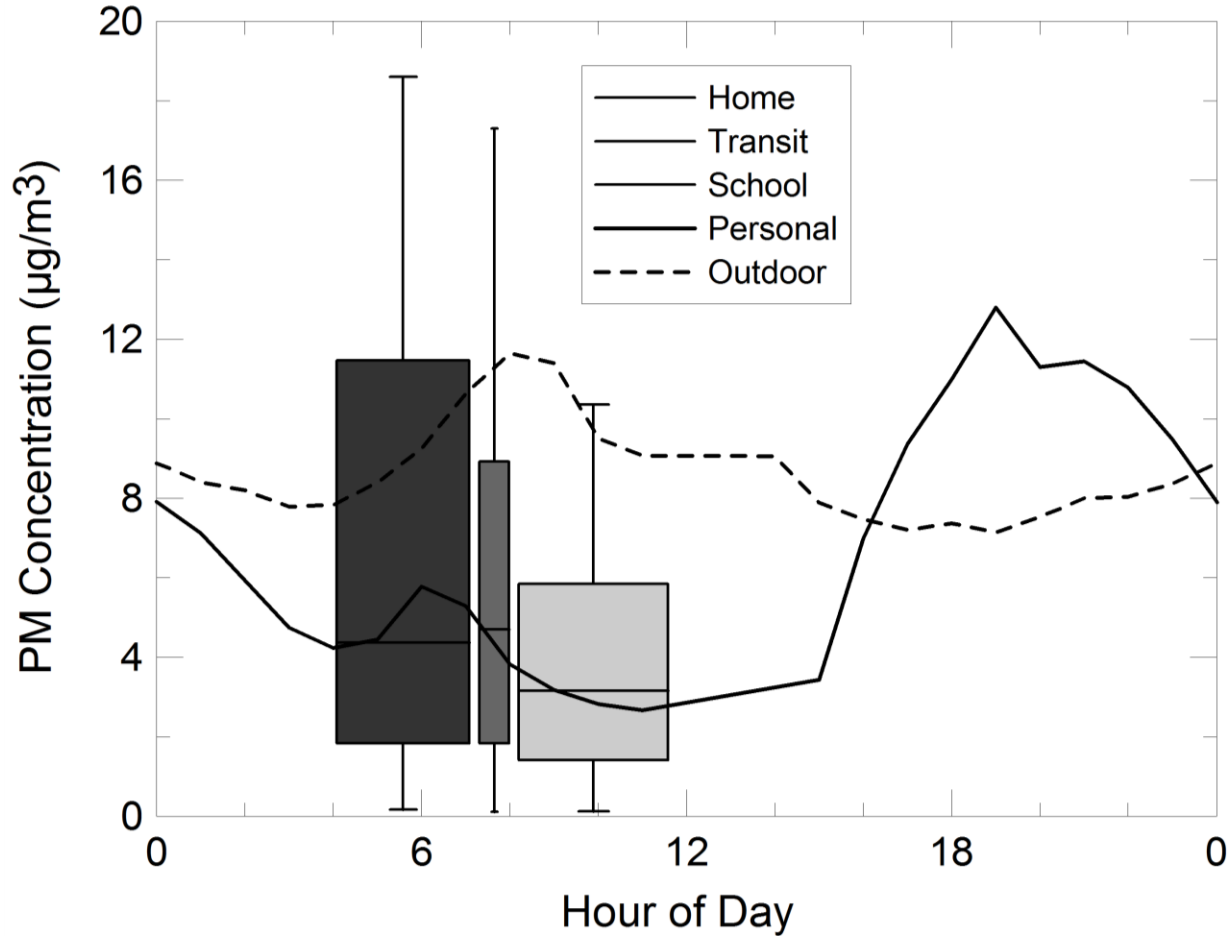

Figure 3.2. Average personal (solid line) and area-wide (dashed line) PM levels during morning hours. Boxplots illustrate medians and ranges for personal PM at home (left whisker plot - black), transit (center whisker plot – dark gray), and school (right whisker plot – light gray).

a.m. period, personal exposures were generally decreasing with a small peak occurring during the 6-8 a.m. period. The personal PM profile (averaged across all subjects and days) indicates relatively low exposures within the school microenvironment. Elevated personal PM exposure occurred at home throughout the late afternoon and evening hours. Ambient $PM_{2.5}$ concentrations tended to be highest from approximately 7-10 a.m., with a smaller peak occurring in the afternoon, around 2 p.m.

Children's transit periods varied each day, with commuting typically beginning near 7 a.m. and lasting 32 min, on average (SD±17, range 10-72 min). Most commutes to school (84%) were via motor vehicle (bus, 3%; vanpool 64%; or car, 17%). The remainder (16%), walked along city streets. The majority of vehicular routes were driven on major city streets with traffic flow managed by stoplights. Mode of transport was not significantly associated with either personal exposure or commute duration.

For modeling purposes, each child's personal exposure was time-averaged to the microenvironmental level. These microenvironments included: the hour before commuting to school (i.e., at home), time spent commuting to school (in transit), and the first hour spent within the school (school). Personal PM concentrations were typically highest at home and lowest at school (mean home, 4.3 $\mu g/m^3$; mean transit, 4.0 $\mu g/m^3$; mean school, 2.7 $\mu g/m^3$) (Figure 3.2 and Table 3.2). Although ambient PM levels tended to rise throughout the morning, personal PM levels tended to decline as children moved from home to transit to school (see Figure 3.2).

3.4.c. Morning Transit exposures are associated with increased $uLTE_4$ levels

The mean $uLTE_4$ value of this study was 78.8 pg/mg creatinine (SD = 63.8 pg/mg) and mean urinary cotinine was 22.1 ng/mg creatinine (SD = 44.3 pg/mg). An IQR increase of personal PM during home, transit or school did not have a significant effect on the level of urinary cotinine within panel subjects. Simple regressions for the relationships between $uLTE_4$ and microenvironmentally-apportioned personal PM exposures (top panels) or concurrently measured ambient $PM_{2.5}$ concentrations (bottom

Table 3.2. Summary statistics for PM Levels by microenvironment and outdoor PM Levels measured concurrently by a community-based monitor.

Concentration metric ($\mu g/m^3$)	Micro-environment	Mean*	SD*	Min Val	25th Quantile	Med	75th Quantile	Max Value
Personal PM	Home	4.3	1.4	0.2	1.8	4.5	8.6	103.3
Personal PM	Transit	4.0	1.3	0.2	2.0	5.2	8.6	56.1
Personal PM	School	2.7	1.2	0.2	1.4	3.1	5.3	24.0
Outdoor $PM_{2.5}$	Home	3.4	1.2	0.1	2.3	4.2	6.4	17.3
Outdoor $PM_{2.5}$	Transit	5.5	0.9	0.2	4.0	6.1	10.0	26.3
Outdoor $PM_{2.5}$	School	6.2	0.8	0.3	4.0	5.9	11.1	30.3

Definition of abbreviations: PM personal samples of airborne particulates <1.6 μm in aerometric diameter; $PM_{2.5}$ airborne particulates < 2.5 μm in aerometric diameter.

* Geometric

panels) measured outside the school are shown in Figure 3.2. These plots demonstrate that the strongest relationship was between transit-related personal PM and $uLTE_4$ and that correlations were much weaker with ambient area-wide concentrations measured at the same times.

In models controlling for second-hand cotinine and daily upper respiratory infection symptoms, an interquartile range increase in personal transit-related PM exposure was associated with a 15.7 % increase in $uLTE_4$ measured within 3-6 hours after exposure (95^{th} CI, 7-46%; $p < 0.001$). Weaker relationships were observed between $uLTE_4$ and personal PM exposures at home (13.9% increase per IQR, 95^{th} CI 2-58, ($p=0.03$) and school (8.6% per IQR, 95^{th} CI, -4, 31, $p=0.15$). Similar associations were not observed with PM concentrations measured by area-wide monitors ($p>0.7$) (Table 3.3 and Figure3.3). Transit-related PM effects of $uLTE_4$ continued to be

TABLE 3.3. Percent increase in urinary leukotriene E_4 per interquartile range increase in pollutant, based on linear mixed model fits for personal PM (nephelometer) and ambient $PM_{2.5}$ (tapered element oscillating microbalance) exposures each morning.

Exposure / Microenvironment	% Change $uLTE_4$	95% CI; (p-value)
Personal PM at Home	13.9	2, 58 (0.03)
Personal PM in Transit	15.7	7, 46 (0.0005)
Personal PM at School	8.6	-4, 31(0.15)
Outdoor Ambient / Home	-2	-10, 7 (0.7)
Outdoor Ambient / Transit	-1	-7, 6 (0.7)
Outdoor Ambient / School	-2	-12, 9 (0.8)

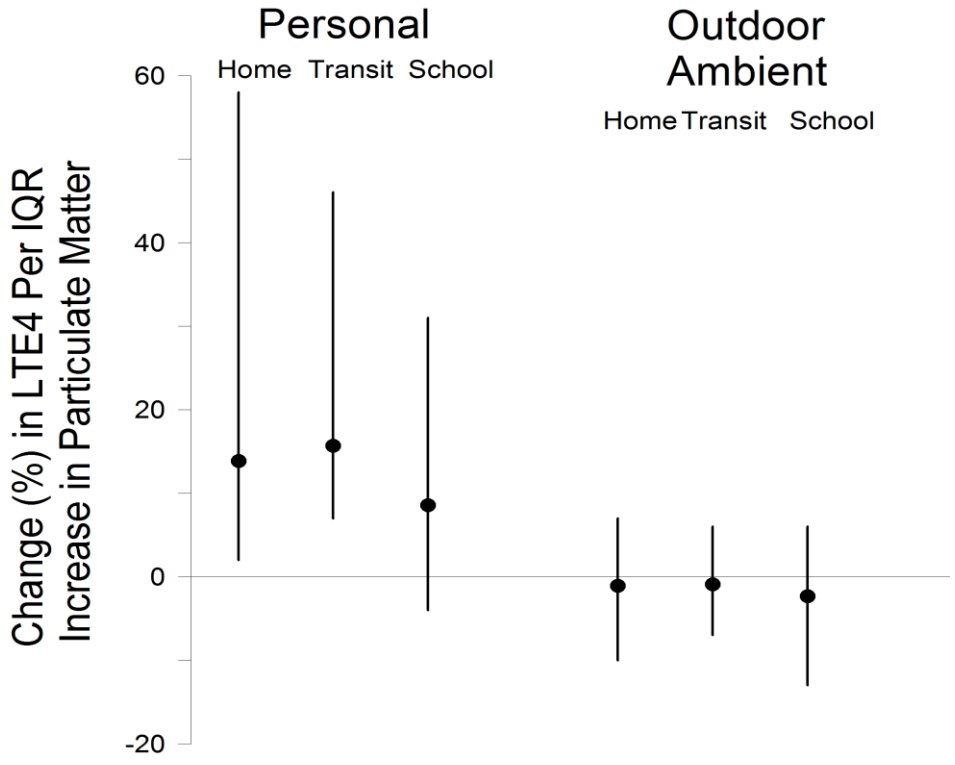

Figure 3.3. Estimated effects of PM exposure (via personal or fixed outdoor monitors) on same-day levels of urinary LTE_4. Estimates represent associations for exposures while subjects were at home, in transit or at school. Error bars represent two standard deviations about the estimate.

significant in 'co-pollutant' models that included all three microenvironments (24% increase in $uLTE_4$ during transit, 95^{th} CI, 4, 48; $p<0.019$). However, in the co-pollutant model, only the effects on $uLTE_4$ per IQR of personal PM from the transit microenvironment remained significant (Transit, p=0.019; Home, p=0.6; School, p=0.16). In all models the self-reported health status (cold/URI) was significant (p< 0.003).

3.5. Discussion

In this study, personal PM exposures measured during the morning commute were associated with $uLTE_4$ values measured within hours of exposure in children with asthma. Cysteinyl leukotrienes (LTC_4, LTD_4, LTE_4), are highly potent mediators closely linked to the pathobiology of asthma (Drazen, Obrien et al. 1992; Kumlin 2000; Rabinovitch 2007; Sanak, Bochenek et al. 2010; Rabinovitch 2012) and other disease processes (Bousquet, Jeffery et al. 2000; Laidlaw and Boyce 2012). They act as potent chemoattractants (Fregonese, Silvestri et al. 2002), leading to hyperresponsiveness of the inflammatory response to various stimuli (Gauvreau, Parameswaran et al. 2001; Rabinovitch 2012). Leukotrienes have been assessed as a marker of asthma exacerbation (Rabinovitch, Strand et al. 2006; Rabinovitch, Reisdorph et al. 2011), as well as an indicator of susceptibility (Rabinovitch 2012). As LTE_4 is thought to be an important mediator of airway inflammation and a marker of cysteinyl leukotriene formation, these results suggest that brief localized exposures to PM especially during transit are related to asthma worsening occurring soon after exposure.

Although we had reported previously that $uLTE_4$ levels increased on days when morning outdoor ambient $PM_{2.5}$ concentrations are elevated, this is the first study to

report a direct link between personal PM exposures and increased $uLTE_4$. We used a direct-reading sampling methodology that recorded personal PM levels, location, and temperature data every 10-seconds throughout the day and categorized the exposure data into predetermined microenvironments (home, transit, and school) (Adams, Riggs et al. 2009). We were able to discern a temporal pattern of brief exposure to traffic-related air pollutants and early asthma-related outcomes. Using this methodology, the magnitude of the dose-response was shown to be considerably greater per IQR (15.7%, 95^{th} CI: 7-46%, p=0.005 based on 89 records) than estimated in our previous reports (6.2% per IQR, 95^{th} CI: 1.9-10.5, p=0.009 based on 388 records) using outdoor ambient $PM_{2.5}$ concentrations measured by an area–wide monitor. This highlights the probability of considerably underestimating effects of PM on asthma with surrogate monitors that lack spatial precision. Similarly, Delfino et al. (2006) found that exhaled nitric oxide (eNO) levels in schoolchildren with asthma were associated with personal exposure but not ambient concentrations.

The findings in our study are consistent with reports of increased markers of airway inflammation within hours of air pollutant exposure (Delfino, Quintana et al. 2004; Delfino, Staimer et al. 2006). Although our sample size (30 subjects, n=89 days) was relatively small, our exposure assessment was very precise. A previous study with this panel using 24-hour averages of ambient air pollution found no significant associations between PM concentrations and daily lung function, asthma symptoms, medication use, or asthma exacerbations (Rabinovitch, Zhang et al. 2004). A follow-up study of this panel found significant associations between the morning hourly maximum $PM_{2.5}$ concentration and medication use highlighting the importance of temporal precision

(Rabinovitch, Strand et al. 2006). In the present study, we did not find an association between concurrently measured or hourly maximum ambient $PM_{2.5}$ and increased $uLTE_4$, possibly due to limited sample size as our previous studies had more than triple the number of samples.

Other asthma exacerbation markers have also been associated with personal exposure to particulate matter air pollution. In a panel study of 45 asthmatic children in urban regions of Southern California, Delfino et al. (2006), found exhaled nitric oxide (eNO) in schoolchildren with asthma was associated with personal exposure and ambient background particulate air pollutants. This association was stronger when the personal $PM_{2.5}$ measurement was near the exhaled NO measurement. They also reported that while the 2-day moving average of personal $PM_{2.5}$ was associated with inflammation, the corollary measurement of outdoor ambient $PM_{2.5}$ was not.

Children's outdoor transit to school accounted for only 2% (about 32 min) of a typical day, yet elevated PM exposures during such transit periods were significantly associated with asthma worsening. Mean Personal PM levels during the morning commute (4.0 µg/m3) were second only to personal concentrations measured at home (4.3 $\mu g/m^3$) (Table 3.2). The children's commute to school (7-8 a.m.) was concurrent with the general population's morning commute (Fig 3.2) resulting in higher ambient concentrations during this time period. Although ambient PM levels tended to increase during the morning timeframe, personal PM concentrations tended to decrease over the same time period suggesting that much of the home exposure was a result of indoor sources of PM. The ambient atmosphere during morning transit was more likely to have calm winds and a lower atmospheric mixing height resulting in higher pollutant

concentrations near roads (Adams, Nieuwenhuijsen et al. 2001; Patel, Chillrud et al. 2009). However, on-road exposures may have been somewhat attenuated in wintertime, as vehicle windows were likely closed. Urban traffic has been identified as a significant source of $PM_{2.5}$ (Kinney, Aggarwal et al. 2000) and is associated with respiratory morbidity and mortality (Peters, Wichmann et al. 1997; Peel, Tolbert et al. 2005; Penttinen, Vallius et al. 2006; Chattopadhyay, Mukherjee et al. 2007; Liu, Poon et al. 2009), with stronger associations in asthmatic populations, especially children (Delfino, Zeiger et al. 1998; Chew 2000; Delfino, Gong Jr et al. 2003; Strickland, Darrow et al. 2010; Lin, Huang et al. 2011). Additionally, traffic-related PM may contain higher concentrations of oxidant-generating pollutants known to induce lung inflammation (Repine, Reiss et al. 2008) explaining some of the potency of the exposure/response relationship. Exposure to traffic-related PM and associated health effects are of specific interest in asthmatic sub-populations (HEI 2010) especially considering that in-vehicle exposure to $PM_{2.5}$ can be higher than concentrations recorded at outdoor community-based ambient monitors (Riediker, Williams et al. 2003; Brown, Sarnat et al. 2012).

The highest mean personal PM concentrations occurred at home, where an IQR increase in personal PM exposure was also significantly associated with $uLTE_4$ ($p=0.03$). However, when the effects of IQR increases were assessed with all microenvironments evaluated in a single 'co-pollutant' model, only the transit microenvironment remained significant (Transit, $p=0.019$; Home, $p=0.6$; School, $p=0.16$). There was likely some collinearity between exposures between these three microenvironments. Additionally, the temporality of the exposure/response relationship may have influenced our ability to detect associations between multiple

microenvironmental exposures and a single biomarker of asthma worsening. Collection of uLTE4 occurred between 11am and 1pm each day; therefore, whether the timing of exposure/response favored an association between Transit exposures and uLTE4 production (as compared to associations between uLTE4 and either home or school exposures) is unknown. Within this study the delay between exposure and response was detected within a fraction of a day, but additional work would be needed to define a more precise relationship between exposure and the expected temporal window of observed effect.

As we were assessing a relatively acute exposure during a defined microenvironment, we did not assess for a lag effect in days following exposure. Our previous study (Rabinovitch, Strand et al. 2006) did not detect a lag effect when assessing morning ambient $PM_{2.5}$ as a predictor of $uLTE_4$. Other studies have found lag effects on health outcomes (e.g. FEV1) when measuring personal exposure over multiple days (Delfino, Quintana et al. 2004; Delfino, Staimer et al. 2006).

The characteristic peaks and valleys of outdoor ambient PM concentrations were evident in the daily average profiles of ambient and personal PM (Figure 3.2). Studies using similar equipment have reported morning and evening personal exposure concentration peaks (LaRosa 2002; Zhu, Aikawa et al. 2005). We saw a similar bi-modal pattern in this study (Figure 3.2). The evening peak in personal exposure likely results from indoor sources including cooking, heating/lighting (e.g., candle-burning), or play activities. In some households the evening peak may be dominated by PM from cigarette smoke, although urinary cotinine was non-significant in our models. The outdoor community-based monitor reported a characteristic peak each morning, likely in

response to traffic-related PM emissions during the morning rush hour. Ambient PM concentrations peaks during afternoon rush hour were not as high (data not shown), perhaps reflecting more turbulent (windy) conditions enhancing atmospheric mixing, and eliminating atmospheric inversions.

Personal PM from any of the three microenvironments did not have a significant effect on the level of urinary cotinine within panel subjects. Most children's transit to school was via bus or vanpool, likely minimizing exposure to SHS during this period. While the median personal PM values at home and in-transit were similar (Fig 3.2) there was more variability in home microenvironments as some homes were very "clean" and some had higher PM concentrations, possibly from tobacco smoke. Children with high cotinine levels were likely exposed to higher PM levels at home (from both SHS and other sources) on a day-to-day basis. As such, the impact of an IQR change in personal home-apportioned PM on uLTE4 levels may have been blunted as children with SHS exposure would most likely be at the higher end of the PM dose range resulting in flatter dose-response curves from home exposures compared to transit (Rabinovitch, Silveira et al. 2011).

The associations reported here are limited to wintertime exposures in an urban setting. Previous studies have shown that seasonality can affect air pollutant concentrations (Rodes, Lawless et al. 2010). In addition, ambient and personal PM exposures were estimated using different techniques; the former was a direct measure of PM mass concentration (TEOM) and the later was an indirect measure of PM mass using scattered light (nephelometer, PDR-1200). However, we attempted to account for measurement error by normalizing our personal exposure data to a filter sample

collected immediately downstream of the nephelometer and weighed for PM mass each day (and for each child). Further studies using new, miniaturized sampling equipment for specific PM constituents, such as black carbon PM, may provide even more precise exposure indices.

In summary, we have reported a strong association between traffic-related personal PM exposure and same-day $uLTE_4$ measurements that was not detectable using measurements from an area-wide monitor. Health estimates from this study, although relatively large, may yet underestimate the association between traffic-related air pollution and airway inflammation in asthmatics since particle mass (measured in our study) may not sufficiently represent the most pathogenic components from fossil fuel combustion (Delfino, Staimer et al. 2006) . The panel investigated in this study may represent only a subfraction of the population of young asthmatics, as the majority of these children suffered from moderate to severe asthma. Also, some of the children in this panel were attending the Kunsberg school because they were at higher risk of asthma exacerbation due to poor disease management. Nonetheless, our findings suggest that personal, spatiotemporal exposure assessment is substantially more precise than using outdoor area-wide monitors and that reliance solely on area-wide measurements may severely underestimate the adverse effects of brief localized PM exposures.

CHAPTER 4

4.1. Summary of Major Findings

One aim of this work was to develop a highly-resolved, temporospatially-referenced method to improve personal exposure assessment for particulate matter health hazards. This method apportioned exposures based on highly-resolved measurements of personal PM levels as a function of location and time. Historically, such data has been difficult to collect and interpret. However, we developed a computer-based algorithm to transform this large amount of exposure data into useable information by interpreting the time and location of each data point taken and assigning a particular microenvironment classification. We then applied this method to study PM exposure and asthma worsening in a panel of urban schoolchildren. Major findings from this work included:

- Our study population of children experienced personal exposures that varied substantially between different microenvironments (home, school, transit) each day. Differences in personal exposures between these microenvironments are most likely generalizable to asthmatic children living in similar urban locales.
- Centrally-located, outdoor, ambient monitors were, at best, only marginally predictive of medium-term (hour-length) personal exposures and only when individuals were proximate to that monitor. Thus, outdoor PM measurements made by a centrally-located ambient monitor represent only a small fraction of an individual's daily PM intake.

- Centrally-located, outdoor, ambient monitor concentrations were not correlated with personal exposures experienced in the home microenvironment, where most subjects received the highest PM exposures.
- A study subject's microenvironment had significant impact on measured personal exposures. Furthermore, personal exposures in one microenvironment were strongly correlated with levels in ensuing microenvironments later in the day. This finding supports a within-day and subject-specific effect, known as the 'personal cloud.' This effect is hypothesized to occur because subjects either create or carry a 'personal cloud' of PM as they move from one microenvironment to the next.
- Within our study population there was a strong association between traffic-related personal PM exposure during the morning commute and same-day $uLTE_4$ levels measured at school. This association was not detected using PM exposure measurements from a centrally-located, outdoor, ambient monitor. This association was stronger than ones previously detected using an outdoor monitor with a substantially larger sample size. Thus, studies that rely on outdoor, area-wide measurements may underestimate both the adverse effects of brief localized PM exposures, for example, during transit or other activities.
- Asthma worsening estimates from this study, although relatively large, may underestimate the association between traffic-related air pollution and airway inflammation in asthmatics since PM mass (measured in this study) may not sufficiently represent the most pathogenic components from fossil fuel combustion (Delfino, Staimer et al. 2006).

- The ability to find associations with a relatively small number of samples suggests that personal, spatiotemporal exposure assessment is substantially more precise than outdoor, area-wide monitors.
- The method was capable of collecting and apportioning over 8600 personal exposure data points per day with both high resolution and accuracy and allowed preparation of a detailed 'exposure budget' for each subject. The highly-resolved, space- and time-referenced data allowed more precise exposure assessment of mobile subjects.

4.2. Limitations of the Method

This method integrated continuous measures of personal PM levels with the corresponding microenvironment (i.e. work/school, home, transit) of the subject. Monitoring equipment include global positioning system (GPS) receiver, a miniature aerosol nephelometer, and an ambient temperature monitor to estimate the location, time, and magnitude of personal exposure to particulate matter air pollution. Application of the method provided greater resolution of personal PM levels in microenvironments and allowed preparation of a more detailed 'exposure budget' for each subject. The production of highly-resolved, space- and time-referenced exposure data permitted rigorous exposure assessment of mobile cohorts in the workforce or community. However, there were limitations experienced with the application of the developed method. Some of the limitations were:

- Nephelometers sense the amount of light (λ = 880 nm) scattered by particles drawn though a sensing zone. The amount of light scattered by an aerosol is dependent not only upon the concentration of particles but also on properties of the particles,

themselves, such as their shape, composition, and index of refraction. Thus, particles from different sources may scatter different amounts of light, leading to biases when PM exposure from one microenvironment is compared to another. This source of bias was likely only partially ameliorated through the use of a gravimetric filter correction, applied each day.

- Cyclones (1.6 μm cutpoint, Model GK2.05, BGI Inc., Waltham MA) used to sample fine particulate matter fine separated aerosols at a 1.6 μm cutpoint. This cutpoint resulted from a volumetric flowrate required to meet the gravimetric limit of detection for the downstream filter. The cutpoint did not match the 2.5 μm diameter that is regulated by the U.S. EPA's National Ambient Air Quality Standard. However, this cutpoint should have collected more than 90% of the ambient $PM_{2.5}$ fraction based on urban aerosol distributions.
- Use of the backpack sampler by youth constrained the placement of the sampling inlet, as minimal protrusion of equipment outside the physical boundaries of the backpack was required. Therefore the inlet location (2 inches above the top surface of the backpack, slightly to the rear of the wearer's left shoulder) was chosen to best approximate the breathing zone. Sampling of adult populations would likely allow the placement of the sampling inlet to be configured closer to the traditional 'lapel' sampling location.
- The pDR is prone to overestimating particle mass, however, correlation values between pDR signals and gravimetrically-derived mass concentrations are quite high. A differential correction based on the daily gravimetric analysis collected was used to normalize the pDR data.

- Although GPS technology is improving in sensitivity it may not be able to receive signals in all environments (i.e. indoors). In addition, the technology is still susceptible to spurious signals (signal bounce) that can provide incorrect geospatial references. In many cases, these spurious signals can be detected and corrected through post-processing algorithms.
- GPS units do not reference outdoors/indoors in their recorded signals. The use of complementary sensors (e.g. light meters and temperature monitors), can help enable these determinations.
- GPS receivers and other miniaturized sensors are relatively expensive, however, this will change as miniaturization and integration continue (e.g. most cell-phones now have GPS receiver chips).

4.3. Potential Future Research

Use of GIS and GPS technologies in concert with highly-resolved sample collection holds potential to provide new insights in the field of human exposure assessment. The combination of the technologies provides new levels of accuracy and precision for defining the relationship between time-location and exposure. Combination of the data within GIS allows for visual and tabular analysis of exposure-related data and other geospatially relevant information. The existing data set from this research is very rich in terms of the amount of temporospatially referenced data, and the related health indicator data. There are potentially many different analyses that that could be accomplished with the data. Avenues for further research include:

- Expanded evaluation of the geospatial aspect of the dataset. Vehicle-based navigation and web-based map delivery applications have generated a

corresponding increase in the geo-location information of businesses, other structures, and public gathering areas (e.g., parks). These geo-location data could be cross-referenced with the existing exposure profile data to potentially identify likely activities (e.g., grocery shopping, eating at restaurants, visiting fueling stations). Knowledge of the activities could produce further associations between microenvironments and personal exposures.

- Similarly, traffic density data with respect to sections of roadways within the study area could be cross-referenced with exposure profile data to investigate potential associations between traffic density and personal exposure.
- Other microenvironmental-based analyses could target relationships between exposures and health indicators, such as home exposures and urinary cotinine levels, or perhaps spirometry data.
- Implementing improved instrumentation/technologies within the sampling method, such as direct reading technologies for specific components of ambient aerosols may provide and enhanced assessment of exposures.
- Investigation of more complex microenvironmental classification algorithms could be assessed to improve precision, especially during transition from one microenvironment to another.

REFERENCES

Adams, C., P. Riggs, et al. (2009). "Development of a method for personal, spatiotemporal exposure assessment." Journal Of Environmental Monitoring **11**(7): 1331-1339.

Adams, H. S., M. J. Nieuwenhuijsen, et al. (2001). "Determinants of fine particle (PM2.5) personal exposure levels in transport microenvironments, London, UK." Atmospheric Environment **35**(27): 4557-4566.

Adgate, J. L., G. Ramachandran, et al. (2002). "Spatial and temporal variability in outdoor, indoor, and personal $PM_{2.5}$ exposure." Atmospheric Environment **36**(20): 3255.

Adgate, J. L., G. Ramachandran, et al. (2003). "Longitudinal variability in outdoor, indoor, and personal $PM_{2.5}$ exposure in healthy non-smoking adults." Atmospheric Environment **37**: 993.

Armstrong, M., A. H. Liu, et al. (2009). "Leukotriene-E4 in human urine: Comparison of on-line purification and liquid chromatography–tandem mass spectrometry to affinity purification followed by enzyme immunoassay." Journal of Chromatography B **877**(27): 3169-3174.

Arrandale, V. H., M. Brauer, et al. (2011). "Exposure Assessment in Cohort Studies of Childhood Asthma." Environmental Health Perspectives **119**(5): 591-597.

Benton-Vitz, K. and J. Volckens (2008). "Evaluation of the pDR-1200 Real-Time Aerosol Monitor." Journal of Occupational and Environmental Hygiene **5**: 353-359.

Bolstad, P., A. Jenks, et al. (2005). "A Comparison of Autonomous, WAAS, Real-Time, and Post-Processed Global Positioning Systems (GPS) Accuracies in Northern Forests." Northern Journal of Applied Forestry **22**: 5-11.

Bousquet, J., P. K. Jeffery, et al. (2000). "Asthma - From bronchoconstriction to airways inflammation and remodeling." American journal of respiratory and critical care medicine **161**(5): 1720-1745.

Braccioni, F., S. C. Dorman, et al. (2002). "The effect of cysteinyl leukotrienes on growth of eosinophil progenitors from peripheral blood and bone marrow of atopic subjects." Journal of Allergy and Clinical Immunology **110**(1): 96-101.

Branis, M. and J. Kolomaznikova (2010). "Year-long continuous personal exposure to $PM_{2.5}$ recorded by a fast responding portable nephelometer." Atmospheric Environment **44**(24): 2865-2872.

Brown, K. W., J. A. Sarnat, et al. (2012). "Concentrations of PM2.5 mass and components in residential and non-residential indoor microenvironments: The

Sources and Composition of Particulate Exposures study." Journal of Exposure Science and Environmental Epidemiology **22**(2): 161-172.

Casella, G. (2002). Statistical inference. Pacific Grove, CA, Duxbury/Thomson Learning.

Chakrabarti, B., P. M. Fine, et al. (2004). "Performance evaluation of the active-flow personal DataRAM PM2.5 mass monitor (Thermo Anderson pDR-1200) designed for continuous personal exposure measurements." Atmospheric Environment **38**(20): 3329-3340.

Chattopadhyay, B. P., A. Mukherjee, et al. (2007). "Exposure to Vehicular Pollution and Assessment of Respiratory Function in Urban Inhabitants." Lung **185**(5): 263-270.

Chew, F. T., Goh, D.Y.T., Ooi, B.C., Saharom, R., Hui, J.K.S., Lee, B.W. (2000). "Association of ambient air pollution levels with acute asthma exacerbation among children in Singapore. ." Allergy **55**(4): 340-347.

Cohen, B., McCammon, CS (2001). Air sampling instruments for evaluation of atmospheric contaminants. Cincinnati, Ohio, ACGIH Worldwide.

Colice, G. L., J. Vanden Burgt, et al. (1999). "Categorizing asthma severity." American journal of respiratory and critical care medicine **160**(6): 1962-1967.

Delfino, R., R. Zeiger, et al. (1998). "Symptoms in pediatric asthmatics and air pollution: differences in effects by symptom severity, anti-inflammatory medication use and particulate averaging time." Environmental Health Perspectives **106**(11).

Delfino, R. J., H. Gong Jr, et al. (2003). "Asthma Symptoms in Hispanic Children and Daily Ambient Exposures to Toxic and Criteria Air Pollutants." Environmental Health Perspectives **111**(4): 647.

Delfino, R. J., P. J. E. Quintana, et al. (2004). "Association of FEV1 in asthmatic children with personal and microenvironmental exposure to airborne particulate matter." Environmental Health Perspectives **112**(8): 932-941.

Delfino, R. J., N. Staimer, et al. (2006). "Personal and ambient air pollution is associated with increased exhaled nitric oxide in children with asthma." Environmental Health Perspectives **114**(11): 1736-1743.

Delfino, R. J., Zeiger, R.S., Seltzer, J.M., Street, D.H., and C. McLaren (2002). "Association of asthma symptoms with peak particulate air pollution and effect modification by anti-inflammatory medication use. ." Environmental Health Perspectives **110**: A607-A617.

Dockery, D. W., C. A. Pope, et al. (1993). An Association between Air Pollution and Mortality in Six U.S. Cities. New England Journal of Medicine, New England Journal of Medicine. **329:** 1753-1759.

Dons, E., L. Int Panis, et al. (2011). "Impact of time–activity patterns on personal exposure to black carbon." Atmospheric Environment **45**(21): 3594-3602.

Drazen, J. M., J. Obrien, et al. (1992). "RECOVERY OF LEUKOTRIENE-E4 FROM THE URINE OF PATIENTS WITH AIRWAY-OBSTRUCTION." American Review of Respiratory Disease **146**(1): 104-108.

Egeghy, P. P., J. J. Quackenboss, et al. (2005). "Determinants of temporal variability in NHEXAS-Maryland environmental concentrations, exposures, and biomarkers." Journal of Exposure Analysis & Environmental Epidemiology **15**(5): 388-397.

Elgethun, K., R. A. Fenske, et al. (2003). "Time-Location Analysis for Exposure Assessment Studies of Children Using a Novel Global Positioning System Instrument." Environmental Health Perspectives **111**(1): 115.

Elgethun, K., M. G. Yost, et al. (2007). "Comparison of global positioning system (GPS) tracking and parent-report diaries to characterize children's timeâ€“location patterns." Journal of Exposure Science & Environmental Epidemiology **17**(2): 196-206.

EPA. (2001, 2003). "Consolidated Human Activity Database." Retrieved 10, 2007, from http://www.epa.gov/chadnet1/.

EPA, U. S. (2004). Air Quality Criteria for Particulate Matter, Vol. 1. . Research Triangle Park, NC, U.S. Environmental Protection Agency

Fischer, S. L. (2007). "Field performance of a nephelometer in rural kitchens: effects of high humidity excursions and correlations to gravimetric analyses." Journal of exposure science & environmental epidemiology **17**(2).

Floyd, R. P. (1978). Geodetic Benchmarks. NOAA.

Freeman, N. C. G., P. J. Lioy, et al. (1999). Responses to the Region 5 NHEXAS time/activity diary. Journal of Exposure Analysis & Environmental Epidemiology, Nature Publishing Group. **9:** 414.

Fregonese, L., M. Silvestri, et al. (2002). "Cysteinyl leukotrienes induce human eosinophil locomotion and adhesion molecule expression via a CysLT(1) receptor-mediated mechanism." Clinical and Experimental Allergy **32**(5): 745-750.

Gauvreau, G. M., K. N. Parameswaran, et al. (2001). "Inhaled leukotriene E-4, but not leukotriene D-4, increased airway inflammatory cells in subjects with atopic asthma." American journal of respiratory and critical care medicine **164**(8): 1495-1500.

Green, R. S., S. Smorodinsky, et al. (2004). "Proximity of California Public Schools to Busy Roads." Environmental Health Perspectives **112**(1): 61-66.

Gulliver, J. and D. Briggs (2007). "Journey-time exposure to particulate air pollution." Atmos Env **41**: 7195-7207.

HEI (2010). Traffic-Related Air Pollution: A Critical Review of the Literature on Emissions, Exposure, and Health Effects. . Boston, MA, Health Effects Institute.

Henderson, S. B., B. Beckerman, et al. (2007). "Application of Land Use Regression to Estimate Long-Term Concentrations of Traffic-Related Nitrogen Oxides and Fine Particulate Matter." Environmental Science & Technology **41**(7): 2422-2428.

Henneberger, P. K., A.-C. Olin, et al. (2005). "The Incidence of Respiratory Symptoms and Diseases Among Pulp Mill Workers With Peak Exposures to Ozone and Other Irritant Gases." Chest **128**(4): 3028-3037.

Hoek, G., R. Beelen, et al. (2008). "A review of land-use regression models to assess spatial variation of outdoor air pollution." Atmospheric Environment **42**(33): 7561-7578.

Hoek, G., B. Brunekreef, et al. (2002). "Association between mortality and indicators of traffic-related air pollution in the Netherlands: a cohort study." Lancet **360**(9341): 1203-1209.

Hsueh-Ting, C., H. Chir-Chang, et al. (2006). A ubiquitous warning system for asthma-inducement. Sensor Networks, Ubiquitous, and Trustworthy Computing, 2006. IEEE International Conference on.

Hutcheon, J. (2010). "Random measurement error and regression dilution bias." BMJ **341**(7762): 1402.

Hystad, P. U., E. M. Setton, et al. (2009). "Modeling residential fine particulate matter infiltration for exposure assessment." Journal of Exposure Science and Environmental Epidemiology **19**(6): 570-579.

IOM (2000). Clearing the Air: Asthma and Indoor Air Exposures. Washington, DC, National Academy Press.

Janssen, N. A. H., B. Brunekreef, et al. (2003). "The Relationship between Air Pollution from Heavy Traffic and Allergic Sensitization, Bronchial Hyperresponsiveness, and Respiratory Symptoms in Dutch Schoolchildren." Environmental Health Perspectives **111**(12): 1512.

Jerrett, M., M. A. Arain, et al. (2007). "Modeling the Intraurban Variability of Ambient Traffic Pollution in Toronto, Canada." Journal of Toxicology and Environmental Health, Part A **70**(3-4): 200-212.

Johannesson, S., S. Rappaport, et al. (2011). "Variability of environmental exposure to fine particles, black smoke, and trace elements among a Swedish population." Journal of Exposure Science & Environmental Epidemiology **21**(5): 506-514.

Kanwal, R., G. Kullman, et al. (2006). Evaluation of Flavorings-Related Lung Disease Risk at Six Microwave Popcorn Plants. Journal of Occupational & Environmental Medicine. **48:** 149-157.

Kim, J. Y., Magari, Shannon R., Herrick, Robert F., Smith, Thomas J., and Christiani, David C. (2004). "Comparison of Fine Particle Measurements from a Direct-Reading Instrument and a Gravimetric Sampling Method." Journal of Occupational and Environmental Hygiene **1**(11): 707 — 715.

Kinney, P. L., M. Aggarwal, et al. (2000). "Airborne Concentrations of PM 2.5 and Diesel Exhaust Particles on Harlem Sidewalks: A Community-Based Pilot Study." Environmental Health Perspectives **108**(3): 213.

Klepeis, N., W. Nelson, et al. (2001). "The National Human Activity Pattern Survey: a resource for assessing exposure to environmental pollutants." J Exp Anal Environ Epidemiol **11**: 231-252.

Koenig, J. Q. (1999). "Air pollution and asthma." The journal of allergy and clinical immunology **104**(4): 717-722.

Kumlin, M. (2000). "Measurement of leukotrienes in humans." American journal of respiratory and critical care medicine **161**(2 II).

Lachenmyer, C. and G. M. Hidy (2000). Urban Measurements of Outdoor-Indoor PM[sub 2.5] Concentrations and Personal Exposure in the Deep South. Part I. Pilot Study of Mass Concentrations for Nonsmoking Subjects. Aerosol Science & Technology, Taylor & Francis Ltd. **32:** 34-51.

Laidlaw, T. M. and J. A. Boyce (2012). "Cysteinyl leukotriene receptors, old and new; implications for asthma." Clinical & Experimental Allergy **42**(9): 1313-1320.

Lanki, T., A. Ahokas, et al. (2007). "Determinants of personal and indoor $PM_{2.5}$ and absorbance among elderly subjects with coronary heart disease." Journal of Exposure Science & Environmental Epidemiology **17**(2): 124-133.

LaRosa, L. E., Buckley, T.J., Wallace, L.A. (2002). "Real-time indoor and outdoor measurements of black carbon in an occupied house: an examination of sources." Journal of the Air & Waste Management Association **52**: 174-185.

Lin, W., W. Huang, et al. (2011). "Acute Respiratory Inflammation in Children and Black Carbon in Ambient Air before and during the 2008 Beijing Olympics." Environmental Health Perspectives **119**(10): 1507-1512.

Liu, L., R. Poon, et al. (2009). "Acute Effects of Air Pollution on Pulmonary Function, Airway Inflammation, and Oxidative Stress in Asthmatic Children." Environmental Health Perspectives **117**(4): 668-674.

McCreanor, J., P. Cullinan, et al. (2007). Respiratory Effects of Exposure to Diesel Traffic in Persons with Asthma. New England Journal of Medicine. **357:** 2348-2358.

McCurdy, T. and S. Graham (2003). "Using human activity data in exposure models: analysis of discriminating factors." J Exp Anal Environ Epidemiol **13**: 294-317.

Michaels, R. A. and M. T. Kleinman (2000). Incidence and Apparent Health Significance of Brief Airborne Particle Excursions. Aerosol Science & Technology, Taylor & Francis Ltd. **32:** 93-105.

Muscat, J. E., M. V. Djordjevic, et al. (2005). "Racial differences in exposure and glucuronidation of the tobacco-specific carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)." Cancer **103**(7): 1420-1426.

NOAA-NWS. (2008). "DENVER, COLORADO TEMPERATURE NORMALS AND EXTREMES." Retrieved Dec 8, 2008, from http://www.crh.noaa.gov/bou/include/showProduct.php?product=febn.txt&parentdir=cli.

NRC-NAS (1998). Research Priorities for Airborne Particulate Matter I: Immediate Priorities and a Long-Range Research Portfolio. Washington, DC, National Academy Press.

Ott, D. K., N. Kumar, et al. (2008). "Passive sampling to capture spatial variability in PM10–2.5." Atmospheric Environment **42**(4): 746-756.

Oudyk, J., A. T. Hatnes, et al. (2003). Investigating Respiratory Responses to Metalworking Fluid Exposure. Applied Occupational & Environmental Hygiene. **18:** 939.

Ozkaynak, H. (1996). "Personal exposure to airborne particles and metals: results from the Particle TEAM study in Riverside, California." Journal of exposure analysis and environmental epidemiology **6**(1): 57-78.

Patel, M. M., S. N. Chillrud, et al. (2009). "Spatial and temporal variations in traffic-related particulate matter at New York City high schools." Atmospheric Environment **43**(32): 4975-4981.

Peel, J. L., P. E. Tolbert, et al. (2005). "Ambient air pollution and respiratory emergency department visits." Epidemiology **16**(2): 164-174.

Penttinen, P., M. Vallius, et al. (2006). "Source-Specific Fine Particles in Urban Air and Respiratory Function Among Adult Asthmatics." Inhalation Toxicology **18**(3): 191-198.

Peters, A., Dockery, D.W., Heinrich, J., Wichmann, H.E. (1997). "Shortterm effects of particulate air pollution on respiratory morbidity in asthmatic children. ." Eur. Respir. J. **10**(4): 872-879.

Peters, A., E. Wichmann, et al. (1997). "Respiratory effects are associated with the number of ultrafine particles." American journal of respiratory and critical care medicine **155**(4): 1376-1383.

Phillips, M., Hall, T., Esmen, N., Lynch, R., and Johnson, D. (2001). "Use of Global Positioning System Technology to Track Subjects' Location During Environmental Exposure Sampling." Journal of exposure analysis and environmental epidemiology **11**: 207-215.

Pope, A. and D. Dockery (2006). "Health Effects of Fine Particulate Air." J. Air & Waste Manage. Assoc **56**: 709-742.

Pope, C. A. (2004). Air Pollution and Health: Good News and Bad. New England Journal of Medicine**:** 1132-1134.

Qing Yu, M., B. J. Turpin, et al. (2005). "Influence of ambient (outdoor) sources on residential indoor and personal PM2.5 concentrations: Analyses of RIOPA data." Journal of Exposure Science and Environmental Epidemiology **15**(1): 17-28.

Quintana, P. J., J. R. Valenzia, et al. (2001). "Monitoring of 1-min personal particulate matter exposures in relation to voice-recorded time-activity data." Environmental research **87**(3): 199-213.

Quintana, P. J. E., J. R. Valenzia, et al. (2001). "Monitoring of 1-Min Personal Particulate Matter Exposures in Relation to Voice-Recorded Time-Activity Data." Environmental Research **87**(3): 199-213.

Rabinovitch, N. (2007). "Urinary leukotriene E-4." Immunology and Allergy Clinics of North America **27**(4): 651-+.

Rabinovitch, N. (2012). "Urinary leukotriene E-4 as a Biomarker of Exposure, Susceptibility and Risk in Asthma." Immunology and Allergy Clinics of North America **32**(3): 433-+.

Rabinovitch, N., N. Reisdorph, et al. (2011). "Urinary leukotriene E-4 levels identify children with tobacco smoke exposure at risk for asthma exacerbation." Journal of Allergy and Clinical Immunology **128**(2): 323-327.

Rabinovitch, N., L. Silveira, et al. (2011). "The Response of Children with Asthma to Ambient Particulate Is Modified by Tobacco Smoke Exposure." American journal of respiratory and critical care medicine **184**(12): 1350-1357.

Rabinovitch, N., M. Strand, et al. (2006). "Particulate levels are associated with early asthma worsening in children with persistent disease." American journal of respiratory and critical care medicine **173**(10): 1098-1105.

Rabinovitch, N., M. Strand, et al. (2008). "Exposure to tobacco smoke increases leukotriene E(4)-related albuterol usage and response to montelukast." Journal of Allergy and Clinical Immunology **121**(6): 1365-1371.

Rabinovitch, N., L. Zhang, et al. (2006). "Urine leukotriene E4 levels are associated with decreased pulmonary function in children with persistent airway obstruction." Journal of Allergy and Clinical Immunology **118**(3): 635-640.

Rabinovitch, N., L. Zhang, et al. (2004). "Effects of wintertime ambient air pollutants on asthma exacerbations in urban minority children with moderate to severe disease." Journal of Allergy and Clinical Immunology **114**(5): 1131.

Rappaport, S. M. and L. L. Kupper (2004). "Variability of environmental exposures to volatile organic compounds." Journal of Exposure Analysis & Environmental Epidemiology **14**(1): 92-107.

Reed, C. L. (2000). "Use of a Continuous Nephelometer to Measure Personal Exposure to Particles During the U.S. Environmental Protection Agency Baltimore and Fresno Panel Studies." Journal of the Air & Waste Management Association **50**(7).

Repine, J. E., O. K. Reiss, et al. (2008). "Effects of fine carbonaceous particles containing high and low unpaired electron spin densities on lungs of female mice." Translational Research **152**(4): 185-193.

Riediker, M., R. Williams, et al. (2003). "Exposure to particulate matter, volatile organic compounds, and other air pollutants inside patrol cars." Environmental Science & Technology **37**(10): 2084-2093.

Robinson, J. (1988). "Time-diary research and human exposure assessment: some methodological considerations." Atmos. Environ. **22**: 2085-2092.

Rodes, C. E., P. A. Lawless, et al. (2001). "The relationships between personal PM exposures for elderly populations and indoor and outdoor concentrations for three retirement center scenarios." J Expo Anal Environ Epidemiol **11**(2): 103-115.

Rodes, C. E., P. A. Lawless, et al. (2010). "DEARS particulate matter relationships for personal, indoor, outdoor, and central site settings for a general population." Atmospheric Environment **44**(11): 1386-1399.

Roosbroeck, S., Li, R, Hoek, G, Lebret, E, Brunekreef, B, Spiegelman, D (2008). "Traffic-Related Outdoor Air Pollution and Respiratory Symptoms in Children." Epidemiology **19**(3): 8.

Salvi, S., A. Blomberg, et al. (1999). "Acute inflammatory responses in the airways and peripheral blood after short-term exposure to diesel exhaust in healthy human volunteers." Am. J. Respiratory Critical Care Med. **159**: 702-709.

Samet, J. M., F. Dominici, et al. (2000). Fine Particulate Air Pollution and Mortality in 20 U.S. Cities, 1987-1994. New England Journal of Medicine, New England Journal of Medicine. **343:** 1742-1749.

Sanak, M., G. Bochenek, et al. (2010). "Elevated urinary leukotriene E4 excretion in asthma: a comparison of HPLC-mass spectrometry and ELISA." Allergy **65**(5): 663-664.

Seinfeld, J. H. (1998). Atmospheric chemistry and physics from air pollution to climate change. New York, Wiley.

Setton, E., J. D. Marshall, et al. (2011). "The impact of daily mobility on exposure to traffic-related air pollution and health effect estimates." Journal of Exposure Science & Environmental Epidemiology **21**(1): 42-48.

Shoval, N. (2008). "Tracking technologies and urban analysis." Cities **25**(1): 21-28.

Sørensen, M., S. Loft, et al. (2005). "Personal exposure to $PM_{2.5}$, black smoke and NO_2 in Copenhagen: relationship to bedroom and outdoor concentrations covering seasonal variation." Journal of Exposure Analysis & Environmental Epidemiology **15**(5): 413-422.

Strand, M., P. K. Hopke, et al. (2007). "A study of health effect estimates using competing methods to model personal exposures to ambient PM2.5." Journal of Exposure Science & Environmental Epidemiology **17**(6): 549-558.

Strickland, M., L. Darrow, et al. (2010). "Short-term Associations between Ambient Air Pollutants and Pediatric Asthma Emergency Department Visits." Am J Respir Crit Care Med **182**: 307 - 316.

Thornburg, J., D. S. Ensor, et al. (2001). "Penetration of Particles into Buildings and Associated Physical Factors. Part I: Model Development and Computer Simulations." Aerosol Science and Technology **34**(3): 284-296.

Van Cleave, J., S. L. Gortmaker, et al. (2010). "Dynamics of Obesity and Chronic Health Conditions Among Children and Youth." JAMA: Journal of the American Medical Association **303**(7): 623-630.

Van Roosbroeck, S., R. F. Li, et al. (2008). "Traffic-related outdoor air pollution and respiratory symptoms in children - The impact of adjustment for exposure measurement error." Epidemiology **19**(3): 409-416.

Wallace, L., R. Williams, et al. (2006). "Continuous weeklong measurements of personal exposures and indoor concentrations of fine particles for 37 health-impaired North Carolina residents for up to four seasons." Atmospheric Environment **40**(3): 399-414.

Wallace, L. A., E. D. Pellizzari, et al. (1987). "The TEAM Study: Personal exposures to toxic substances in air, drinking water, and breath of 400 residents of New Jersey, North Carolina, and North Dakota." Environmental research **43**(2): 290-307.

Weis, B. K., D. Balshaw, et al. (2005). "Personalized Exposure Assessment: Promising Approaches for Human Environmental Health Research." Environmental Health Perspectives **113**(7): 840-848.

Weisel, C., J. Zhang, et al. (2005). Relationships of Indoor, Outdoor, and Personal Air (RIOPA). Part I, Collection Methods and Descriptive Analyses Boston, MA, Health Effects Institute.

Williams, R., J. Suggs, et al. (2003). "The Research Triangle Park particulate matter panel study: PM mass concentration relationships." Atmospheric Environment **37**(38): 5349-5363.

Williams, R., J. Suggs, et al. (2000). "The 1998 Baltimore Particulate Matter Epidemiology Exposure Study: Part 1. Comparison of ambient, residential outdoor, indoor and apartment particulate matter monitoring." Journal of Exposure Analysis & Environmental Epidemiology **10**: 518.

Wilson, W. E. and M. Brauer (2006). "Estimation of ambient and non-ambient components of particulate matter exposure from a personal monitoring panel study." J Expos Sci Environ Epidemiol **16**(3): 264-274.

Wu, C.-F., R. J. Delfino, et al. (2005). "Evaluation and quality control of personal nephelometers in indoor, outdoor and personal environments." Journal of Exposure Analysis & Environmental Epidemiology **15**: 99-110.

Wu, C. F., R. J. Delfino, et al. (2005). "Exposure assessment and modeling of particulate matter for asthmatic children using personal nephelometers." Atmospheric Environment **39**(19): 3457-3469.

Wu, J., C. Jiang, et al. (2011). "Automated time activity classification based on global positioning system (GPS) tracking data." Environ. Health(10).

Yu, O., Sheppard, L., Lumley, T., Koenig, J.Q., Shapiro, G.G. (2000). "Effects of ambient air pollution on symptoms of asthma in Seattle area children enrolled in the CAMP study." Environ. Health Perspect. **108**(12): 1209-1214.

Zhu, J., B. Aikawa, et al. (2005). "Measurement of fine particles in diesel emissions using a real-time aerosol monitor." Journal Of The Air & Waste Management Association **55**(7): 978-983.

APPENDIX 1

"Spatiotemporal Profiles of Particulate Matter Exposure Among Asthmatic Children"

Paper Supplemental Information

A1.1. Censored Data Imputation Procedure

Censored (below limit of detection) data is commonly addressed with a substitution process. A commonly used heuristic substitution value is one-half of the smallest value of quantification. This procedure, however, leaves much to be desired when applied to observed data. In many cases substitution skews the representation of data, as it does not represent the likely overall distribution of the collected data.

An imputation operation was performed on this dataset in order to maintain censored PM exposure data collected within this research. This imputation procedure was performed five different times so that the resulting values could be compared to ensure the operation was performing as expected. The probability transform employed was designed to model the estimated values for the censored data based on the distribution observed in the remainder of the collected PM exposure data. The data were log-normally distributed which required a transformation operation to acquire the distribution parameters needed for the imputation procedure. Prior to transforming the data, a small constant was substituted for zero values to enable the lognormal transformation as part of the imputation procedure.

The procedure for the imputation followed these steps:

1. Direct-reading PM exposure data were stratified based on the subject.
2. A small constant replaced concentration values equal to zero (non-detects). The value used was equal to one half of the smallest measurable value reported by the nephelometer (0.5 $\mu g/m^3$).

3. The subject-stratified data were then log-transformed and distribution parameters (mean and standard deviation) specific to each subject were calculated.
4. The censored data values (zeros) were then replaced with values generated by a probability integral transform (Eq. A1.1) based on the subject specific distribution parameters.

   R code for Probability Integral Transform value imputation step:

   Imputed value <- pnorm(log(0.001), sub_spec_ave, sub_spec_stdev) (Eq A1.1)

The issue of simple substitution of censored data with a heuristic value is displayed in Figure A1.1. The subset of data appears to be bimodal with a smaller peak located at the arbitrarily selected substitution value. In Figure A1.2 values for the censored data have been imputed and are the resulting histogram is displayed. This process has produced a distribution based on the non-censored data and provides the expected characteristic 'tail' shape. When the imputed values were substituted for the censored data, the histograms of the entire dataset (Figure A1.3) were unimodal and generally normal. Multiple imputation procedures were performed and the parameters were evaluated for consistency (Table A1.1). The resulting change in the mean for the censored data was less than 0.4%.

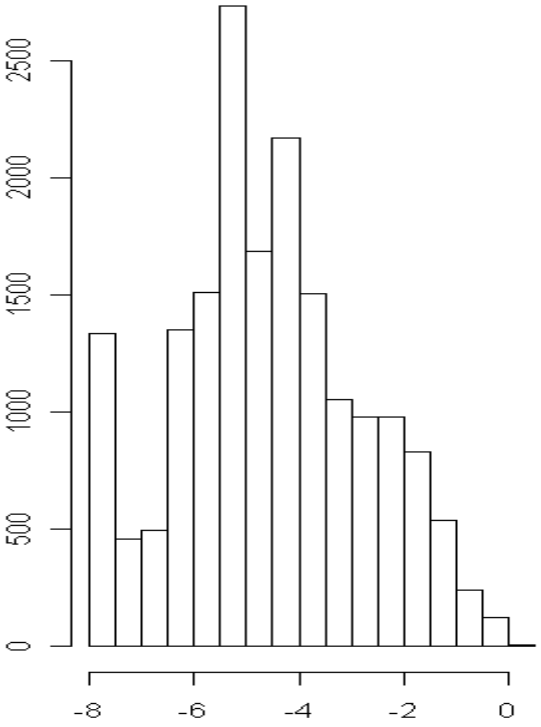

Figure A1.1. Histogram of personal PM data with heuristic substitution for censored data

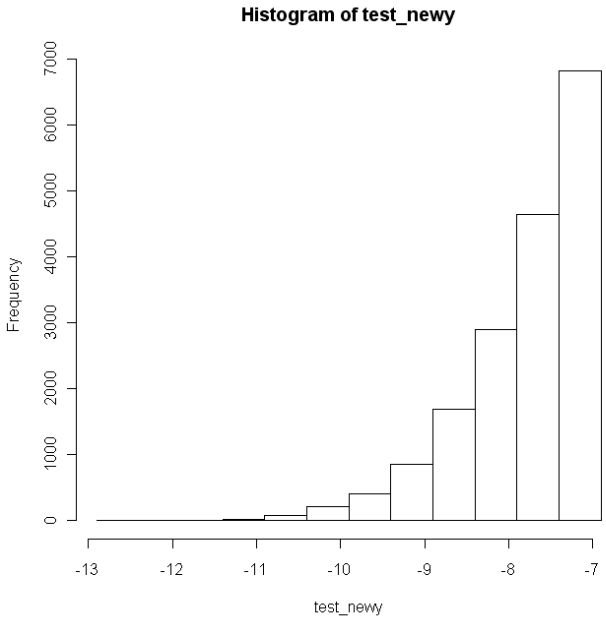

Figure A1.2. Sample distribution of imputed values for censored data

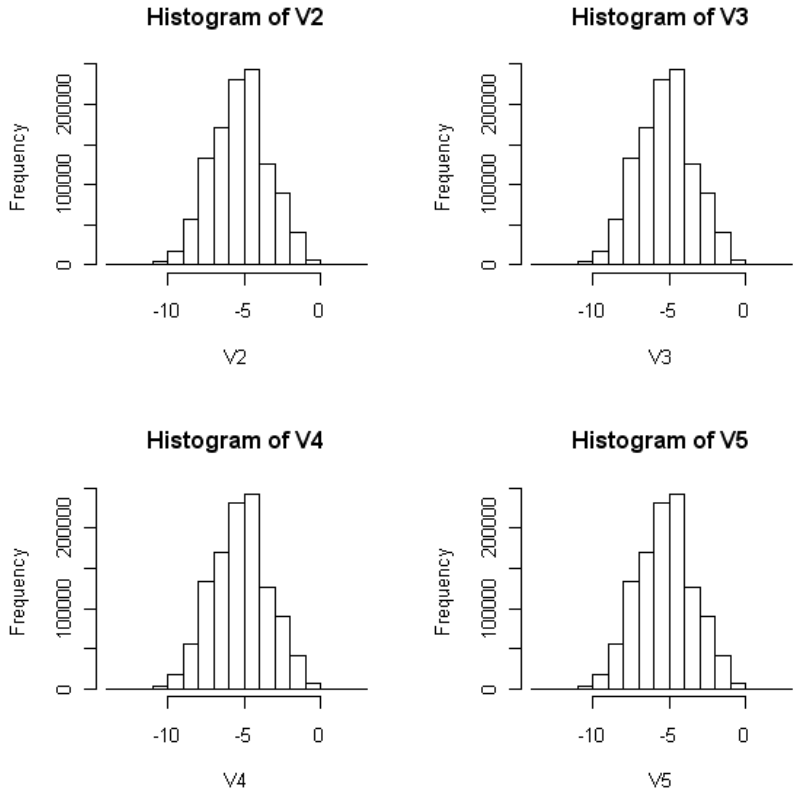

Figure A1.3. Sample histograms of data with imputed values substituted for zero readings

Table A1.1. Sample Distribution Parameters from Datasets with Imputed Values

Dataset	Mean (mg/m^3)	Std Dev
Uncensored	0.02654	0.1051
Imputed 1	0.02664	0.1051
Imputed 2	0.02663	0.1050
Imputed 3	0.02663	0.1050

A1.2. Nephelometer (10-sec PM) Data Normalization Procedure

Direct-reading data from the nephelometer were normalized using a factor consisting of the ratio of the daily time-weighted average calculated from each gravimetric sample and the daily time-weighted average of the nephelometer during the concurrent sampling timeframe. This normalization factor was applied to the 10-sec

nephelometer data to obtain a corrected PM concentration (Eq. A1.2). The normalization occurred in post processing following the imputation procedure.

$$C_{corrected,\ i} = C_{pdr,uncorr} \frac{C_{filter,TWA}}{C_{pdr,uncorr,TWA}} \quad \text{(Eq. A1.2)}$$

A1.3. Model Development

An additive approach using a linear mixed model was used to build a model to explore personal PM exposure relationships (Table A1.2). The subject's microenvironment was assessed as a predictor of the mean log-normalized exposure concentrations for each subject's microenvironments (or shorter averaging times). There were multiple samples per child, requiring inclusion of a repeated measures term in the model. A nested structure of child (samples within child) was also addressed with a random effects term in the model. With this model the location-activity classification was a significant predictor ($p<0.0001$) of the exposure. Other random effects evaluated included the sampling instrument IDs. The IDs did not explain much of the covariance in the model and did not improve the AIC value and were therefore excluded.

Additional covariates examined included the outdoor ambient $PM_{2.5}$ concentrations (NJ TEOM) which were significant in modeling the mean personal PM exposure within the microenvironment. The impact of the $PM_{2.5}$ concentration was not great, but the improvement of the model overall, as indicated by the AIC value, warranted inclusion. Other covariates evaluated and found to be non-significant included personal ambient temperature ($p=0.66$) and sampling date ($p=0.1$).

Table A1.2. Summary of Model Building

Variable Included in Model		Model							
	Type	1	2	3	3a	4	5	8	9
Classifcation	Fix	X	x	X	X	X	X	X	
NJ TEOM	Fix			X	X				X
Degrees	Fix						X		
StartDate	Fix							x	
	Covariance								
Child_id	Rdm	0.14	0.054	.43	0	.022	.051	.08	0
Sample_id	Rdm								
sample_id (child_id)	Rdm	0.43	0.51	1.39	.43	.445	0.51	.49	.49
Classification(child_id)	Rdm		0.36	.094	.35	.36	.36	.36	.58
PDR_ID	Rdm				.18	.173			
Residual		.85	.51	.46	.46	.51	.51	.51	.46
AIC Value		1653	1567	1529	1519	1560	1574	1575	1560

A1.4. Model Descriptions (SAS Code and Output)

Table A1.3. Model Descriptions

Model	Period	Code	Model #

Simple	10 sec	**proc mixed** data=sampdata.samp_data ratio noclprint;
		class classification sample_id child_id;
		model mean_lognorm = classification / solution;
		random child_id sample_id(child_id);
		lsmeans classification/ pdiff;
		run;
			(1)

Full	5 min	**proc mixed** data=sampdata.samp_hour5min_rep ratio noclprint;
		class classification sample_id child_id;
		model lognorm = classification NJ25 / solution;
		random sample_id(child_id);
		repeated / type=sp(exp)(samp_date_5min) subject=child_id;
		lsmeans classification/ pdiff;
		run;
			(2)

Uncon-strained	10 sec	class sample_id child_id;
		model lognorm = /solution;
		random intercept / sub = child_id;
			(3)

Personal Cloud	ME/ hour	**proc mixed** data=Pigpen.pigpen_model_merge
		class sample_id child_id date;
		model School_lognorm = avgNJ25_6_11 home_lognorm/ solution;
		random child_id date / solution;
		repeated / type=sp(exp)(date) subject=child_id;
			(4)

Predict	ME	class sample_id child_id;
		model [microenvironment] = [preceding microenvironment]/ solution;
		random child_id;
		repeated / type=sp(exp)(date) subject=child_id;
			(5)

A1.4.a. Simple (Model 1)

```
proc mixed data=sampdata.samp_data ratio noclprint;
class classification sample_id child_id;
model lognorm = classification / solution;
random child_id sample_id(child_id);
lsmeans classification/ pdiff;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Ratio	Estimate
child_id	0.1111	0.2015
sample_id(child_id)	0.2943	0.5340
Residual	1.0000	1.8142

Solution for Fixed Effects

Effect	classification	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		-6.1689	0.1049	29	-58.79	<.0001
classification	Aftern	0.2275	0.005893	1E6	38.61	<.0001
classification	Home	1.0591	0.003275	1E6	323.40	<.0001
classification	Mornin	0.6658	0.008571	1E6	77.68	<.0001
classification	School	0	.	.	.	.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
classification	3	1E6	38527.7	<.0001

A1.4.b. Full (model 2) repeated measures avg period = 1 hr

```
proc mixed data=sampdata.samp_hour_rep ratio noclprint;
class classification sample_id child_id;
model lognorm = classification NJ25 / solution;
random sample_id(child_id);
repeated / type=sp(exp)(samp_date_hour) subject=child_id;
lsmeans classification/ pdiff;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Ratio	Estimate
sample_id(child_id)		0.01403	0.02817

SP(EXP)	child_id	0.1002	0.2012	
Residual		1.0000	2.0080	

Solution for Fixed Effects

Effect	classification	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		-6.2585	0.08769	136	-71.37	<.0001
classification	Aftern	0.3130	0.06479	2811	4.83	<.0001
classification	Home	0.8800	0.06494	2811	13.55	<.0001
classification	Mornin	0.6177	0.07941	2811	7.78	<.0001
classification	School	0	.	.	.	.
NJ25		0.01035	0.003754	2811	2.76	0.0059

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
classification	3	2811	65.76	<.0001
NJ25	1	2811	7.61	0.0059

A1.4.c. Full (model 2) repeated measures: avg period = 15 min

```
proc mixed data=sampdata.samp_hourqtr_rep ratio noclprint;
class classification sample_id child_id;
model lognorm = classification NJ25 / solution;
random sample_id(child_id);
repeated / type=sp(exp)(samp_date_qtr) subject=child_id;
lsmeans classification/ pdiff;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Ratio	Estimate
sample_id(child_id)		0.04322	0.09432
SP(EXP)	child_id	0.07756	0.1692
Residual		1.0000	2.1821

Solution for Fixed Effects

Effect	classification	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		-6.0716	0.08014	136	-75.76	<.0001
classification	Aftern	0.3558	0.03721	11E3	9.56	<.0001
classification	Home	0.6804	0.04146	11E3	16.41	<.0001
classification	Mornin	0.2882	0.03769	11E3	7.65	<.0001
classification	School	0	.	.	.	.
NJ25		0.002266	0.002219	11E3	1.02	0.3072

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF

Effect	DF	DF	F Value	Pr > F
classification	3	11E3	90.23	<.0001
NJ25	1	11E3	1.04	0.3072

A1.4.d. Full (model 2) repeated measures: avg period = 5 min

```
proc mixed data=sampdata.samp_hour5min_rep ratio noclprint;
class classification sample_id child_id;
model lognorm = classification NJ25 / solution;
random sample_id(child_id);
repeated / type=sp(exp)(samp_date_5min) subject=child_id;
lsmeans classification/ pdiff;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Ratio	Estimate
sample_id(child_id)		0.07533	0.1692
SP(EXP)	child_id	0.05606	0.1259
Residual		1.0000	2.2462

Solution for Fixed Effects

Effect	classification	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		-5.8599	0.07443	136	-78.73	<.0001
classification	Aftern	0.1468	0.02414	34E3	6.08	<.0001
classification	Home	0.4185	0.02774	34E3	15.08	<.0001
classification	Mornin	0.1358	0.02374	34E3	5.72	<.0001
classification	School	0	.	.	.	.
NJ25		-0.00047	0.001524	34E3	-0.31	0.7579

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
classification	3	34E3	81.48	<.0001
NJ25	1	34E3	0.10	0.7579

A1.4.e. Full (model 2) repeated measures: avg period = microenvironment

```
proc mixed data=sampdata.samp_hourmicro_rep ratio noclprint;
class classification sample_id child_id;
model lognorm = classification NJ25/ solution;
random child_id sample_id(child_id) ;
repeated / type=sp(exp)(samp_date_sec) subject=child_id;
lsmeans classification/ pdiff;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Ratio	Estimate
child_id		0.1359	0.1139
sample_id(child_id)		0.4775	0.4002
SP(EXP)	child_id	6.2E-17	5.2E-17
Residual		1.0000	0.8382

Solution for Fixed Effects

Effect	classification	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		-6.8331	0.1736	29	-39.35	<.0001
classification	Aftern	0.4237	0.1489	406	2.84	0.0047
classification	Home	1.2816	0.1474	406	8.69	<.0001
classification	Mornin	0.6017	0.1428	406	4.21	<.0001
classification	School	0	.	.	.	.
NJ25		0.05939	0.01053	406	5.64	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
classification	3	406	34.07	<.0001
NJ25	1	406	31.82	<.0001

A1.4.f. Unconstrained (model 3)

```
proc mixed data= sampdata.samp_data ratio noitprint noclprint;
class sample_id child_id;
model lognorm = / solution;
random intercept/ sub = child_id;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Ratio	Estimate
Intercept	child_id	0.1245	0.3035
Residual		1.0000	2.4372

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-5.3857	0.1006	29	-53.54	<.0001

A1.4.g. Personal Cloud (Model 4)

```
proc mixed data=Pigpen.pigpen_model_merge ratio noitprint noclprint;
class sample_id child_id date;
model School_lognorm = avgNJ25_6_11 home_lognorm/ solution;
random child_id date / solution;
repeated / type=sp(exp)(date) subject=child_id;
run;
```

The Mixed Procedure

Covariance Parameter Estimates

Cov Parm	Subject	Ratio	Estimate
child_id		0.5983	0.4046
date		0	0
SP(EXP)	child_id	1.0099	0.6830
Residual		1.0000	0.6762

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	-4.0556	0.4027	29	-10.07	<.0001
avgNJ25_6_11	0.04547	0.01442	60	3.15	0.0025
home_lognorm	0.4312	0.06192	60	6.96	<.0001

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
avgNJ25_6_11	1	60	9.94	0.0025
home_lognorm	1	60	48.49	<.0001

A1.4.h. Prediction (Model 5):

```
proc mixed data=predict.predict ratio noitprint noclprint;
class sample_id child_id;
model pmstransit = pmschool / solution;
random child_id;
repeated / type=sp(exp)(date) subject=child_id;
run;
```

APPENDIX 2

"Commute-related Particulate Matter Exposure Is Associated with Acute Asthma Worsening in Children" Paper Supplemental Information

A2.1. Model Development

An additive approach using a linear mixed model was used to build a model to explore personal microenvironmental exposures and $uLTE_4$ relationships. Three morning microenvironments (home, transit, and school) from each personal exposure were initially assessed as a predictor of the $uLTE_4$ levels collected once per day. There were multiple samples per child requiring a repeated measures term to be included within the model. A nested structure of child (samples within child) was also addressed with a random effects term in the model.

A child's upper respiratory infection status (cold) was significant (p=0.005) and included in the model. Additional covariates evaluated (Table A2.1) and found to be non-significant included mode of transport (p=0.35), smoking family member (p=0.52), breakfast location (p=0.37), body mass index (p=0.91), outdoor temperature (p=0.39), and barometric pressure (p=0.71).

Table A2.1. Summary of Evaluated Covariates

Covariate	p-value
Upper Respiratory Infection (cold)	0.005
Mode of Transport to School	0.35
Smoking Family Member	0.52
Breakfast Location	0.37
Body Mass Index	0.91
Outdoor Temp	0.39
Barometric Pressure	0.71

A2.2. SAS Model Code and Output

A2.2.a. Co-pollutant model

```
proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id cold;
model logLTE = lognorm_h lognorm_t lognorm_s cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
run;
```

The Mixed Procedure

Model Information

Data Set	FOUR10.PTHALF_MULTI
Dependent Variable	logLTE
Covariance Structures	Variance Components, Spatial Exponential
Subject Effect	child_id
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	6
Columns in Z	29
Subjects	1
Max Obs Per Subject	125

Number of Observations

Number of Observations Read	125
Number of Observations Used	89
Number of Observations Not Used	36

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	198.97529638	
1	4	133.93051941	0.00336159
2	1	133.89405524	0.00003254
3	1	133.89371967	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3376	0.1031	3.27	0.0005
SP(EXP)	child_id	1.91E-17	.	.	.
Residual		0.1112	0.02085	5.33	<.0001

Fit Statistics

-2 Res Log Likelihood	133.9
AIC (smaller is better)	137.9

```
                    AICC (smaller is better)        138.0
                    BIC (smaller is better)         140.6

                         Solution for Fixed Effects
                                          Standard
Effect       cold            Estimate       Error      DF    t Value    Pr > |t|
Intercept                      4.9430      0.3109      28      15.90      <.0001
lognorm_h                     0.02508     0.04619      56       0.54      0.5893
lognorm_t                      0.1381     0.05694      56       2.43      0.0185
lognorm_s                     -0.0957     0.06662      56      -1.44      0.1561
cold                   0      -0.5053      0.1664      56      -3.04      0.0036
cold                   1            0           .       .         .         .

                        Type 3 Tests of Fixed Effects
                              Num     Den
                    Effect     DF      DF    F Value    Pr > F
                    lognorm_h   1      56       0.29    0.5893
                    lognorm_t   1      56       5.88    0.0185
                    lognorm_s   1      56       2.07    0.1561
                    cold        1      56       9.22    0.0036
```

A2.2.b. Model with PPM Transit and cold

```
proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id;
model logLTE = lognorm_t cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
run;
```

```
                        The Mixed Procedure
                         Model Information

Data Set                     FOUR10.PTHALF_MULTI
Dependent Variable           logLTE
Covariance Structures        Variance Components,
                             Spatial Exponential
Subject Effect               child_id
Estimation Method            REML
Residual Variance Method     Profile
Fixed Effects SE Method      Model-Based
Degrees of Freedom Method    Containment

                        Dimensions
                 Covariance Parameters            3
                 Columns in X                     3
                 Columns in Z                    29
                 Subjects                         1
                 Max Obs Per Subject            125


                      Number of Observations
```

```
Number of Observations Read            125
Number of Observations Used             89
Number of Observations Not Used         36
```

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	194.90402405	
1	4	130.63343498	0.12216144
2	1	128.56118724	0.02801822
3	1	128.08189380	0.00244296
4	1	128.04300928	0.00002468
5	1	128.04263625	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3310	0.09994	3.31	0.0005
SP(EXP)	child_id	3.37E-17	.	.	.
Residual		0.1123	0.02064	5.44	<.0001

Fit Statistics

-2 Res Log Likelihood	128.0
AIC (smaller is better)	132.0
AICC (smaller is better)	132.2
BIC (smaller is better)	134.8

Solution for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	4.6111	0.2075	28	22.22	<.0001
lognorm_t	0.09392	0.03218	58	2.92	0.0050
cold	0.5358	0.1657	58	3.23	0.0020

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
lognorm_t	1	58	8.52	0.0050
cold	1	58	10.45	0.0020

A2.2.c. Model with PPM Home and cold

```
proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id cold;
model logLTE = lognorm_h cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
run;
```

The Mixed Procedure

Model Information

```
Data Set                     FOUR10.PTHALF_MULTI
```

Dependent Variable	logLTE
Covariance Structures	Variance Components, Spatial Exponential
Subject Effect	child_id
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	4
Columns in Z	29
Subjects	1
Max Obs Per Subject	125

Number of Observations

Number of Observations Read	125
Number of Observations Used	89
Number of Observations Not Used	36

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	202.43345600	
1	4	131.73136365	0.00354071
2	1	131.68155926	0.00004457
3	1	131.68096628	0.00000001

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3752	0.1120	3.35	0.0004
SP(EXP)	child_id	5.43E-17	.	.	.
Residual		0.1133	0.02086	5.43	<.0001

Fit Statistics

-2 Res Log Likelihood	131.7
AIC (smaller is better)	135.7
AICC (smaller is better)	135.8
BIC (smaller is better)	138.4

Solution for Fixed Effects

Effect	cold	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		5.0008	0.2651	28	18.86	<.0001
lognorm_h		0.07059	0.03254	58	2.17	0.0341
cold	0	-0.5104	0.1671	58	-3.05	0.0034
cold	1	0	.	.	.	.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
lognorm_h	1	58	4.71	0.0341
cold	1	58	9.33	0.0034

A2.2.d. Model with PPM school and cold

```
proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id cold;
model logLTE = lognorm_s cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
run;
```

The Mixed Procedure

Model Information

Data Set	FOUR10.PTHALF_MULTI
Dependent Variable	logLTE
Covariance Structures	Variance Components, Spatial Exponential
Subject Effect	child_id
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	4
Columns in Z	29
Subjects	1
Max Obs Per Subject	125

Number of Observations

Number of Observations Read	125
Number of Observations Used	89
Number of Observations Not Used	36

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	199.96290080	
1	4	200.55280736	0.00125118
2	2	182.39642414	0.00796189
3	2	165.42076562	0.08719233
4	2	150.61614382	0.23382287
5	2	139.51952889	0.15861151
6	2	134.01315779	0.03406621
7	2	133.76879891	0.00573247
8	1	133.69350117	0.00010554
9	1	133.69219888	0.00000004
10	1	133.69219839	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3551	0.1073	3.31	0.0005
SP(EXP)	child_id	6.3E-17	.	.	.

```
Residual                  0.1205     0.02215      5.44      <.0001

                        Fit Statistics
                  -2 Res Log Likelihood           133.7
                  AIC (smaller is better)         137.7
                  AICC (smaller is better)        137.8
                  BIC (smaller is better)         140.4

                     Solution for Fixed Effects
                                   Standard
Effect       cold        Estimate       Error      DF    t Value    Pr > |t|
Intercept                 4.9763      0.3200      28      15.55      <.0001
lognorm_s                0.05912     0.04089      58       1.45      0.1536
cold                1     -0.5312      0.1726      58      -3.08      0.0032
cold                2           0           .       .        .         .

                    Type 3 Tests of Fixed Effects
                          Num     Den
                Effect     DF      DF    F Value    Pr > F
                lognorm_s   1      58       2.09    0.1536
                cold        1      58       9.47    0.0032
```

A2.2.e. Model with Ambient transit and cold

```
proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id cold;
model logLTE = log_nj25_t cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
run;
```

```
                    The Mixed Procedure
                     Model Information

Data Set                     FOUR10.PTHALF_MULTI
Dependent Variable           logLTE
Covariance Structures        Variance Components,
                             Spatial Exponential
Subject Effect               child_id
Estimation Method            REML
Residual Variance Method     Profile
Fixed Effects SE Method      Model-Based
Degrees of Freedom Method    Containment

                      Dimensions
           Covariance Parameters             3
           Columns in X                      4
           Columns in Z                     29
           Subjects                          1
           Max Obs Per Subject             125

                Number of Observations
     Number of Observations Read             125
```

Number of Observations Used 89
Number of Observations Not Used 36

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	201.51453094	
1	4	238.29056498	0.00004996
2	3	201.51453094	.
3	1	177.73469005	1.37096296
4	1	159.63000562	11.93714663
5	1	147.19423640	1.03359007
6	1	139.89612294	0.29448858
7	1	136.52005569	0.08114217
8	1	135.47069363	0.01225326
9	1	135.31739587	0.00042159
10	1	135.31248578	0.00000060
11	1	135.31247900	0.00000000

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3637	0.1101	3.31	0.0005
SP(EXP)	child_id	2.12E-17	.	.	.
Residual		0.1233	0.02269	5.43	<.0001

Fit Statistics

-2 Res Log Likelihood	135.3
AIC (smaller is better)	139.3
AICC (smaller is better)	139.5
BIC (smaller is better)	142.0

Solution for Fixed Effects

Effect	cold	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		4.6238	0.2107	28	21.95	<.0001
LOG_NJ25_t		-0.01070	0.05054	58	-0.21	0.8332
cold	0	-0.4971	0.1733	58	-2.87	0.0057
cold	1	0	.	.	.	.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
LOG_NJ25_t	1	58	0.04	0.8332
cold	1	58	8.23	0.0057

A2.2.f. Model with Ambient home and cold

```
proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id cold;
model logLTE = nj25_h cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
```

run;

The Mixed Procedure
Model Information

Data Set	FOUR10.PTHALF_MULTI
Dependent Variable	logLTE
Covariance Structures	Variance Components, Spatial Exponential
Subject Effect	child_id
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	4
Columns in Z	29
Subjects	1
Max Obs Per Subject	125

Number of Observations

Number of Observations Read	125
Number of Observations Used	89
Number of Observations Not Used	36

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	201.99999719	
1	4	209.01039323	0.00065122
2	2	190.59722181	0.00379055
3	2	173.13359494	0.02822489
4	2	157.44461986	2.05221463
5	2	144.87634956	0.19994737
6	2	137.24481432	0.27700652
7	2	136.21994381	0.03371739
8	1	135.79511103	0.00266898
9	1	135.76372186	0.00002212
10	1	135.76347383	0.00000000

Convergence criteria met.

The Mixed Procedure
Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3643	0.1102	3.31	0.0005
SP(EXP)	child_id	0	.	.	.
Residual		0.1230	0.02264	5.43	<.0001

Fit Statistics

-2 Res Log Likelihood	135.8
AIC (smaller is better)	139.8
AICC (smaller is better)	139.9
BIC (smaller is better)	142.5

Solution for Fixed Effects

Effect	cold	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		4.6162	0.1964	28	23.51	<.0001
nj25_h		-0.01587	0.03772	58	-0.42	0.6755
cold	0	-0.4870	0.1751	58	-2.78	0.0073
cold	1	0	.	.	.	.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
nj25_h	1	58	0.18	0.6755
cold	1	58	7.74	0.0073

A2.2.g. Model with Ambient school and cold

proc mixed data= four10.pthalf_multi covtest noclprint;
class child_id cold;
model logLTE = nj25_s cold /solution;
random child_id;
repeated / type=sp(exp)(sampledate) subject=child_id;
run;

The Mixed Procedure
Model Information

Data Set	FOUR10.PTHALF_MULTI
Dependent Variable	logLTE
Covariance Structures	Variance Components, Spatial Exponential
Subject Effect	child_id
Estimation Method	REML
Residual Variance Method	Profile
Fixed Effects SE Method	Model-Based
Degrees of Freedom Method	Containment

Dimensions

Covariance Parameters	3
Columns in X	4
Columns in Z	29
Subjects	1
Max Obs Per Subject	125

Number of Observations

Number of Observations Read	125
Number of Observations Used	89
Number of Observations Not Used	36

Iteration History

Iteration	Evaluations	-2 Res Log Like	Criterion
0	1	201.13191949	
1	4	194.32709513	0.00249577
2	2	176.57284008	0.01726515
3	2	160.34893057	0.43299367

4	2	146.86605857	0.20805334
5	2	137.85603339	0.88244724
6	2	135.12075838	0.00368328
7	1	135.07572930	0.00004260
8	1	135.07523588	0.00000001

Convergence criteria met.

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error	Z Value	Pr > Z
child_id		0.3635	0.1100	3.31	0.0005
SP(EXP)	child_id	0	.	.	.
Residual		0.1230	0.02265	5.43	<.0001

Fit Statistics

-2 Res Log Likelihood	135.1
AIC (smaller is better)	139.1
AICC (smaller is better)	139.2
BIC (smaller is better)	141.8

Solution for Fixed Effects

Effect	cold	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept		4.6513	0.2188	28	21.26	<.0001
nj25_s		-0.02350	0.05262	58	-0.45	0.6568
cold	0	-0.5003	0.1730	58	-2.89	0.0054
cold	1	0	.	.	.	.

Type 3 Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
nj25_s	1	58	0.20	0.6568
cold	1	58	8.36	0.0054

APPENDIX 3

Sampling Backpack Preparation and Collection Procedures

Sampling Backpack Preparation:

1) Insert new batteries in GPS unit, pDR-1200, and TR-52 (temperature monitor), attach charged battery to air sampling pump
2) Place pre-weighed filter in filter assembly on pDR-1200 sensor chamber, record filter number on sample form
3) Open and then close petri dishes containing filter blanks (2 filters each day)
4) Attach sample pump to sampling train
5) Calibrate pump flowrate (6.8 lpm) with Gillibrator, record on sampling form
6) Power on and Zero calibrate the pDR with HEPA filter assembly attached
7) Power on GPS receiver ensure that signal lock acquired on at least four satellites,
8) Verify internal clocks of the pDR and TR-52 are synchronized to within one second of the the clock of the GPS Receiver. If not adjust clocks as needed.
9) Zero out instrument memory (GPS, pDR-1200, and temperature monitor)
10) Prepare GPS, pDR-1200, and TR-52 for data-logging
11) Secure equipment backpack internal frame
12) Activate data-logging and the engage sampling pump.

Sampling Backpack Collection:

1) Collect backpack from child
2) Visually verify that GPS unit, pDR-1200, TR-52 and sample pump are operating
3) Suspend operation of monitoring equipment and sample pump
4) Perform survey questionnaire with child and record answers
5) Measure pump flowrate (~6.8 lpm) with Gillibrator, record on form
6) Remove filter and place in petri dish, ensure label matches with form number
7) Download recorded data (GPS unit, pDR-1200, TR-52) to laptop
8) Power off monitors, store in backpack and place pump battery on charger

APPENDIX 4

Sampling Form /

Personal Behavior / PM Sources Survey Questionnaire

39034

Sample ID Year Filter Sub #

Air Pollution School Study
2007 - 2008
Personal Monitor Survey

Subject Number

Subject Initials

Coordinator Portion

Possession Time

Start Date / / Start Time Start Time

Stop Date / / Stop Time Stop Time

Filter ID Pre-weight . mg

Post-weight . mg

Blank 1 ID Pre-weight . mg

Post-weight . mg

Blank 2 ID Pre-weight . mg

Post-weight . mg

Pump pre-flow . Pump post-flow .

○ Smoking home

○ Non-smoking home

Hose stayed intact ○ Yes ○ No

Functioned Full Time

GPS ID ○ Yes ○ No

PDR ID ○ Yes ○ No

Pump ID ○ Yes ○ No

DCC Use Only

APL005J

39034

Personal Monitor Survey
1 of 3

39034

	Yes	*No*	
Pack was taken home	○	○	
Pack was returned on time	○	○	
Recess outside	○	○	If yes, time ☐☐☐☐
Gym outside	○	○	If yes, time ☐☐☐☐

Questions for Kids

1. How did you get to school?

   ○ RTD Bus ○ Car ○ Transport van ○ Walking ○ Other ☐☐☐☐☐☐☐☐☐☐

2. How did you get home from school?

   ○ RTD Bus ○ Car ○ Transport van ○ Walking ○ Other ☐☐☐☐☐☐☐☐☐☐

3. What did you do for dinner last night?

   ○ Parent cooked ○ Ate out ○ Takeout/Drive thru ○ Didn't eat

4. What did you eat for dinner last night?

   ○ Fried food ○ Barbeque ○ Stir fry ○ Other

5. What did you do for breakfast this morning?

   ○ Parent cooked ○ Ate out ○ Takeout/Drive thru ○ Didn't eat ○ Ate at school

6. Did you eat any fried food?

   ○ Yes ○ No

7. Were you around candles/incense since you left school yesterday?

   ○ Yes ○ No

8. Were you around a fireplace or barbeque since you left school yesterday?

   ○ Yes ○ No

39034

9. Did anyone smoke around you since you left school yesterday?

○ Yes ○ No

If yes, where did they smoke?

○ Inside ○ Outside ○ During transport ○ Other

If yes, when did they smoke?

○ Last night ○ This morning ○ Both

10. Did you go anywhere else besides home and school while you were carrying the pack?

○ Babysitter/After school program

○ Errands with parent

○ Evening activity

○ Other

11. School arrival time

12. Home arrival time

13. Bed time

14. Wake time

15. Yellow Filter ○ 0 ○ 1 ○ 2 ○ 3

APPENDIX 5

Basic Apportionment Algorithm

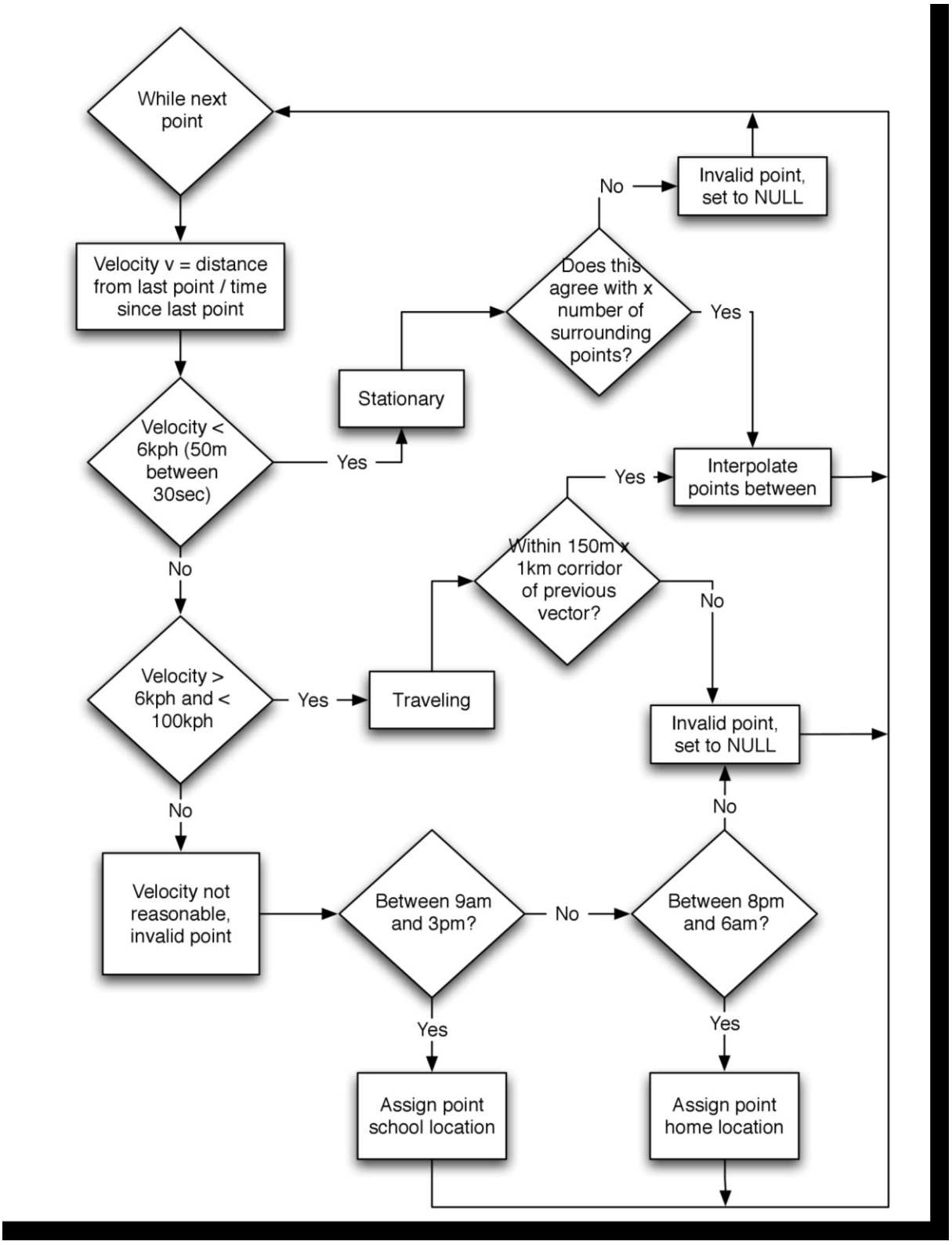

Figure A5.1. Microenvironment Classification Flowchart