Evaluating environmental modeling and sampling data with biomarker data to identify sources and routes of exposure

Hyeong-Moo Shin\textsuperscript{a,}\textsuperscript{*}, Thomas E. McKone\textsuperscript{b,c}, Deborah H. Bennett\textsuperscript{a}

\textsuperscript{a}Department of Public Health Sciences, University of California, One Shields Avenue, MS1-C, Davis, CA 95616, USA
\textsuperscript{b}University of California, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA
\textsuperscript{c}School of Public Health, University of California, Berkeley, CA 94720, USA

\textbf{HIGHLIGHTS}

\begin{itemize}
  \item We modeled PAHs intake from multiple exposure pathways.
  \item Predicted PAH intake were compared to observed intake from NHANES samples.
  \item The total modeled intake was within a factor of 3.4 of the median observed intake.
  \item Evaluation of both indoor and outdoor exposures is needed to evaluate biomarkers.
\end{itemize}

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\textbf{ABSTRACT}

Exposure to environmental chemicals results from multiple sources, environmental media, and exposure routes. Ideally, modeled exposures should be compared to biomonitoring data. This study compares the magnitude and variation of modeled polycyclic aromatic hydrocarbons (PAHs) exposures resulting from emissions to outdoor and indoor air and estimated exposure inferred from biomarker levels. Outdoor emissions result in both inhalation and food-based exposures. We modeled PAH intake doses using U.S. EPA's 2002 National Air Toxics Assessment (NATA) county-level emissions data for outdoor inhalation, the CalTOX model for food ingestion (based on NATA emissions), and indoor air concentrations from field studies for indoor inhalation. We then compared the modeled intake with the measured urine levels of hydroxy-PAH metabolites from the 2001–2002 National Health and Nutrition Examination Survey (NHANES) survey as quantifiable human intake of PAH parent-compounds. Lognormal probability plots of modeled intakes and estimated intakes inferred from biomarkers suggest that a primary route of exposure to naphthalene, fluorene, and phenanthrene for the U.S. population is likely inhalation from indoor sources. For benzo[a]pyrene, the predominant exposure route is likely from food ingestion resulting from multi-pathway transport and bioaccumulation due to outdoor emissions. Multiple routes of exposure are important for pyrene. We also considered the sensitivity of the predicted exposure to the proportion of the total naphthalene production volume emitted to the indoor environment. The comparison of PAH biomarkers with exposure variability estimated from models and sample data for various exposure pathways supports that both indoor and outdoor models are needed to capture the sources and routes of exposure to environmental contaminants.

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1. Introduction

There is growing interest in evaluating exposures to environmental chemicals using biomonitoring data, including blood, urine, and hair, etc. Exposure to environmental chemicals can be attributed to multiple sources, environmental media, and exposure routes (McKone, 1993; Shin et al., 2011a). While biomonitoring data alone cannot reveal how these exposures are linked to the source or route of exposure, they do integrate exposure over multiple pathways, enabling us to compare with cumulative modeled exposure estimates.

Biomarkers are now commonly used to provide direct evidence of human exposure to environmental contaminants (Shin et al., 2011b; Savitz et al., 2012). The Centers for Disease Control and...
Prevention (CDC) have released the National Reports on Human Exposure to Environmental Chemicals to provide an ongoing assessment of the U.S. population exposure to environmental contaminants based on biomonitoring data (CDC, 2005, 2009). These reports capture both the magnitude and variation of exposures for the U.S. population.

There are many multimedia environmental and exposure models developed to capture exposures from a variety of sources and routes (Egeghy et al., 2011). However, these models often cannot compare their exposure estimates with biologic samples over a wide range of organic compounds because they focus only on either near-field (from consumer products used indoors) or far-field (from overall environmental dispersion) exposures (Egeghy et al., 2011). Thus, both near-field and far-field exposures are required to evaluate exposure estimates with biomonitoring data.

Polycyclic aromatic hydrocarbons (PAHs) are a chemical group for which CDC collected biomarkers in 2001–2002 and 2003–2004, through its ongoing National Health and Nutrition Examination Survey (NHANES) (CDC, 2005, 2009). PAHs are derived from tobacco smoke, cooking, and vehicle exhaust as well as incomplete combustion of organic compounds such as coal, gas, oil, and wood (Mastral and Callen, 2000). PAHs give rise to human exposure and intake from multiple sources, including indoor air, outdoor air, and food, because they are ubiquitous in rural and urban environments (Wilson et al., 1999; Cirillo et al., 2006; Loh et al., 2007). Upon entering the body, PAHs are readily and predominantly metabolized to hydroxylated (OH−) metabolites. These metabolites are good indicators of recent exposure to PAH parent-compounds, because metabolism and excretion processes typically happen very quickly (Strickland et al., 1996). For example, the half-life estimates for metabolized pyrene and naphthalene in human urine collected from 20 road-paving workers are 13 and 26 h, respectively (Sobus et al., 2009).

In 2009 the U.S. Environmental Protection Agency (EPA) released its 2002 National Air Toxics Assessment (NATA) data, which includes county-level air toxic emissions inventories (U.S. EPA, 2009). The county-level emission rates of both mobile and stationary PAHs are critical inputs to models, allowing us to estimate not only human exposure to PAHs through inhalation, but also the exposure from food consumption. Additionally, since some PAHs are used in consumer products, including mothballs, caulking, adhesives, flooring materials, dyes, and plastics (Jia and Batterman, 2010; U.S. EPA), we also need to account for exposures resulting from these near-field emissions. Studies have measured PAH indoor concentrations in the U.S. homes (Van Winkle and Scheff, 2001; Naumova et al., 2002), allowing us to estimate exposures from indoor sources.

In this study, we modeled exposure from indoor and outdoor emissions and compared resulting exposures using biomarker data with a set of PAHs as a case study. The set of PAHs addressed in this analysis include naphthalene, fluorene, phenanthrene, pyrene, and benzo(a)pyrene. We modeled intake estimates resulting from outdoor inhalation and food ingestion using the 2002 NATA emission data and from indoor air inhalation using field studies. We then compared these intake estimates with the distribution of PAH urinary metabolites collected in the 2001–2002 NHANES survey. This comparison supports the premise that evaluation of both indoor and outdoor exposures is needed to capture the sources and routes of exposure to environmental contaminants.

The objectives of this study are to (1) compare the magnitude and variation of PAH biomarker levels with those of PAH exposures resulting from various sources and routes of exposure, including indoor air, outdoor air, and food, (2) understand the importance of accounting for the correct exposure scenario, and (3) find exposure pathways of PAHs that primarily impact the general population.

2. Materials and methods

2.1. Selected PAHs and hydroxy-PAH metabolites

We selected five PAHs, including naphthalene, fluorene, phenanthrene, pyrene, and benzo(a)pyrene because the primary metabolites of these compounds were measured in urine samples from the 2001–2002 NHANES survey with concentrations above the limit of detection (LOD) and the emission data of these compounds were available at the county-level in the 2002 EPA NATA data. The selected PAHs represent a range of environmental properties, spanning from relatively volatile compounds (e.g. naphthalene) to those with a high affinity for organic materials and thus for bioaccumulation (e.g. benzo(a)pyrene). Chemical properties of the selected PAHs and their hydroxylated metabolites are listed in Table 1.

2.2. National variation of air emissions and resulting outdoor concentrations

The county-level emission rates, including combustion of fuels and from wildfires, for all selected PAHs are available in the 2002 NATA data, but total outdoor exposure concentrations simulated from the Assessment System for Population Exposure Nationwide (ASPIN) model are only available for naphthalene (U.S. EPA, 2009). The ASPEN model applied the 2002 NATA emission data as input to estimate county-specific naphthalene exposure concentrations and we assumed that modeled outdoor air concentrations are proportional to the county-specific emission rates. Therefore, we computed the outdoor air concentrations for the other PAHs by assuming the same source-to-concentration ratio applied to these other PAHs using the following equation.

$$C_{D,i} = C_{O,naphthalene} \times \frac{E_i}{E_{naphthalene}}$$

where $C_{O,i}$ is the outdoor air exposure concentration of the compound $i$ (ng m$^{-3}$), $C_{O,naphthalene}$ is the outdoor air exposure concentration of naphthalene (ng m$^{-3}$), $E_i$ is the emission rate of the compound $i$ (kg year$^{-1}$), and $E_{naphthalene}$ is the emission rate of naphthalene (kg year$^{-1}$). For example, the annual emission rates of naphthalene and pyrene for the Los Angeles County in 2002 were 361,580 and 3620 kg year$^{-1}$, respectively, and the average outdoor air exposure concentration of naphthalene computed from the ASPEN model was 188 ng m$^{-3}$. Therefore, using Eq. (1), the

<table>
<thead>
<tr>
<th>PAH</th>
<th>MW$^a$</th>
<th>$K_{ow}^b$</th>
<th>VP$^c$</th>
<th>Hydroxy-PAH metabolites</th>
<th>MW$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naphthalene</td>
<td>128.2</td>
<td>2.4E+03</td>
<td>1.2E+01</td>
<td>1-Hydroxynaphthalene</td>
<td>144.2</td>
</tr>
<tr>
<td>Fluorene</td>
<td>166.2</td>
<td>1.5E+04</td>
<td>9.0E-01</td>
<td>2-Hydroxylfluorene</td>
<td>182.2</td>
</tr>
<tr>
<td>Phenanthrene</td>
<td>178.2</td>
<td>3.5E+04</td>
<td>2.7E-02</td>
<td>1-Hydroxyphenanthrene</td>
<td>194.2</td>
</tr>
<tr>
<td>Pyrene</td>
<td>202.3</td>
<td>1.0E+05</td>
<td>6.1E-04</td>
<td>1-Hydroxypyrene</td>
<td>218.3</td>
</tr>
<tr>
<td>Benzo(a)pyrene</td>
<td>252.3</td>
<td>2.2E+06</td>
<td>7.1E-07</td>
<td>3-Hydroxybenzo(a)pyrene</td>
<td>268.3</td>
</tr>
</tbody>
</table>

Table 1

Chemical properties of selected PAHs and hydroxy-PAH metabolites.

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$^a$ Molecular weight (g mol$^{-1}$)

$^b$ Octanol–water partition coefficient (unitless).

$^c$ Vapor pressure (Pa).
predicted pyrene outdoor air exposure concentration for the Los Angeles County is 1.9 ng m⁻³ in 2002. This is comparable to the measured concentration of pyrene (=1.6 ng m⁻³) in 2002 from Naumova et al. (2002) (see Table A1 in the Appendix for comparison of predicted and measured concentrations for other compounds).

Based on measurement studies (Hoff et al., 1996; Simcik et al., 1997; Gigiotti et al., 2000; Park et al., 2001; Dachs et al., 2002), about 98% of fluorene and phenanthrene are in the gas phase in the air. For pyrene, about 86% is in the gas phase and 14% in the particle phase, whereas benzo(a)pyrene is primarily in the particle phase. We expect that benzo(a)pyrene has different patterns of air dispersion compared to the other four PAHs, and thus the estimates of outdoor air concentrations for benzo(a)pyrene using Eq. (1) are expected to be less reliable than those for the more volatile PAHs.

To estimate the daily intake dose (nmol day⁻¹) from outdoor inhalation resulting from environmental emissions, we used the following equation.

\[ I_{OC} = C_0 \cdot BR \cdot (1/MW) \cdot (1 - F_{IN}) \]  

(2)

where \( I_{OC} \) is the intake dose from outdoor inhalation, \( C_0 \) is the outdoor air exposure concentrations from the NATA data and Eq. (1) (ng m⁻³), \( BR \) is the average breathing rate for adults (= 15 m³ day⁻¹) (US EPA, 2011), MW is the molecular weight of the compound (ng nmol⁻¹), and \( F_{IN} \) is the fraction of time spent indoors (= 0.7) (U.S. EPA, 2011).

2.3. Modeled estimates of exposure from food ingestion due to outdoor air emissions

We used the CalTOX multimedia total exposure model (McKone, 1993) to estimate PAH daily intake (nmol day⁻¹) from food ingestion, including vegetables, meat, milk, eggs, and fish. However, this model does not account for intake that would occur during food preparation due to limited information of PAH concentrations in the U.S. diet after cooking, thus we might be underestimating exposure from food intake. The CalTOX model considers chemical transformation in the environment (see Table A2 in the Appendix for the environmental degradation half-lives used in the CalTOX model) and uses biotransfer and bioconcentration factors, including partition coefficients between soil and plants; between air and plants; between animal feed intake and animal-based food products; and between surface water and fish (Hsieh et al., 1995) (see Table A3 in the Appendix for the biotransfer and bioconcentration factors used in the CalTOX model). The CalTOX model has been widely used for environmental contaminant distributions and multimedia exposure and risk assessments (Hertwich et al., 2001; Dör et al., 2003; Glorennec et al., 2005). The model can estimate direct inhalation exposure from environmental releases to ambient air and also track indirect exposures through food or water ingestion attributable to the environmental releases in a particular study area. Thus, we applied the 2002 NATA county-level emissions data to the CalTOX model as input and assigned the individual landscape properties of each state that corresponds to each county.

2.4. Modeled estimates of exposure from indoor sources

To model indoor exposures, we relied on the data of field studies, which collected indoor measurements, to provide insight on the contributions to cumulative intake from the indoor environment. For phenanthrene, pyrene, and benzo(a)pyrene, we used indoor PAH concentration distributions collected from 55 nonsmoking residences in Los Angeles, California; Houston, Texas; and Elizabeth, New Jersey, during June 1999—May 2000 (Naumova et al., 2002). For naphthalene and fluorene, we used indoor concentration distributions collected from 10 nonsmoking houses in the Chicago area during 1994–1995 (Van Winkle and Scheff, 2001), because Naumova et al. study did not collect naphthalene and fluorene samples. There are several other studies that measured naphthalene and fluorene concentrations indoors in the United States. However, these were measured in a much earlier (1986–1987) time period (Mitra and Ray, 1995) or in low-income houses, which could result in potential bias of air concentration due to heavy mothball usage (Chuang et al., 1999).

Although all of these field samples were collected in urban areas, we expect that both naphthalene and fluorene indoor concentrations from Van Winkle and Scheff (2001) may be representative of the U.S. population. Because the indoor concentrations were much greater than outdoor concentrations, indoor concentrations are not dependent on regional variability of outdoor concentrations, but depend on variability of indoor emission rates and housing properties such as air exchange rate (Li et al., 2005). For phenanthrene, pyrene, and benzo(a)pyrene, outdoor regional concentration differences may influence indoor concentrations as outdoor concentrations are more significant contributors to indoor levels (Dubowsky et al., 1999; Naumova et al., 2002; Li et al., 2005). We summarized PAH indoor air concentrations (ng m⁻³) from these field studies as well as annual emission rate (kg year⁻¹) and outdoor air concentrations (ng m⁻³) in Table 2.

To estimate the daily intake dose (nmol day⁻¹) from indoor inhalation, we used the following equation.

\[ I_{IC} = C_I \cdot BR \cdot (1/MW) \cdot F_{IN} \]  

(3)

where \( I_{IC} \) is the intake dose from indoor inhalation, \( C_I \) is the indoor air exposure concentrations (ng m⁻³) from Naumova et al. (2002) and Van Winkle and Scheff (2001), BR is the average breathing rate for adults (= 15 m³ day⁻¹), MW is the molecular weight of the compound (ng nmol⁻¹), and \( F_{IN} \) is the fraction of time spent indoors (= 0.7).

2.5. Natural variations of exposure based on biomarkers

Hydroxy-PAH metabolites were measured in urine from a random one-third subsample of participants 6 years old and older in the 2001–2002 NHANES survey (CDC, 2005). Generation of single hydroxylated PAH products is a result of initial metabolism of the compound by the cytochrome P450 enzyme. NHANES does not measure metabolites generated from multiple cycles of P450 metabolism. It should be noted that this is another source of uncertainty that might lead to an underestimation of cumulative PAH intake based on CDC biomarker data. Nevertheless, since the measurements of hydroxylated metabolites reflect exposure to parent PAHs that has occurred in the last few days, these

<table>
<thead>
<tr>
<th>Compound</th>
<th>NATA annual emission rate</th>
<th>Predicted outdoor exposure concentration from ASPEN</th>
<th>Measured indoor concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naphthalene</td>
<td>911.9(5.9)²</td>
<td>18.8(1.4)²</td>
<td>900(4.5)²</td>
</tr>
<tr>
<td>Fluorene</td>
<td>42.4(3.7)²</td>
<td>0.57(1.2)²</td>
<td>59(3.5)²</td>
</tr>
<tr>
<td>Phenanthrene</td>
<td>126.0(4.0)²</td>
<td>1.80(1.5)²</td>
<td>30(2.8)²</td>
</tr>
<tr>
<td>Pyrene</td>
<td>28.3(6.4)²</td>
<td>0.87(3.5)²</td>
<td>2(2.8)²</td>
</tr>
<tr>
<td>Benzo(a)pyrene</td>
<td>6.3(4.4)²</td>
<td>0.19(3.6)²</td>
<td>0.06(2.8)²</td>
</tr>
</tbody>
</table>

² EPA (2009).

² Computed from annual emission rate and ASPEN modeled naphthalene concentrations.


² Naumova et al. (2002).
metabolites of PAHs provide a method to assess human exposures to PAHs (Strickland et al., 1996). Although there are some environmental transformations that produce hydroxy-PAHs prior to human ingestion, they are not considered to be significant sources of the hydroxy-PAHs observed in human urine (Barrado et al., 2012).

Since a majority of naphthalene (94.7%), fluorene (94.6%), and pyrene (94.7%) samples had levels above the LOD during the 2001–2002 survey, we used the distribution of urine concentrations that NHANES has released (CDC, 2005) or the 2002 survey, we used the distribution of urine concentrations that NHANES has released (CDC, 2005). The inverse of a lognormal cumulative distribution function (cdf) was used to estimate two concentrations at two percentiles, we estimated two unknown percentiles (75th and 95th percentiles) of urine concentrations summarized in the NHANES survey (ng L⁻¹). Thus, we used two percentiles (e.g., 75th and 95th percentiles) of urine concentrations summarized in the CDC’s report to fit an assumed lognormal distribution of the U.S. population intake for phenanthrene and benzo(a)pyrene. Given two concentrations at two percentiles, we estimated two unknown mean and standard deviation of lognormal distribution using the inverse of a lognormal cumulative distribution function (cdf) (Ramaswami et al., 2005).

\[ C_U = F^{-1}(p|\mu, \sigma) \]  

where \( C_U \) is the urinary PAH metabolite concentration at the probability of \( p \) of the inverse lognormal cdf with parameters \( \mu \) (mean) and \( \sigma \) (standard deviation) of \( \ln(C_U) \).

To estimate the daily intake dose (nmol day⁻¹) from urine concentrations, we used the following equation.

\[ I_{UC} = C_U \times \text{Output} \times (1/MW) \]  

where \( I_{UC} \) is the intake dose from urine concentrations, \( C_U \) is the urine concentrations from the NHANES survey (ng L⁻¹), Output is the average urine output per day (= 1.5 L day⁻¹), and MW is the molecular weight of the compound (ng nmol⁻¹).

2.6. Impact of indoor emission rates

Ultimately, one would like to be able to compare total production volume of compounds to measured biomarkers of exposure. As emissions to the indoors may be important for some compounds, we determined the impact of accounting for what portion of that total production volume was released indoors versus outdoors. We estimated the indoor residential emission rate for PAHs whose primary exposure pathway is likely indoor inhalation by comparing to the estimated exposure from the biomarkers. For example, given the total naphthalene outdoor emission rates (\( E \)), median naphthalene intake from outdoor emissions (\( I_{OC} \)), and naphthalene total intake inferred from urinary concentrations (\( I_{UC} \)), we analyzed the fraction of total naphthalene emission amount released to indoor residential environments (\( f \)). Assuming that naphthalene food intake is negligible due to low octanol–water partition coefficient (\( K_{ow} \)), we can estimate the total intake from outdoor and indoor inhalation using the following equation.

\[ I_{TOT} = I_{OC} + \frac{f \times E}{N} \times iF_{IN} \times CF \]  

where \( I_{TOT} \) is the total intake dose from both indoor and outdoor inhalation (mg day⁻¹), \( I_{OC} \) is the intake dose from outdoor inhalation (mg day⁻¹), \( f \) is the fraction of total emission to indoor residential environments (unitless), \( E \) is the emission rate (kg day⁻¹), \( N \) is the total number of household in the U.S. in 2002 (=10⁸ homes), \( iF_{IN} \) is the indoor intake fraction (i.e., the integrated incremental intake per unit emission) for a male adult from continuous releases (=2.1 × 10⁻³ mg day⁻¹ per 1 mg day⁻¹/home of naphthalene emission), and \( CF \) is the conversion factor (10⁶ mg kg⁻¹). Varying \( f \) in Eq. (6) allows us to find an optimal value of \( f \) that matches the total intake (\( I_{TOT} \)) to the intake inferred from urinary concentrations (\( I_{UC} \)). Thus, we estimated the average naphthalene indoor emission rate per household by multiplying the total naphthalene emission (\( E \)) and the estimated fraction of emission to indoors (\( f \)) and dividing by the number of household in the U.S. in 2002 (\( N \)).

3. Results

3.1. Intake distributions

Using the NATA county-level emission data, the CalTOX model, and indoor concentrations from field studies, we estimated daily intake dose (nmol day⁻¹) for five PAHs found in both the 2001–2002 NHANES survey and the 2002 NATA emissions inventories. Fig. 1 illustrates the lognormal cumulative distribution of naphthalene intake from outdoor inhalation (NATA data and ASPEN model), food ingestion (CalTOX), and indoor inhalation (field studies) as well as intake inferred from biomarkers (NHANES). We transformed the y-axis of the cdf plot to Z-scores to reflect variability rather than cumulative probabilities because the slope of each line reflects the variability of intake distributions. The closely matched intake distributions from NHANES (red) and indoor inhalation (blue) in Fig. 1 indicate that the total naphthalene intake inferred from biomarkers is predominantly driven by indoor inhalation and that the standard deviation of both distributions appears to be very close; they both vary over about four orders of magnitude between the 1st and 99th percentile. However, we note that the predicted intake from indoor inhalation was larger than the estimated intake from biomarkers and that this is likely due to the potential temporal variation of naphthalene indoor concentrations between an indoor field sampling time period (1994–1995) and our targeting time period (2001–2002) along with spatial variation of naphthalene uses between study homes and the U.S. general households.

Similar to naphthalene, the major exposure route of fluorene, phenanthrene, and pyrene is likely indoor inhalation based on the slope and standard deviation of two distribution curves from Fig. 1. Log-probability plot for naphthalene intake in nmol day⁻¹.
NHANES and indoor concentrations [see Appendix, Figs. A1–3]. However, as the vapor pressure of the substances decreases as one goes from fluorene to pyrene, we note that the distance between the estimated intake inferred from biomarkers and the modeled intake from indoor concentrations increases, indicating that the contribution of exposure from indoor sources to the total intake becomes smaller with decreasing vapor pressure values. Different from the other four PAHs, Fig. 2 shows that the modeled national variation of benzo(a)pyrene intake from food ingestion is closely matched with the variation of intake inferred from the biomarkers, indicating that models including multiple pathways of exposure are necessary to estimate actual benzo(a)pyrene exposure. Due to its low volatility, both indoor and outdoor inhalation have a negligible contribution to the total benzo(a)pyrene intake.

In Table 3, we present the median daily intake rate in nmol day$^{-1}$ and the relative contribution of each exposure route to the total intake for the five selected PAHs. For volatile compounds with vapor pressure values larger than 0.01 Pa, including naphthalene, fluorene, and phenanthrene, more than 97% of intake is due to indoor sources. For less volatile and more persistent compounds, including benzo(a)pyrene, more than 95% of intake is from food ingestion resulting from overall environmental dispersion. Based on the predicted food ingestion intake by food type, including produce, meat, milk, eggs, and fish from the CalTOX model, the primary sources of benzo(a)pyrene food intake are meat (41%) and milk (35%) (see Table A4 in the Appendix for estimated percent ingestion intake by different food type for each PAH). For pyrene, with moderate volatility and persistence in the environment, indoor inhalation is still dominant, but outdoor inhalation becomes the second most important exposure pathway to the total exposure. The ratio of predicted (from indoor and outdoor inhalation and food intake) to estimated (from biomarkers) intake for pyrene is the smallest among the compounds, indicating that there are other likely important exposure routes for pyrene or we were underestimating either food or indoor air concentrations. Overall, total predicted intakes from the sum of food ingestion and indoor and outdoor inhalation were within a factor of 3.4 of the median estimated intake from NHANES samples for each of the five PAHs.

3.2. Sensitivity of indoor emissions on total intake

To determine the amount of change in the predicted naphthalene exposure with increasing indoor emissions, we assumed indoor emissions increases as a function of total outdoor emissions (e.g. assume indoor emissions are 0.1% of outdoor emissions), and plotted this versus the projected total naphthalene intake (mg day$^{-1}$) in Fig. 3. However, the predicted median naphthalene intake from outdoor inhalation, assuming no indoor emissions, is $5.5 \times 10^{-5}$ mg day$^{-1}$, whereas the estimated median intake from NHANES is about two orders of magnitude higher ($2.6 \times 10^{-3}$ mg day$^{-1}$) than this value. Assuming additional emissions to the indoor environment of 0.3% of total outdoor emissions results in the projected total naphthalene intake (blue dotted line) meeting the median intake from NHANES (red line). This suggests that the estimates of indoor emission rate for volatile organic chemicals are more important than those of outdoor emission rate although the magnitude of indoor emissions is much smaller (0.3%) than that of outdoor emissions. Based on the number of household in the U.S. in 2002 (N), the total naphthalene emission ($E$), and the estimated fraction of emission to indoors ($f$), the average naphthalene emission rate per household is about 1.1 mg day$^{-1}$.

4. Discussion

There has been a lack in understanding about how environmental modeling and sampling data can be used to evaluate contributions to total intake inferred from biomarkers. This work is an effort to address the importance of applying both indoor and outdoor models to evaluating biomarker data using PAHs as a case study. Comparison of estimated intake from biomarkers with predicted intake from multiple sources allows us to evaluate the performance of our approach for assessing exposure. However, there are many sources of uncertainty in model predictions. We grouped them into three categories: (1) uncertainty associated with modeled exposures from the three exposure pathways that are included in the total intake, (2) uncertainty associated with potential exposure pathways that are not included in the total intake, and (3) uncertainty associated with estimated intake inferred from biomarkers.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Outdoor inhalation based on NATA emissions (a)</th>
<th>CalTOX food intake based on NATA emissions (b)</th>
<th>Indoor inhalation intake based on indoor sources (c)</th>
<th>Total predicted intake from food and outdoor and indoor air (a + b + c) (d)</th>
<th>Estimated intake based on NHANES biomarkers (e)</th>
<th>Ratio of predicted to estimated intake (d)/(e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naphthalene</td>
<td>0.4(0.7%)</td>
<td>0.001(0.1%)</td>
<td>63.1(99.3%)</td>
<td>63.5</td>
<td>18.6</td>
<td>3.4</td>
</tr>
<tr>
<td>Fluorene</td>
<td>0.01(0.3%)</td>
<td>0.01(0.1%)</td>
<td>3.7(99.6%)</td>
<td>3.7</td>
<td>3.3</td>
<td>1.1</td>
</tr>
<tr>
<td>Phenanthrene</td>
<td>0.03(1.8%)</td>
<td>0.01(0.4%)</td>
<td>1.8(97.9%)</td>
<td>1.8</td>
<td>3.1</td>
<td>0.6</td>
</tr>
<tr>
<td>Pyrene</td>
<td>0.01(9.7%)</td>
<td>0.003(2.5%)</td>
<td>0.1(87.8%)</td>
<td>0.12</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>Benzo(a)pyrene</td>
<td>0.002(2.1%)</td>
<td>0.09(95.2%)</td>
<td>0.002(2.7%)</td>
<td>0.09</td>
<td>0.06</td>
<td>1.5</td>
</tr>
</tbody>
</table>
4.1. Uncertainty in modeled exposure

Uncertainties in modeled exposures included in the total intake result from variability and uncertainty of indoor and outdoor concentrations and food concentrations. Although indoor inhalation is likely the predominant exposure pathway for phenanthrene and pyrene, the predicted intake from indoor inhalation for all PAHs has significant uncertainty. This uncertainty arises because all of the indoor air concentrations were measured in urban areas where outdoor concentrations resulting from a high density of mobile sources could contribute significantly to indoor concentrations (Dubousky et al., 1999; Naumova et al., 2002; Li et al., 2005). The uncertainties in naphthalene and fluorene indoor concentrations are likely associated with a small sample size (N = 10) of the Van Winkle and Scheff study (2001). More studies with a larger sample size are needed to reduce the uncertainties in indoor inhalation intake for this study population.

There are uncertainties in outdoor air concentrations as well. County-level estimates of average outdoor concentrations from the ASPEN model (see Table A1 in the Appendix) were compared with measured concentrations and found to be lower. The concentrations may be lower because we are comparing county average values to measured values collected either in areas with high density of traffic or in highly industrialized areas. Therefore, we may have underestimated phenanthrene and pyrene exposure from outdoor inhalation intake. Moreover, the uncertainties of about a factor of 2–3 in the ASPEN model predictions could result in uncertainties in outdoor concentration predictions (Hanna et al., 2007).

Based on a previous uncertainty analysis, the estimated uncertainties in the CalTOX model predictions for food ingestion are about a factor of 5 (McKone, 1994). Thus, uncertainties in the total intake could result from food intake for benzo(a)pyrene, as its predominant exposure pathway is likely from food intake due to its high K<sub>ow</sub>. Some research indicates that PAHs may be metabolized in the general U.S. population (2009). Therefore, smoking is an important pathway in comparing PAH exposure to biomarkers for smokers and second-hand smokers. However, the contribution from smoking was not added to the total intake, because urine samples for phenanthrene and benz(a)pyrene could not be linked to smoking status and adding exposure from smoking is beyond the scope of this study. In addition, exposure to carbaryl could result in increased levels of 1-hydroxynaphthalene (i.e., 1-Naphthol) (Meeker et al., 2004), but information to quantify this pathway is limited and thus excluded in our study. Occupational exposure was also not included because distributions of occupational exposure for the population are not available and occupations of individuals sampled in NHANES are not known.

Another potential exposure is through food intake of PAHs formed during thermal processes and cooking over open fires or charcoal (Chung et al., 2011). Chung et al. reported that the levels of PAHs on smoked meat products depend on the cooking method and type of heat sources (2011). Several studies reported that consumption of roasted, grilled, or broiled meat resulted in increased urinary PAH metabolite concentrations (Buckley and Lioy, 1992; Kang et al., 1995; Sithisarankul et al., 1997). Thus, dietary exposure from cooking can be an important exposure pathway for people who consume primarily roasted, grilled, or broiled meat. Food intake could theoretically have been assessed through measured concentrations rather than modeled values. However, we did not include this contribution in the total intake because PAH food concentrations were limited and dietary information including cooking styles and food types was not available for the study population.

As PAHs are commonly found in household dust, the other potential exposure pathway of PAHs with the high octanol–air partition coefficient (K<sub>oa</sub>) for younger children could be non-dietary dust ingestion through hand-to-mouth and object-to-mouth activities (Wilson et al., 2000; Maertens et al., 2004; Gevao et al., 2007; Langer et al., 2010). Wilson et al. reported that for PAHs, which are probable human carcinogen, non-dietary ingestion was the most important exposure pathway for 9
children at day care and at home, followed by dietary ingestion, and inhalation (2000). Maertens et al. reported that settled house dust may be an important source for exposure to indoor PAHs for preschool children (2004). Gevao et al. (2007) and Langer et al. (2010) reported that non-dietary dust ingestion in the indoor environment might be an important exposure route for pyrene for younger children. However, we did not add the contribution of dust ingestion to the total intake, because urine samples used in our study were measured from the participants in the NHANES survey who are 6 years old and older (CDC, 2005), and non-dietary dust ingestion is only important for children who are younger than 7 years old (Shin et al., 2012).

4.3. Uncertainty associated with biomarkers

Temporal variability of urine concentrations from the NHANES survey might result in uncertainties in estimated intake inferred from biomarkers, because a single spot urine sample might not fully capture the actual daily intake of a PAH for an individual due to the short half-life of PAHs in the body (Li et al., 2010). Metabolic variability of PAHs in human bile is another source of uncertainties in intake inferred from biomarkers. However, the population variance of PAH metabolites includes both person-to-person variance of PAH intake and uncertainty related to excretion/ intake ratios based on issues such as time-of-day, spot vs. daily urine, and creatinine levels (Li et al., 2010). The coefficient of variation (CV) for all PAH metabolites for this population ranging from 1.6 to 2.0 is greater than the within-person variation (CV) for 1-hydroxypyrene from 30 children ranging 0.14 to 1.1 (Li et al., 2010). The constructed distributions of urine concentrations for phenanthrene and benzo(a)pyrene from two percentiles are another limitation of our study, because more than half of urine samples for these compounds were detected below LOD.

5. Conclusions

Despite the lack of exposure intake from other potential exposure pathways such as cigarette smoking, carbaryl exposure, non-dietary ingestion, and food intake of smoked products and the uncertainties resulting from modeled exposure and biomarkers, preliminary comparisons of predicted intake with estimated intake from the NHANES biomarkers suggest that the predicted intake doses for the selected PAHs are within a factor of roughly 3.4 of the median estimated intake inferred from the NHANES biomarkers. Model predictions could be improved with inclusion of other potential exposure pathways, including cigarette smoking, carbaryl exposure, non-dietary ingestion, and food intake as a result of cooking as well as by reducing uncertainties associated with input parameters and biomarkers.

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Appendix A. Supplementary material

Supplementary material related to this article can be found at http://dx.doi.org/10.1016/j.atmosenv.2012.02.027.

References


Centers for Disease Control and Prevention (CDC), 2003. Third National Report on Non-dietary dust ingestion to the total intake, because urine samples used in our study were measured from the participants in the NHANES survey who are 6 years old and older (CDC, 2005), and non-dietary dust ingestion is only important for children who are younger than 7 years old (Shin et al., 2012).


