Personal inhalation risk assessment based on a hybrid method using CFD-CSP-PBTK modelling: quantification of time-averaged and peak concentration differences

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Abstract. Human health has been intimately linked to the indoor environment, highlighting the relevance of indoor air quality (IAQ). Although various techniques have been developed to maintain the well-being of building residents/workers, a convergence between IAQ and personal inhalation exposure risk under realistic conditions has yet to be achieved due to the heterogeneous nature of contaminant transfer. In this regard, computational fluid dynamics (CFD) is a promising tool when analysing detailed three-dimensional flow and gas-phase contaminant transport in a building. From this viewpoint, this study performs a comprehensive inhalation exposure analysis in the working environment, integrating outdoor airflow to the indoor environment of a factory under cross-ventilation for an 8-hour occupational period, a factory worker in the form of a computer simulated person (CSP) and a semi-coupled virtual respiratory tract. A physiologically-based toxicokinetic (PBTK) model has been added to the respiratory tract to predict tissue dose distribution, i.e., inhalation exposure risk. Three cases were analysed to confirm the differences between maximum/minimum and time-averaged inhaled dose for a comprehensive source-to-dose study. Results confirmed the relevance of calculated personal inhalation exposure for an accurate time-averaged intake and the danger of acute exposures at given times of a working day.

1. Introduction
Air pollution directly affects human health, potentially causing cardiopulmonary and respiratory diseases, as well as raising levels of mortality and morbidity [1][2][3]. Although air pollution was previously deemed an outdoor issue, it has been documented that air pollutants also concern the indoor environment because modern society spends roughly 90% of the day indoors (home, school, work, hospital…) [4]. Therefore, the control of indoor air quality (IAQ) becomes crucial for public health improvement and inhalation risk assessment.

IAQ is affected by several factors due to the complexity of indoor environments: pollutant properties, building design, dwellers’ behaviour and outdoor environment conditions such as air temperature and urban wind velocity/direction [5][6]. The outdoor environment is particularly relevant in the case of natural ventilation (i.e. cross-ventilation) since variation in building ventilation rate has a direct impact on IAQ. Specifically, the prediction of the physiological effects on the human body caused by poor IAQ while considering outdoor/indoor environment interaction becomes crucial for realistic personal inhalation exposure and for quantification of dose intake.

In the past decades, computational fluid dynamics (CFD) has been applied to various issues regarding outdoor and indoor environmental design as well as IAQ prediction because it provides detailed heterogeneous characteristics of airflow, temperature, humidity and contaminant
concentration [7]. While CFD has been previously used to predict local zone and breathing air contaminant concentration [8], it has not yet been used to predict source-to-dose path under realistic working conditions to quantify inhaled pollutants. In order to quantify this inhaled pollutant dose and its potential effects on the human body – particularly the human respiratory tract –, the implementation of a physiologically-based toxicokinetic (PBTK) coupled with CFD becomes necessary [9].

Furthermore, for most industrial environments analysis, the prediction of average concentrations – i.e. time-averaged – is a commonly used approach. However, analysis of instantaneous “peaks” where contaminant concentration can be higher or lower than the average value are just as essential for a comprehensive risk assessment during short-period fluctuations in terms of acute exposure [10].

Against this background, this study has developed a comprehensive technique that joins the transient interactions of outdoor/indoor environment for IAQ prediction based on variable building ventilation rate. In order to analyze contaminant concentration of breathing air, a computer simulated person (CSP) was integrated to the target building and a virtual human respiratory tract model was semi-coupled. A PBTK model was integrated to the respiratory tract to precisely quantify inhaled (absorbed) contaminant dose in the lumen. Finally, differences between the effects of time-averaged contaminant concentration and short-time peaks were quantified.

2. Methodology
In order to analyse the influence of urban airflow variation around the target building under cross-ventilation, outdoor conditions were analysed by coupling Weather Research and Forecasting model (WRF) and CFD dynamic downscaling method [11]. Global parameters of wind velocity/direction, temperature and turbulence were calculated and downcaled to be analysed in an urban domain. These results were previously reported and used in the present study to generate indoor airflow and variation in ventilation rate from 08:00 to 17:00 hours in the target building. Urban flow characteristics were calculated at every prevailing hourly wind direction during the established period under steady-state conditions and urban flow was transported into the building by way of wind pressure coefficient concept, as already reported [11].

![Figure 1](image.png)

**Figure 1.** Design of (a) building, (b) local CSP surroundings, (c) CSP and (d) respiratory tract

2.1. Indoor environmental contaminant exposure
Cross-ventilation airflow was generated inside a factory building with an integrated CSP, which was previously validated [12]. Factory–CSP design is shown in Figure 1 (a) and Figure 1 (b) depicts the CSP location inside the working area of the building. Complex CSP geometry is shown in Figure 1 (c). The building analytical domain was discretized by an unstructured mesh of 2.97 million elements. The CSP was discretized by a mesh of 1.95 million elements and at least five layers of prism cells with a thickness of less than 0.5 mm were added to the surface of the CSP for a detailed analysis of the viscous sub-layer.
Urban airflow entered the building through open windows and turbulence was analysed using the shear stress transport (SST) $k-\omega$ model while boundary conditions at the windows (pressure, temperature $k$ and $\omega$) were set according to previously obtained outdoor results. To analyse indoor exposure risk, six indoor-only contaminant sources were fixed in the form of industrial machines, surface contaminant sources have been highlighted in Figure 1 (a). A working schedule was established to generate the passive contaminant: contaminant flux was set to $f = 0$ g/s during lunch break and fixed constant at $f = 4$ g/s during working hours for realistic conditions. Contaminant was nasally breathed by the CSP at a constant respiration rate of 7.5 lt/min and skin temperature was maintained constant. The overarching objective of this step was to calculate contaminant concentration at the nares of the CSP based on realistic indoor environmental conditions.

2.2. Personal inhalation exposure

To perform a personal inhalation risk assessment by predicting the amount of contaminant adsorbed on the surface of the respiratory tract, a PBTK model was applied. Contaminant transport was modelled in the air and mucus layer of tissue through flux conservation and partition coefficient by using equation (1), which applies a linear contaminant concentration profile in the mucus layer and treats the concentration at the interface as zero [13]:

$$\frac{\partial C_a}{\partial x} + \frac{D_a P_{aw}}{D_m h_m} C_{1w}=0$$  \hspace{1cm} (1)

Where $C_a$ and $C_i$ are the contaminant concentrations in the air and mucus layer, respectively; $D_a$ and $D_i$ are the diffusion coefficients of the cyclohexanone in the air and mucus layer. Here, $D_a$ and $D_i$ have been treated as the diffusion coefficients of the contaminant in air and water ($7.83\times10^{-6}$ and $8.38\times10^{-10}$ m$^2$/s), respectively; and $h_m$ is the thickness of the mucus layer adopted (15 $\mu$m). $P_{aw}$ is the partition coefficient, adopted from literature and corrected for use at 36 °C, considered the standard temperature inside the human respiratory tract, by using equation (2); thereafter, equation (3) was used to calculate dimensionless $P_{aw}$:

$$H^{CP}(T) = H^{CP}(T^0) \exp\left[\frac{d \ln H^{CP}(T)}{d(1/T)} \left(\frac{1}{T} - \frac{1}{T^0}\right)\right]$$  \hspace{1cm} (2)

$$H^{CC} = H^{CP} \times RT$$  \hspace{1cm} (3)

Where $H^{CP}(T^0)$ is the partition coefficient at 25 °C and $d \ln H^{CP}(T) / d(1/T)$ is Henry’s law constant, adopted from literature [14]; $R$ is the gas constant and $T$ is the absolute temperature. The PBTK model was adjusted to the wall surfaces of the semi-coupled respiratory tract model in Figure 1 (d). This domain was discretized by an unstructured mesh of 7.53 million elements and has been previously validated [15]. The Low Reynolds $k-\varepsilon$ (AKN) model was used to analyse turbulence due to the complex geometry of the region. Furthermore, respiration rate 7.5 L/min was maintained and temperature of breathed air was set according to results obtained from the factory–CSP analysis. Wall surface temperature at the lumen was set constant at 309.80 K, according to standard human body conditions. Based on the contaminant concentration results calculated at the nares of the CSP, three cases of personal inhalation exposure have been analysed to assess their differences and impact on the human body. These are: highest instantaneous peak concentration $C_{in} = 62.76$ mg/m$^3$ at 11:49 hours, lowest instantaneous concentration $C_{in} = 0.030$ mg/m$^3$ at 12:58 hours and 9-hour time-averaged concentration $C_{in} = 41.52$ mg/m$^3$.

3. Results and discussion

Figure 2 (a) and (b) show contaminant concentration distribution inside the factory building and around the CSP at representative times before the peaks 11:30 and 12:30 hours, respectively.
High concentration levels can be seen at 11:30 hours, particularly near the emission source depicted with varying gradients of contaminant around the CSP. In contrast, contaminant distribution around the CSP at 12:30 diminishes greatly and becomes almost uniform due to stagnation of airflow.

Figure 2 (c) shows transient contaminant concentration at the nares of the CSP based on realistic conditions of diurnal ventilation rate, building design and CSP position inside the building. High contaminant levels were observed during the day despite the change in ventilation rate except during lunch break, when the change in contaminant emission ($f = 0$ g/s) had a major impact on inhaled amount. From these results, it was confirmed that the close location of the CSP to the contaminant sources had a major impact on inhaled contaminant.

Figure 2. Contaminant concentration results of (a) distribution in factory-CSP at 11:30 h, (b) at 12:00 h and (c) transient at the nares of CSP and time-averaged
Peak inhaled cyclohexanone concentration occurred at 11:49 hours while lowest inhalation of contaminant concentration was at 12:58 hours. Then, the schedule set for contaminant sources had a direct effect on contaminant levels and personal exposure.

Figure 3 shows the three cases of inhalation dose calculated in terms of (1) adsorption flux at the lumen (mucus) tissue of the respiratory tract and (2) normalized contaminant concentration distribution inside the respiratory tract. Highest peak, lowest and time-averaged results are presented in Figure 3 (a), (b) and (c), respectively. In the three cases, cyclohexanone had a major impact inside the nasal cavity while only less than 20% of the gas-phase contaminant was adsorbed further along the trachea and/or bronchial tubes. Furthermore, non-uniform tissue dose was found in all cases. Lowest peak presented in Figure 3 (c) was considered unimportant when compared to the other two cases; however, traces of contaminant were still found despite that 0 g/s generation rate was set. A marked difference was found between short-term acute exposure (Figure 3 (a)) and time-averaged exposure (Figure 3 (c)) since time averaging was affected by the working schedule and change in contaminant generation rate during break.

Finally, a linear relationship was confirmed between the route of exposure (inhaled contaminant) and toxicity (absorbed contaminant). This is because toxicity exposure through inhalation, as opposed to ingestion, results in the entry of the chemical directly to the systemic circulation, giving no time for metabolic activity. Inhalation is therefore considered the primordial exposure issue and has been addressed in this study.

![Figure 3](image-url)

**Figure 3.** Results of the three inhalation cases in terms of (1) wall adsorption flux and (2) normalized contaminant distribution inside respiratory tract

### 4. Conclusion

In this study, a personal inhalation risk assessment in the form of inhaled dose distribution was performed using an integrated CFD-CSP-PBTK method. Outdoor/indoor environment and IAQ transient conditions were analysed from 08:00 to 17:00 hours in order to calculate inhaled contaminant at the surface of the CSP’s nares. Thereafter, a virtual respiratory tract model was semi-coupled to the CSP to calculate inhaled dose distribution of contaminant in three cases: highest peak, lowest peak and time-average concentration of cyclohexanone.
Estimating the maximum/minimum value of concentration (highest and lowest peak) inhaled at a given time is an essential factor of IAQ as well as time-averaged values to define air quality standard in the industrial field. Therefore, this study focused on quantitatively analysing both conditions. Quantitative results showed a noticeable difference between the three cases: in this study, the lowest peak was considered negligible; furthermore, acute instantaneous exposure (highest peak) was roughly 30% higher than time-averaged concentration. The nasal cavity was primordially affected in both cases under the realistic working conditions described. Then, by applying this method, it was possible to quantify personal inhalation exposure and difference between peaks and time-averaged conditions.

References

[1] HEI, WHO 2018 State of global air. Special report Boston MA Health Effects Institute
[2] International Agency for Research and Cancer 2013 Air pollution and cancer IARC Scientific Publication No. 161 Lyon, France, WHO 2013
[3] Dockery DW, Pope CA, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG and Speizer FE 1993 An association between air pollution and mortality in six US cities N. Engl. J. Med 329 (24) 1753–59
[4] Klepeis NE, Nelson WC, Ott WR, Robinson JP, Tsang AM, Switzer P, Behar JV, Hern SC and Engelman WH 2001 The national human activity pattern survey (NHAPS): a resource for assessing exposure to environmental pollutants J. Expo. Anal. Environ. Epidemiol. 11 (3) 231–52
[5] Kelly FJ and Fussell JC 2019 Improving indoor air quality, health and performance within environments where people live, travel, learn and work Atmos. Environ. 200 90–109
[6] Jantunen M, Oliveira Fernandes E, Carrer P, Kephalopoulos S 2011 European Comission, Directorate General for Health & Consumers, Promoting Actions for Healthy Indoor Air (IAIAQ), European Commission, Luxembourg
[7] Spengler JD and Chen Q 2000 Indoor air quality factors in designing a healthy building Annu. Rev. Energ. Environ. 25 (1) 567–600
[8] Ito K 2014 Integrated numerical approach of CFD and epidemiological model for multi-scale transmission analysis in indoor spaces Indoor Built Environ. 23 (7) 1029–49
[9] Yoo SJ and Ito K 2018 Assessment of transient inhalation exposure using in silico human model integrated with PBPK–CFD hybrid analysis Sustain Cities Soc. 40 317–25
[10] Singer IA 1961 The relationship between peak and mean concentrations J. Air Pollut. Control Assoc. 11 (7) 336–41
[11] Murga A, Sano Y, Kawamoto Y and Ito K 2017 Integrated analysis of numerical weather prediction and computational fluid dynamics for estimating cross-ventilation effects on inhaled air quality inside a factory Atmos. Environ. 167 11–22
[12] Li C and Ito K 2014 Numerical and experimental estimation of convective heat transfer coefficient of human body under strong forced convective flow J. Wind. Eng. Ind. Aerodyn. 126 107–17
[13] Keyhani K, Scherer PW and Mozell MM 1997 A numerical model of nasal odorant transport for the analysis of human olfaction J. Theor. Biol. 186 279–301
[14] Sander R 2015 Compilation of Henry’s law constants (Version 4.0) for water as solvent. Atmos. Chem. Phys. 15 4399–981
[15] Phuong NL and Ito K 2015 Investigation of flow pattern in upper human airway including oral and nasal inhalation by PIV and CFD Build. Environ. 94 504–15
[16] Ito K, Inthavong K, Kurabuchi T, Ueda T, Endo T, Omori T, Ono H, Kato S, Sakai K, Suwa Y, Matsumoto H, Yoshino H, Zhang W, Tu J. 2015 CFD Benchmark Tests for Indoor Environmental Problems: Part 3 Numerical thermal manikins, Int. Journal of Architectural Engineering Technology, 2 (1), 50-75 (doi:10.15377/2409-9821.2015.02.01.3)