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Research article

Estimation of sources and factors affecting indoor VOC levels using basic numerical methods

Sibel Mentese*, Deniz Tasdibi, and Ersin Orak

Canakkale Onsekiz Mart University, Faculty of Engineering, Department of Environmental Engineering, Terzioglu campus, Canakkale, 17100, Turkey

* **Correspondence:** Email: sibelmentese@gmail.com; Tel: +90-286-2180018/ext2174;
Fax: +90-286-2180541.

Abstract: Volatile Organic Compounds (VOCs) are a concern due to their adverse health effects and extensive usage. Levels of indoor VOCs were measured in six homes located in three different towns in Çanakkale, Turkey. Monthly indoor VOC samples were collected by passive sampling throughout a year. The highest levels of total volatile organic compounds (TVOC), benzene, toluene, and xylenes occurred in industrial, rural, and urban sites in a descending order. VOC levels were categorized as average values annually, during the heating period, and non-heating period. Several building/environmental factors together with occupants' habits were scored to obtain a basic indoor air pollution index (IAP*i*) for the homes. Bivariate regression analysis was applied to find the associations between the pollutant levels and home scores. IAP*i* scores were found to be correlated with average indoor VOC levels. In particular, very strong associations were found for occupants' habits. Furthermore, observed indoor VOC levels were categorized by using self-organizing map (SOM) and two simple scoring approaches, rounded average and maximum value methods, to classify the indoor environments based on their VOC compositions (IAPvoc). Three classes were used for both IAP*i* and IAPvoc approaches, namely "good", "moderate", and "bad". There is an urgent need for indexing studies to determine the potential sources and/or factors affecting observed VOCs. This study gives a basic but good start for further studies.

Keywords: building characteristics; environmental factors; indoor air pollution; occupants' habits; volatile organic compounds

1. Introduction

Volatile Organic Compounds (VOCs) include a large group of compounds which are named according to their boiling points, from very volatile organic compounds (VVOCs) with boiling point around 50 °C to semi-volatile organic compounds (SVOCs) with boiling points of 220–260 °C [1]. VOCs consist of different functional groups such as aliphatic hydrocarbons, aromatic hydrocarbons, halogens etc. In terms of health, some VOCs have severe adverse health effects due to acute or chronic exposure [2]. Among them, benzene is one of the most worrying compounds due to its confirmed human carcinogenicity [2,3]; thus its limit value in air has been regulated by many countries (mostly around <5 $\mu g/m^3$ annually).

Sources of VOCs indoors are ubiquitous such as building and decoration products, air fresheners, household cleaning agents, some cooking and heating fuels, many consumer products, office equipment etc. [4-7]. Indoor VOCs are influenced by climatic factors, such as humidity and temperature, as well as occupants' behaviours, such as smoking indoors, household cleaning activity (both frequency, duration and household cleaning agent preferences etc.), ventilation activity (type of ventilator i.e., natural/mechanical and ventilation amount) [8,9].

In addition to the direct effect of indoor temperature fluctuations, season also has an indirect effect on observed indoor VOC levels by means of heating or cooling intentions of the occupants. Thus, occupants tend to close indoor environments during wintertime in order to prevent heat loss, while they tend to cool their indoor environments during the summertime by any means of ventilation. Studies have shown that indoor VOC levels vary seasonally similar to outdoor VOC levels, depending on the predominant source at the time of measurements such as type of domestic heating fuel/industrial fuel or photochemical activity [6,7,10-13].

There are plenty of studies in the literature on indoor VOC levels, yet few of them focus on their potential sources or factors influencing observed indoor VOCs [14]. Residential VOC levels and their sources are not associated with a single source or a single factor; they are due to a mixture of multiple sources. Thus, all potential sources and factors that may influence indoor VOC levels should be taken into account to obtain a basic indoor air pollution index (IAP*i*).

Self-Organizing Maps (SOM) are competitive and unsupervised forms of artificial neural networks (ANNs), pioneered by the Finnish professor Teuvo Kohonen (1981) [15]. One of the most widely used ANN algorithms is SOM, which is used extensively for information extraction without prior knowledge and efficiency of visualization [16]. In this study, SOM is used for overall air pollution classification including all target VOCs.

The aims of this study are: (i) assessment of long-term indoor VOC exposure levels in six different homes in three different towns in Çanakkale, Turkey; (ii) characterizing the indoor environments by scoring the building/environmental factors and occupants' habits; (iii) estimating the associations between indoor VOC levels and building/environmental factors and occupants' habits to form a IAP*i*, and (iv) creating an indoor air pollution index for observed VOC levels (IAPvoc) by categorizing the target VOC levels from good towards bad by using basic numerical methods (i.e. SOM, rounded average, and maximum value).

2. Materials and Methods

2.1. Study design

Indoor VOC levels were measured in homes (n = 6) located in three different towns which are

Çanakkale city center (urban and marine-road traffic), Çan (semi-urban and industrial), and Lapseki (rural and marine-road traffic) in Çanakkale, Turkey. Sampling points are shown in Figure 1. Three of the homes were located in the city center, one home was located in Lapseki, and two homes were located in Çan. All indoor environments were selected randomly from among volunteer participants of a previous health survey of the *Çanakkale HealthAir* Study [10]. Indoor VOC samples were collected every month from living rooms of the sampling sites for a year. Also, temperature and relative humidity values were recorded at the time of sampling. All sampling sites were naturally ventilated homes.

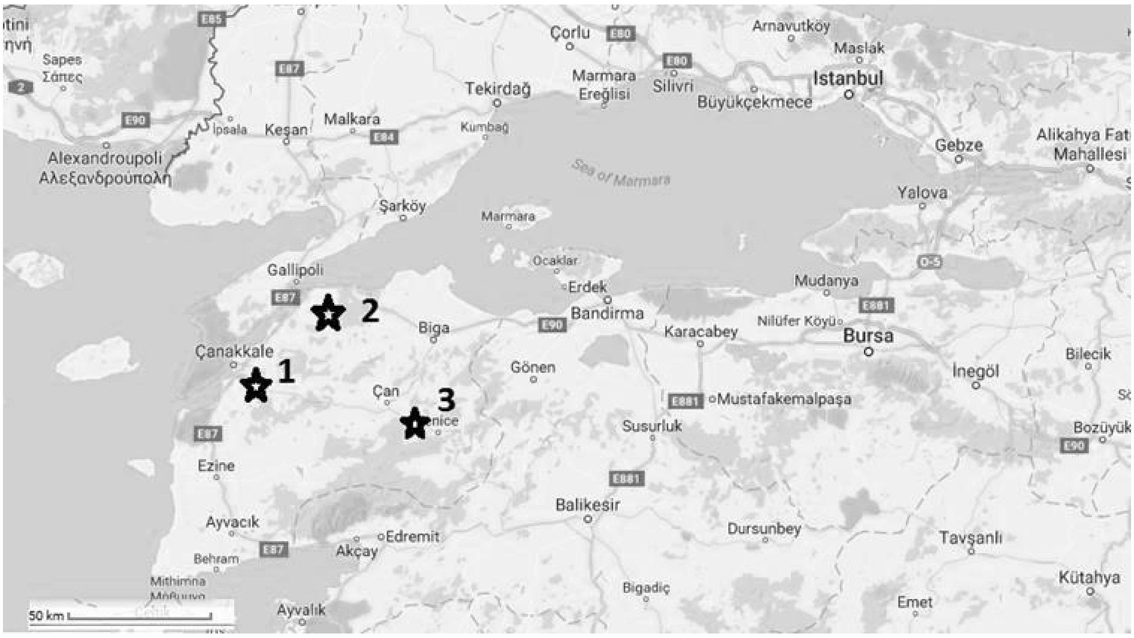


Figure 1. Sampling sites (*denotes the sampling sites 1: Center, 2: Lapseki, and 3: Can).

2.2. VOCs sampling and analyses

Monthly indoor VOC samples were collected from the sampling sites using a passive sampling principle throughout one year [17]. VOC samples were collected on Tenax TA-Carbograph1TD dual-bed sorbent tubes and analyzed by Thermal Desorber (Unity-2, Markes Inc., USA) - Gas Chromatography-Flame Ionization Detector (7890A, Agilent Technologies Inc., USA). A capillary column (DB-VRX, 75 m × 0.45 mm × 2.55 mm, Agilent Technologies Inc., USA) was used to detect VOCs. Concentrations of benzene, toluene, xylenes, i.e. BTX, and total volatile organic compounds (TVOC) were assessed. TVOC concentrations were quantified as toluene-equivalent from C_6 (n-hexane) to C_{16} (n-hexadecane) [10,18,19]. A certified standard VOC mixture (Volatile Arom. + Unsat. Org. Comp. Mix 1, Dr. Ehrenstorfer, Germany) was used for five-point calibration. The limit of quantification (LOQ) for individual VOCs was calculated [10,20] to be around 1.0 $\mu g\ m^{-3}$ on average. Quality Assurance/Quality Control (QA/QC) procedures followed in this study were the same as those in Mentese et al. [10].

2.3. Home inventory

A detailed questionnaire was given to an occupant of each sampling site, including questions about building and environmental parameters (i.e. floor number, room area, flooring material type, last floor covering/wall painting time, and amount of carpet/wooden product in the room), as well as occupants' habits (i.e. home cleaning frequency, pesticide/naphthalene-air freshener usage, cooking/heating fuel type, and average daily ventilation duration) [21]. The sites were investigated visually to monitor the building/environmental related factors for IAPi scoring [14].

2.4. Evaluation of the data

Bivariate regression analyses and other basic computations were applied using MS Excel. Indoor VOC concentrations were analyzed as independent variables; while scores of building/environmental factors, occupants' habits and total factors were dependent variables to find the associations between IAQ parameters and other factors. VOC levels below LOQ were assigned with 1/2 LOQ values to increase the precision of the computations.

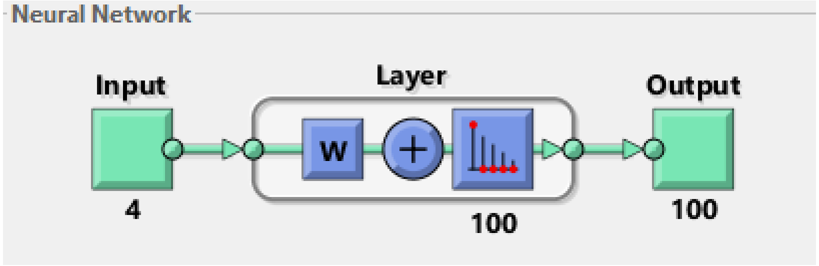
Three different basic numerical methods were used to classify the quality of indoor environments in terms of target compounds of TVOC, benzene, toluene, and xylenes: They are (i) self-organizing map (SOM), (ii) rounded average approach and (iii) maximum value approach.

Artificial Neural Networks (ANNs), divided into supervised and unsupervised learning, are widely used in environmental models. Supervised learning is generally used for data estimation based on prior knowledge, while unsupervised learning is useful for classification of problems without previous knowledge [22]. In this study, Self-Organizing Map (SOM), an unsupervised form of artificial neural networks, was used for indoor air quality (IAQ) classification. There are three procedures for applying SOM: data normalization, training, and extracting information.

In the normalization step, we transformed the pollutants within the range of 0–1, since all parameters had equal importance. The formula used for normalization is given in the equation below:

$$N_i = \frac{X_i - X_{min}}{X_{max} - X_{min}}$$

where X_i is the value of pollutant, X_{min}, and X_{max} are minimum and maximum values of pollutant, respectively. In this study, MATLABR2014a's Neural Clustering toolbox was used for SOM modelling with 10x10 neurons on the output layer (Scheme 1). The training strategy is based on "winner takes all". After the training of SOM, the results can be post-processed based on visualization and clustering [23]. Indoor environments were classified into three categories by SOM: (i) good, (ii) moderate, and (iii) bad.



Scheme 1. Neural network flow chart.

Besides SOM, two other basic numerical methods were used to classify the indoor environments according to their VOC levels. For the rounded average and the maximum value approaches, self-performed VOC classes tending from good towards bad for each target VOC were used (see Table 1). To set the upper and lower limits of each class for the target VOCs, available guideline values, building certification/rating system limit values, suggested levels for health, and the typical values of the VOCs observed in extensive studies were taken into account as a whole.

For the rounded average method, exceeding or non-exceeding the upper limits of each class (“good” = 0, “moderate” = 1, and “bad” = 2) was scored for each target compound, given in Table 1. Thus, the total score for an environment for four target pollutants ranged between zero (all of the target compounds are in “good” class) and eight (all of the target compounds are in “bad” class). Final IAPvoc for the rounded average method is computed using total average score of the environment and rounding the IAPvoc, if it is a floating point number. Estimating the IAPvoc class by the maximum value method is quite similar to the rounded average method. The only difference is the maximum score value amongst the four target pollutants’ scores for each environment is used to estimate the final IAPvoc class, instead of rounding the average score.

Table 1. IAPvoc criteria* used for the rounded average and the maximum value methods.

IAPvoc	Concentration (μg/m^3)			
	TVOC	Benzene	Toluene	Xylenes
Good	< 200	< 2	< 15	< 5
Moderate	≥ 200–1000	≥ 2–5	≥ 15–30	≥ 5–10
Bad	> 1000	> 5	> 30	> 10

*coding: “good” = 0, “moderate” = 1, “bad” = 2

3. Results and Discussion

3.1. Indoor VOC levels

The highest levels of TVOC, benzene, toluene, and xylenes occurred in industrial, rural, and urban sites, in descending order. In general, VOC levels were found to be higher throughout the heating season (October-March) compared to other months (Figures 2–5). Exceptionally, summertime VOC levels were higher in Ind-1 sampling site than wintertime levels, probably due to the enhanced reactions due to photochemical activity together with the industrial emissions. TVOC levels were lower than 1000 μg/m^3 in urban and rural sampling sites, while it was over 1000 μg/m^3 for the industrial ones (see Figure 2).

Benzene levels exceeded the limit value of 2008/50/EC, 5 μg/m^3 [24], only at Ind-1 sampling site during the heating period, while the rest of the time it was below its limit value in all sampling sites (see Figure 3). The lowest benzene levels occurred during the non-heating period in all sampling sites, and in general, the highest benzene levels occurred during the heating period.

Similar to the trends were observed for TVOC and benzene, levels of toluene and xylenes were found to be higher in the industrial town, particularly Ind-1 sampling site, compared to other towns (see Figures 4–5). Similar to TVOC levels trend occurred in Ind-1, the highest toluene/xylene levels were found during the non-heating period, probably due to more frequent ventilation with outdoors where the enhanced photochemistry of toluene/xylenes might have occurred due to industrial sources.

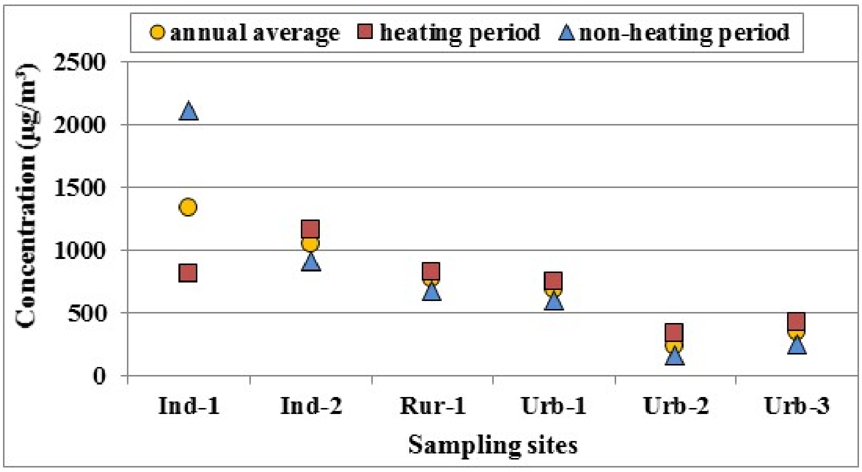


Figure 2. Levels (μg/m^3) of Indoor TVOC (Urb: urban, Rur: rural, and Ind: industrial).

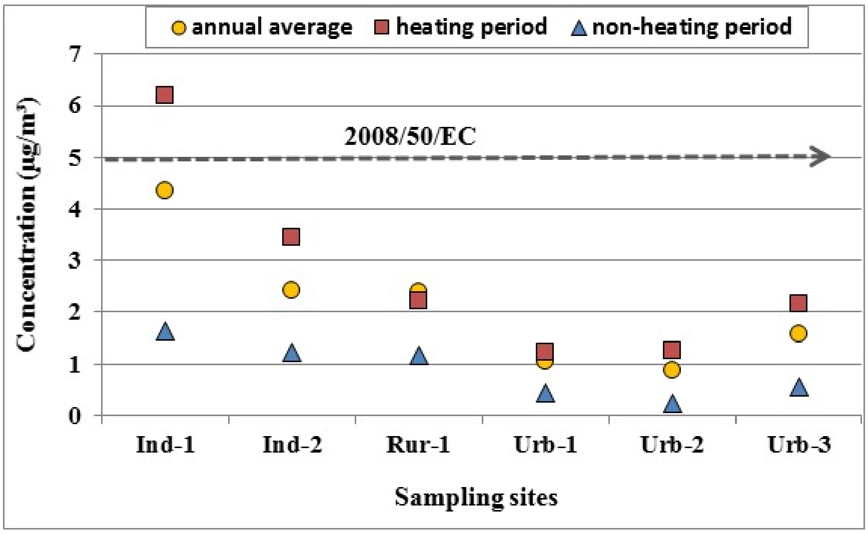


Figure 3. Levels (μg/m^3) of Indoor Benzene (Urb: urban, Rur: rural, and Ind: industrial).

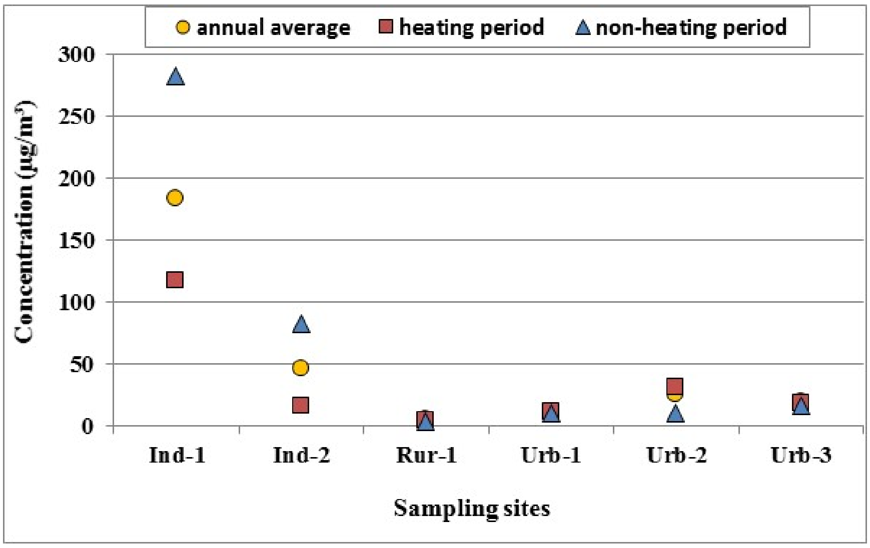


Figure 4. Levels (μg/m^3) of Indoor Toluene (Urb: urban, Rur: rural, and Ind: industrial).

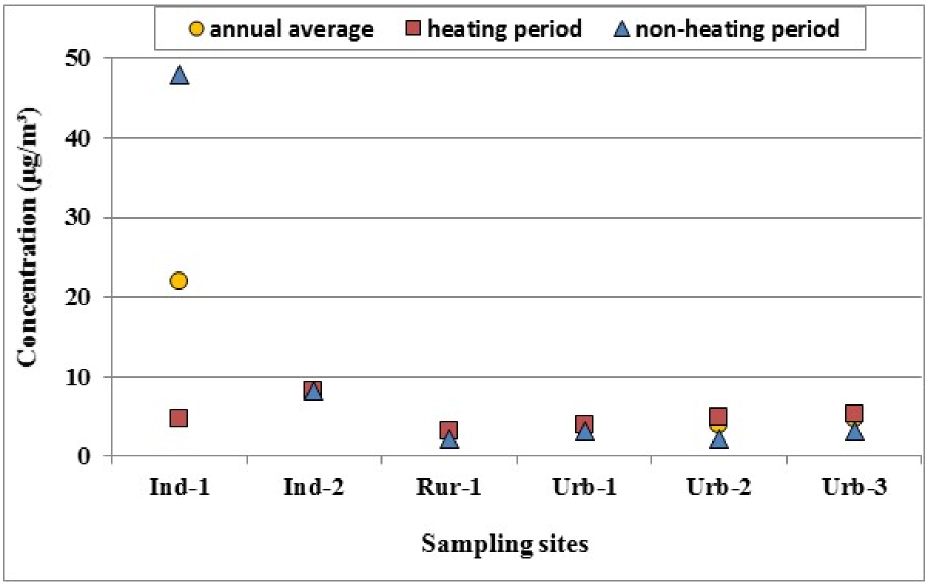


Figure 5. Levels (µg/m^3) of Indoor Xylenes (Urb: urban, Rur: rural, and Ind: industrial).

Similar to this study results, toluene was the first ranked compound among BTEX in another study conducted in Ankara, Turkey [6]. Also, BTEX levels were related to the proximity of outdoor BTEX sources such as traffic and gas stations or availability of VOC sources indoors such as activities related to construction/renovation, kitchen, and smoking [7,25-28].

As mentioned earlier, among BTX, benzene is a concern due to it carcinogenicity [2,29]. The limit value for annual average benzene concentration (5 µg/m^3), set by European Union [24], was only exceeded in one of the sampling sites located in the industrial region only during the heating season not for annual average value. Thus, it can be said that benzene levels can be assumed to be "safe" at the time of sampling, but definitely must be improved particularly in industrial sites. Mentese et al. (2012) also observed the average benzene concentration as > 5 µg/m^3 in some sampling sites with smokers and sites that were close to high density traffic sources in wintertime [6]. Smoking and traffic related activities are the major sources of benzene exposure [30-31]. Benzene levels ranged widely in the EXPOLIS study and the highest benzene levels were observed at sampling sites in Greece, Czech Republic and Italy [32].

3.2. Indoor air pollution index (IAPi)

Building and environmental factors together with occupants' habits were scored to obtain a basic IAP*i* for the homes (Table 2). A total of 14 factors were scored between 5 to 25; building/environmental factors were scored between 4 and 16, and the occupants' habits were scored between 1 and 9. The higher score the environment has, the worse the indoor air quality (higher IAPi value). Some questions have yes/no answers (coded as 0 and 1), while some are multiple choice and thus they were classified logically according to their potential to influence the indoor air pollution, e.g. as the home is located on the lowest floors, contribution of VOC emissions from traffic sources assumed is assumed to be higher. Thus, answers with high scores (2 or 3) are expected to influence the IAQ more, when compared to answers with low scores (0 or 1). For some of the questions scores start from 0 (e.g. no observable effect or negligible effect), while some start from 1 (e.g. this factor has a certain degree of effect anyway).

Table 3 shows the indoor air pollution indexing criteria applied in this study. Accordingly, the environments were classified into three groups: “good”, “moderate”, and “bad” with the IAP*i* approach. IAP*i* is includes two main sub-groups that affect the observed IAQ, which are building/environmental factors and occupants’ habits. Also, these two subgroups were evaluated separately in addition to the total score computed for each environment (IAP*i* value) to find the predominant group with most influence on IAQ. Notice that one of the factors is available or active only during the heating period (i.e. heating fuel type). Hence, the contribution of this factor during the non-heating period was computed as well.

Table 3 also shows the scores for each sampling site ($n = 6$). Similar to indoor VOC levels, the highest IAP*i* scores were found in industrial, rural, and urban sites in descending order. Only one of the sampling sites (Urb-2) was classified as “good” in terms of total IAP*i*, building/environmental conditions and present occupants’ habits, while the other sampling sites fell mostly in “moderate” indoor air quality class. One of the sampling sites located in an industrial region was “bad” in terms of occupants’ habits during the heating season (Ind-1). Finally, IAP*i* value of both sites located in industrial areas were in the “bad” class for the heating period (i.e. Ind 1-2) and in “bad” class in Ind-1 for the annual IAP*i* value.

Table 2. Ranges and scoring criteria for the basic indoor air pollution index (IAP*i*).

Building/Environmental factors	IAP*i* range	Scoring		
Floor number	0–2	0: > 2nd floor	1: 2nd flor	2: ≤ 1st floor
Distance to traffic	1–3	1: less	2: moderate	3: much
Room area	1–2	1: > 15 m^2	2: < 15 m^2	
Flooring material type	0–1	0: concrete	1: wooden	
Last floor covering time	0–1	0: > 1 year	1: < 1 year	
Carpeting amount in the room	1–3	1: < 1/4 of the room	2: 1/4–1/2 of the room	3: > 1/2 of the room
Wooden product amount in the room	1–3	1: < 1/4 of the room	2: 1/4–1/2 of the room	3: > 1/2 of the room
Last wall painting time	0–1	0: > 1 year	1: ≤ 1 year	
Total score for building/environmental factors	*4–16*	*4*	*12*	*+11*
Occupants’ habits				
House cleaning frequency	1–2	1: maximum once a week	2: more than once a week	
Pesticide usage	0–1	0: no	1: yes	
Naphthalane/air freshener usage	0–1	0: no	1: yes	
Cooking fuel type	0–2	0: natural gas	1: butane-propane cylinder	
Heating fuel type	0–2	0: natural gas	1: coal	2: coal & wood
Average daily ventilation duration	0–1	0:> 3 h d^{-1}	1:>3 h d^{-1}	
Total score for occupants’ habits	*1–9*	*1*	*7*	*+2*
Total score	*5–25*			

Table 3. Indexing Criteria and IAP*i* of the sampling sites

Building/Environmental factors	Range	Class code	Urb-1	Urb-2	Urb-3	Rur-1	Ind-1	Ind-2
Good	4–7	0		6				
Moderate	10–12	1	10		10	9	10	12
Bad	13–16	2						
Occupants' habits								
Good	1–3	0	3*	3 (3*)	2 (2*)			
Moderate	4–6	1	4			5 (4*)	6*	5 (4*)
Bad	7–9	2					8	
IAPi (total score)								
Good	5–10	0		9 (9*)				
Moderate	11–16	1	14 (13*)		12 (12*)	14 (13*)		16*
Bad	17–25	2					(17*)	17

*refers to non-heating season score

3.3. Association between observed VOC levels and indoor air pollution index (IAPi)

In addition to indexing the indoor environments according to their building/environmental conditions as well as occupants' habits, associations between IAP*i* and observed VOC levels were examined. For this aim, average levels of annual, heating-period, and non-heating period TVOC, benzene, toluene, and xylenes gathered from a total of 112 samples (see Table 4) and scores of building/environmental factors, occupants' habits, and total factors were analyzed with bivariate regression analyses. Table 5 shows the bivariate regression analysis results with correlation coefficients (r^2). In terms of correlations between the scores and observed VOC levels, there were strong correlations ($r^2 > 0.7$) for annual/heating period TVOC levels and annual benzene levels with total score/occupants' habits; with xylenes during annual/non-heating period occupants' habits; and with occupants' habits and toluene levels during the non-heating period and benzene levels for all three periods. As mentioned earlier, heating activity both at the sampling sites and around their outer surroundings can influence the observed VOC composition and therefore it might have a masking effect on the correlations. Thus, in addition to annual averages, non-heating period averages of the VOCs were used for the regression analyses as well. Finally, only a good relationship was found ($r^2 > 0.6$) between building/environmental factors and heating period TVOC levels. Hence, these results indicate that the most significant factors affecting observed VOC levels are occupants' habits, other than building/environmental factors.

Another study, investigating the source apportionments of indoor VOC levels used a factor analysis approach and found a significant effect of VOC including product usage indoors as a main mechanism, but they did not include the occupants' habits directly in the analyses [6].

3.4. Basic numerical methods for classification of indoor environments according to observed indoor VOC levels (IAPvoc)

Three basic numerical methods, namely SOM, the rounded average approach, and the maximum

Table 4. Number of data used for the data analysis at each sampling point.

Sampling point	N
Urb-1	12
Urb-2	10
Urb-3	12
Rur-1	10
Ind-1	11
Ind-2	12
Total	*114*

Table 5. R^2 values between the average VOC concentrations and IAP*i* scores.

TVOC	Total score	Occupants' habits	Building/Environmental factors
annual concentrations	0.94 (0.92*)	0.87	0.40
heating concentrations	0.73	0.37	0.61
non-heating concentrations	0.36*	0.93*	0.17
Benzene			
annual concentrations	0.67 (0.71*)	0.81	0.18
heating concentrations	0.64	0.73	0.18
non-heating concentrations	0.55*	0.73*	0.30
Toluene			
annual concentrations	0.41 (0.46*)	0.68	0.04
heating concentrations	0.23	0.56	0.01
non-heating concentrations	0.57*	0.84*	0.09
Xylenes			
annual concentrations	0.49 (0.54*)	0.70	0.08
heating concentrations	0.08	0.01	0.26
non-heating concentrations	0.48*	0.84*	0.05

*refers to non-heating season scores; $n = 114$; $R^2 \geq 0.70$ were underlined.

value approach were used here to classify the indoor environments in terms of VOC abundance (IAPvoc). Similar to IAP*i* approach, the higher score the environment has, the worse the IAQ of the environment regarding VOC pollution (higher IAPvoc score). The other similarity of IAPvoc approach with IAP*i* approach is that indoor environments were classified into three classes: "good", "moderate, and "bad".

Figure 6 depicts the SOM results. In Figure 6 (A) represents SOM Neighbor Weight Distances that displays air quality classes, and (B) represents SOM Sample Hits that display how sample unit presents 10 × 10 neuron units. Evaluated classes (Class 1: "good", class 2 = "moderate", class 3 = "bad") are visualized on Figure 6. Similar classes are shown with the same color. Where the disparity of light color shows small differences, the disparity of darker color shows huge differences. Figure 7 shows the classes of indoor environments ($n = 6$) estimated by SOM, the rounded average, and the maximum value approaches for (A) annual; (B) heating period; and (C) non-heating period average values of TVOC and BTX. According to Figure 7, all three approaches are strictly consistent for Ind-

1 sampling site during all sampling periods, while SOM underestimated the class of environment in urban sampling sites as annual averages, and also SOM overestimated the class of the environment in Rur-1 for annual average and heating period; in Urb-2 during non-heating period; and in Urb-1 during heating period. When we compare the rounded average and the maximum value approaches, they were in good agreement except in Urb-2 during the heating period and in Ind-2 during the non-heating period.

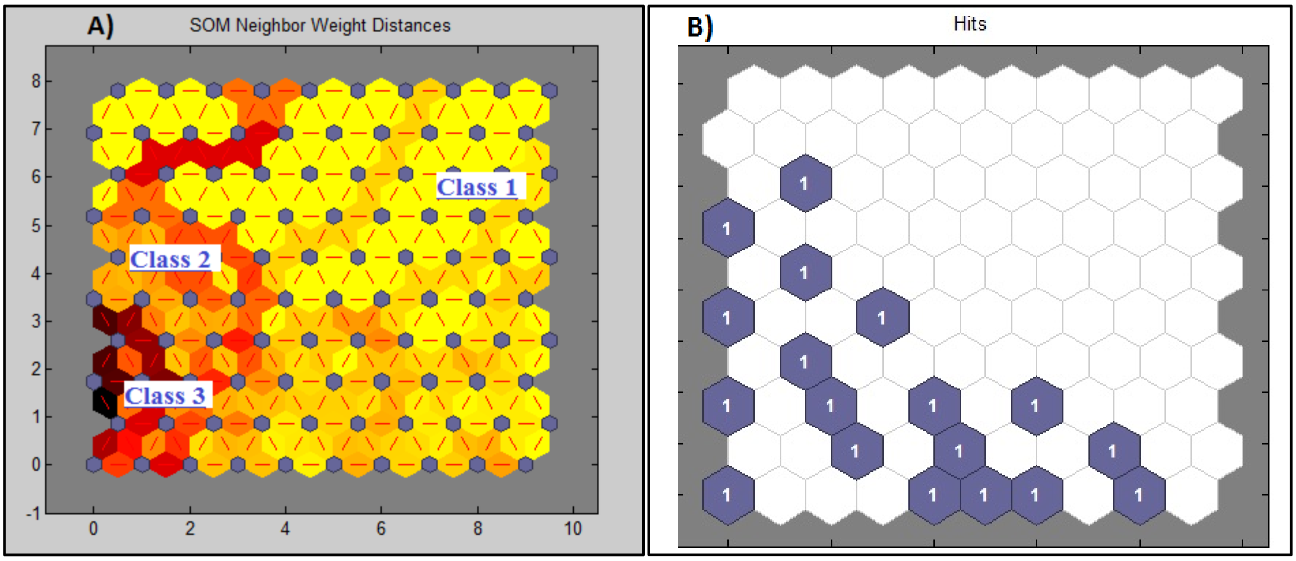


Figure 6. Clustering of Data According to SOM at the sampling sites for IAPvoc: A) SOM Neighbor Weight Distances, B) SOM Sample Hits (10 × 10 matrix; the lighter nests: Class 1 "good", grey nests: Class 2 "moderate", the darkest nests: Class 3 "bad").

Table 6 shows the summary of the estimation of the three methods as a pairwise comparison. As can be seen from both Figure 7 and Table 6, the rounded average and the maximum value approaches have 88.9% agreement while classifying the indoor environments according to their VOC composition. When it comes to the SOM classification, only around 30% match was found with the other two methods. Also, the environments were in better classes with SOM methods than other two methods.

Table 6. Comparison table of three IAPvoc methods* for the estimated classes of the sampling sites.

Method pairs	N	n (%n)			
		Identical	Worse in SOM	Worse in rounded average	Worse in maximum value
SOM vs. Rounded average	18	6 (33.4)	4 (22.2)	8 (44.4)	-
SOM vs. Maximum value	18	5 (27.8)	4 (22.2)	-	9 (50)
Rounded average vs. Maximum value	18	16 (88.9)	-	0	2 (11.1)

*annual, heating period, and non-heating period IAPvoc scores were used (N = 6 sampling sites × 3 periods = 18; n: number of data for each group, %n: frequency of each group (n/N × 100))

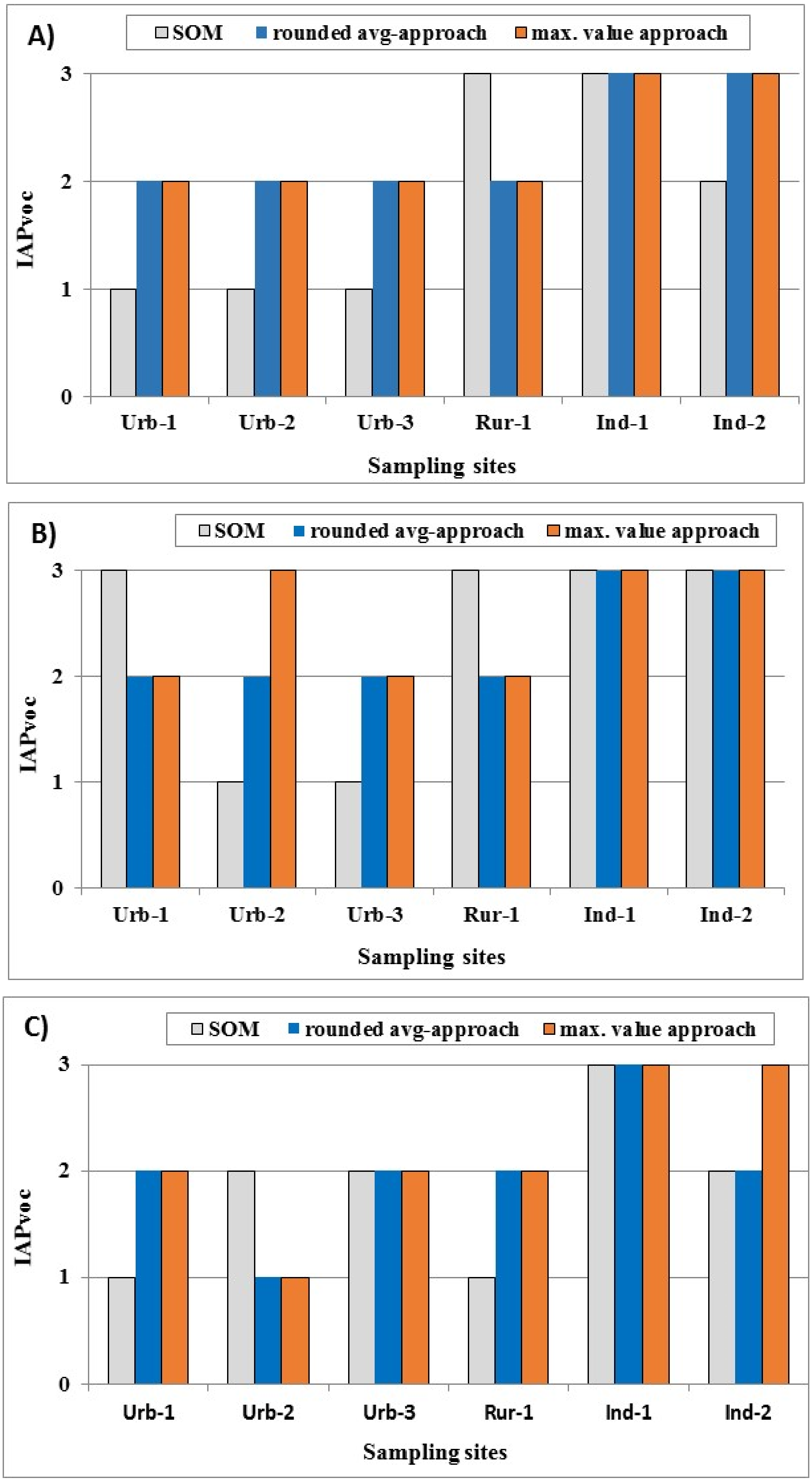


Figure 7. IAPvoc classes estimated by SOM, the rounded average, and the maximum value methods at the sampling sites for target VOC concentrations: A) annual avg, B) heating period, and C) non-heating period.

4. Conclusions

Levels of TVOC, benzene, toluene, and xylenes were measured in six different homes in Çanakkale city, Turkey throughout a year. Levels of TVOC and BTX were found to be higher in industrial areas, particularly in Ind-1 sampling site, compared to other towns. VOC levels were higher during the heating season except in the industrial region, probably due to more frequent ventilation with the outdoor air where the enhanced photochemistry of toluene/xylenes might have occurred due to additional industrial sources.

IAP*i* for the factors affecting IAQ can be a useful tool in typical indoor environments with natural ventilation in terms of assessing the availability of potential sources and triggering factors for VOCs. This study showed that both building/environmental factors and occupants' habits contributed to observed indoor VOC levels. Among those factors, occupants' habits were found to be the most significant group according to the bivariate regression results ($r^2 > 0.70$).

Ecological data analysis is very complex. Similar to IAP*i*, the IAPvoc approach was used to classify the indoor environments into three classes (good-moderate-bad) according to their VOC composition. For this aim, three different basic numerical methods were utilized here. Among them, SOM is a very powerful tool for analyzing environmental data. Although SOM is frequently used for water and surface water modelling etc., it is not commonly used for indoor air pollution modelling. In this study, SOM gave an overall class for IAQ. With the SOM method, the sampled environments were in better classes than the other two methods, which were the rounded average and the maximum value methods. The rounded average and the maximum value approaches were in a very good agreement (88.9%) in terms of classifying the indoor environments according to their VOC composition. When it comes to the SOM classification, only around 30% similarity was found with other two methods.

Even so, SOM is a good visualization method but less data may not provide good results. Since plenty of studies are available in the literature measuring the VOCs in different types of indoor environments, there is no indexing study for the potential sources and/or factors of observed VOCs. Although there are some limitations in this study such as small sample size for indoor environments, low number of individual VOCs and occupants, it gives a basic but start for further studies. Increasing the number of sampled environments and occupants would result in more precise and significant conclusions for numerical analyses than those obtained from this study.

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Conflict of Interest

All authors declare no conflicts of interest in this paper

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