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Analysis of Solvent Vapors in Breath and Ambient Air with a Surface Acoustic Wave Sensor Array

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This article describes the development and evaluation of a small prototype instrument employing an array of four polymer-coated surface acoustic wave (SAW) sensors for rapid analysis of organic solvent vapors in exhaled breath and ambient air. A thermally desorbed adsorbent preconcentrator within the instrument is used to increase sensitivity and compensate for background water vapor. Calibrations were performed for breath and dry nitrogen samples in Tedlar bags spiked with 16 individual solvents and selected binary mixtures. Responses were linear over the 50- to 400-fold concentration ranges examined and mixture responses were additive. The resulting library of vapor calibration response patterns was used with extended disjoint principal components regression and a probabilistic artificial neural network to develop vapor-recognition algorithms. In a subsequent analysis of an independent data set all individual vapors and most binary mixture components were correctly identified and were quantified to within 25% of their actual concentrations. Limits of detection for a 0.25 l. sample collected over a 2.5-min period were <0.3×TLV for 14 of the 16 vapors based on the criterion that all four sensors show a detectable response. Results demonstrate the feasibility of this technology for workplace analysis of breath and ambient air.

Keywords: volatile organic compounds; breath analysis; surface acoustic wave sensor; biological monitoring; sensor array

INTRODUCTION

Exposure to volatile organic solvent vapors results in absorption by the pulmonary blood supply and distribution throughout the body. Following exposure, a fraction of the absorbed dose is excreted in the breath. Thus, the concentration of vapor in breath can provide insight into the body burden and thereby assist in the assessment of individual vapor uptake levels and the risk of possible adverse health effects (Wilson, 1986; Manolis, 1983; Droz and Guillemin, 1986; American Conference of Governmental Industrial Hygienists, 1996).

The non-invasive nature of breath monitoring makes it more convenient than monitoring blood or urine. However, the high concentration of background water vapor, the presence of multiple endogenous and exogenous vapors, and the short biological half-lives of most absorbed vapors in the breath make it difficult to perform breath analyses in the field. Current approaches to breath analysis typically rely on the collection of a discrete breath sample in an inert container followed by laboratory analysis (Droz and Guillemin, 1986; Ho and Dillon, 1987; Pleil *et al.*, 1998; Wallace *et al.*, 1996). Direct analysis using conventional instrumentation has been reported (Benoit *et al.*, 1985; Ewers *et al.*, 2000; Franzblau *et al.*, 1992; Anon, 1994), but the cost and complexity associated with these methods limit their application in clinical and occupational settings.

Arrays of various partially selective microfabricated sensors have been used for gas and vapor analysis (Ballantine, 1997; Grate and Klusty, 1991; Rose-Pehrsson *et al.*, 1988; Carey and Kowalski, 1986; Grate, 2000; Jurs *et al.*, 2000; Hierlemann *et al.*, 1995; Gardner, 1991; Sundgren *et al.*, 1990). Those

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*Author to whom correspondence should be addressed. Current address: Industrial Health and Safety Program, Department of Energy and Geo-Environmental Engineering, Pennsylvania State University, University Park, PA 16802-5000. Tel.: +1-814-863-1618; Fax: +1-814-865-3248; E-mail: wag10@psu.edu based on surface-acoustic-wave (SAW) and related acoustic-wave (AW) sensor technology have a number of potential advantages for analyzing organic vapors. SAW sensors detect changes in the mass and viscoelastic properties of interfacial surface-coating films (Grate and Zellers, 2000; Martin *et al.*, 1994). Responses are rapid and reversible, isotherms are linear over fairly wide ranges of vapor concentration, and responses to vapor mixtures are generally additive (Park *et al.*, 2000; Zellers and Han, 1996; Zellers *et al.*, 1995). It has been shown that an array of only 3–6 SAW sensors coated with a diverse set of amorphous polymers can produce characteristic response patterns for identifying and quantifying a large number of individual vapors and the components of various vapor mixtures (Park *et al.*, 1999, 2000; Cai *et al.*, 2000; Zellers and Han, 1996; Zellers *et al.*, 1993, 1995; Grate *et al.*, 1993; Patrash and Zellers, 1993; Rose-Pehrsson *et al.*, 1988; Wohltjen, 1984). Previous studies from our laboratory have shown that instrumentation similar to that reported on here can be used for several occupational hygiene applications, including personal exposure monitoring and the determination of solvents permeating through chemical protective clothing (Park *et al.*, 2000; Park and Zellers, 2000a,b).

Various pattern recognition methods have been used to interpret sensor array response data (Zellers *et al.*, 1993; Massart, 1988; White *et al.*, 1996; Carey *et al.*, 1986; Sutter and Jurs, 1997; Stetter *et al.*, 1986; Gardner *et al.*, 1990; Sundgren *et al.*, 1990; Jurs *et al.*, 2000). Among these is the extended disjoint principal components regression (EDPCR) method that we have used to analyze SAW sensor array response data in a number of recent studies (Zellers *et al.*, 1993, 1995; Park *et al.*, 2000; Cai *et al.*, 2000; Park *et al.*, 1999; Zellers and Han, 1996; Park and Zellers, 2000a,b). Artificial neural networks (ANN) have also been successfully applied to the problem of classifying sensor responses (Dickinson *et al.*, 1996; Eklov and Lundstrom, 1999; Jurs *et al.*, 2000; Hierlemann *et al.*, 1995; Gardner *et al.*, 1992; Shaffer and Rose-Pehrsson, 1999). In a recent study of seven different pattern recognition algorithms for processing of chemical sensor array data, it was found that ANN based approaches produced the most accurate classifications (Shaffer *et al.*, 1999), thus providing validation for the utility of this approach.

This article is the third in a series describing the development and laboratory testing of a simple prototype instrument designed to analyze organic vapors in exhaled breath and ambient air (Groves and Zellers, 1996b; Groves *et al.*, 1998). The instrument utilizes a thermally desorbed adsorbent preconcentrator to capture samples and reduce the influence of background humidity, and an array of four polymer-coated surface-acoustic-wave (SAW) sensors to detect the vapors. The first article in this series provided preliminary data on instrument performance and the second provided a detailed analysis of the preconcentrator adsorbent, with an emphasis on humidity compensation. Due to the limited sensitivity of polymer-coated SAW sensors, sample preconcentration is needed to achieve the low- or sub-part-per-million (ppm) detection limits generally required for breath analysis (Park *et al.*, 1999, 2000; American Conference of Governmental Industrial Hygienists, 1996; Groves and Zellers, 1996a). This article presents a more comprehensive evaluation of the instrument for breath monitoring. A sampling and analytical protocol applicable to both breath and ambient air samples is presented, the effects of sample humidity are assessed, and the application of EDPCR and ANN pattern recognition methods is demonstrated for vapor identification and quantification.

EXPERIMENTAL METHODS

Instrument description and operation

The key functional components of the instrument used in this study are shown schematically in Fig. 1. Included are an array of four 250-MHz polymer-coated surface-acoustic-wave (SAW) resonators with matched reference resonators, two diaphragm pumps, four Teflon® solenoid valves, and an adsorbent-packed preconcentrator tube (PCT). The instrument, which was constructed to our design specifications by Microsensor Systems, Inc. (Bowling Green, KY), measures approximately 16×12×4 cm, weighs less than 5 kg, and can be powered by AC or battery.

Each pair of working and reference sensors is mounted on a 3×5 cm circuit board that also supports the circuitry needed to drive the sensors and mix the output signals. The four boards are clamped onto a brass block having machined receptacles for the sensors. Four parallel channels within the block, emanating from a common inlet, distribute airflow to the four working sensors. The reference sensors are not exposed to the sample stream, but are in the same thermal environment as the working sensors. A Peltier device affixed to the underside of the brass block maintains all sensors at 20°C to minimize baseline disturbances and improve the reproducibility of responses. The instrument microprocessor controls the pneumatic and thermal cycling, and collects the difference frequencies from the four working/reference sensor pairs at a rate of 0.5 Hz. Output signals are routed via an RS-232 port to an external computer for display and processing. The microprocessor was programmed by the instrument manufacturer to allow for modification of valve switching and thermal desorption timing through the use of a menu driven software program also provided by the manufacturer.

The PCT was constructed from 3-mm i.d. glass tubes approximately 4.4 cm long wrapped with twelve turns of 32-gauge NiCr wire to give a heated length of about two cm. A thermocouple for monitor-

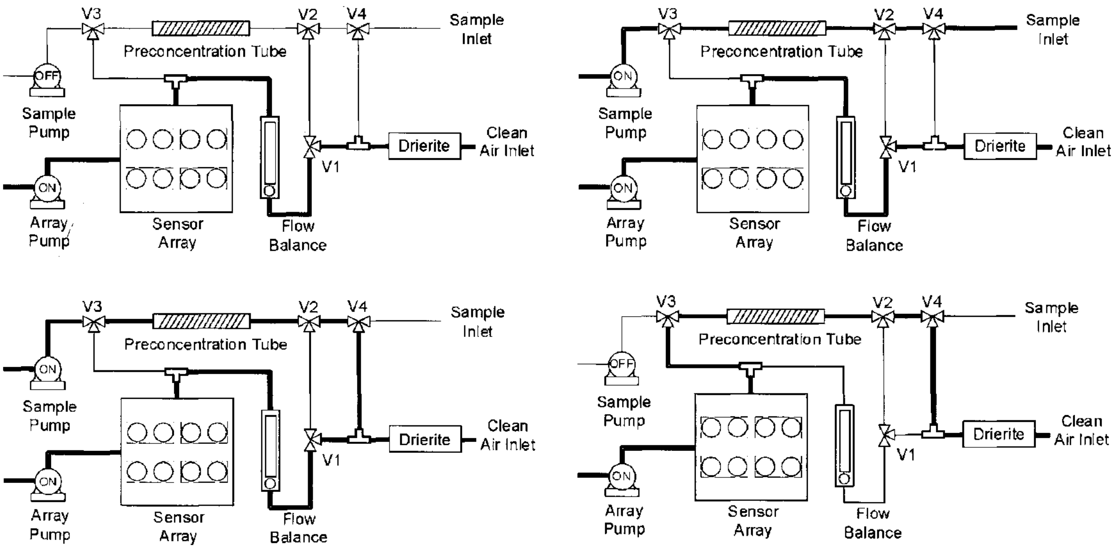

Fig. 1. Simplified schematic and flow diagram for (a) Warm-up, (b) Sample, (c) Purge, and (d) Analysis modes.

ing and controlling temperature is attached to the outside of the NiCr wire using a silicon-rubber heat-transfer compound. Temperature control is provided by a PID Universal Temperature/Process Controller (Omega Engineering, Inc., Stamford, CT). The PCT is packed with 40 mg of XUS 43565.01 adsorbent (Dow Chemical, Midland, MI; currently available from Supelco, Bellefonte, PA), which is a 20/50 mesh spherical resin composed of a methylene-bridged copolymer of styrene and divinylbenzene. Selection of the type and quantity of adsorbent was the subject of the second paper in this series (Groves *et al.*, 1998) and was based upon breakthrough studies for a subset of vapors. The adsorbent was used as received. Sample flow-path materials consisted of Teflon®, stainless steel, glass, and brass, all of which were selected to minimized loss of analyte and sample carry-over. Further details about the instrument and preconcentrator design are given elsewhere (Groves and Zellers, 1996b; Groves *et al.*, 1998).

The following four polymers are used as sensor coatings: poly(epichlorohydrin) (PECH), poly(isobutylene) (PIB), poly(bis-allylcyanosiloxane) (OV-275), and poly(diphenoxyphosphazene) (PDPP). One additional coating of an acrylonitrile-butadiene copolymer (ABC) was examined during preliminary tests but was not included in the final set of coatings due to baseline instabilities observed at low humidity (note: this effect was reproducible and could be resolved by increasing the background relative humidity to 20%). Polymers were obtained from Scientific Polymer Products, Inc., Ontario, NY (PIB, PECH, PDPP, and ABC), and Anspec, Ann Arbor, MI (OV-275). PIB, PECH, PDPP, and ABC are amorphous rubbery solids and OV-275 is a viscous liquid at room temperature. These polymers were selected as sensor coatings for the array on the basis of previous studies indicating that response patterns derived from them provide a relatively high degree of selectively among solvent vapors within and between structural classes (Zellers and Han, 1996; Zellers *et al.*, 1995) Coatings were applied to thicknesses in the range of 20–30 nm, corresponding to a frequency shift of ~225 kHz (Grate and Klusty, 1991; Park *et al.*, 2000), using an airbrush and a dilute solution of each polymer in chloroform.

All calibration and test samples were prepared in 1-l. Tedlar® bags and connected to the inlet port by a short section of 1/8 in o.d. Teflon® tubing. Once activated, the instrument proceeds automatically through a series of four pre-set operating modes. In Warm-up Mode [Fig. 1(a)], clean dry air is passed over the sensor array. In Sample Mode [Fig. 1(b)], a 0.25-l. sample is drawn through the PCT at 0.1 l./min. Valve V4 is then switched and 0.25 l. of clean, dry air is passed through the PCT at the same flow rate [Purge Mode, Fig. 1(c)] in order to remove the majority of co-adsorbed water vapor from the adsorbent. Then, valves V1–V3 are switched, the flow rate is reduced to 0.04 l./min, and the PCT is heated to 170°C at a rate of 15°C/s to desorb the trapped organic vapors and draw them across the sensor array [Analysis Mode, Fig. 1(d)]. After 2.5 min, the instrument returns to Warm-Up Mode in preparation for the next cycle.

The protocol for purging water vapor from the PCT in this study differs from that used in our preliminary study (Groves and Zellers, 1996b). In the current approach, the water vapor bypasses the sensor array during Purge Mode, which avoids unnecessarily exposing the array to high water vapor concentrations. In addition to maintaining a flow of clean, dry air across the sensor array at all times, the flow rate over the array is held constant at 0.04 l./min. This yields lower LODs due to a decreased and more reproducible baseline, and also allows a single set of calibration data to be used for samples collected under different conditions of humidity. The main disadvantage of using a dried purge stream is the need to replace the drying agent (Drierite®) periodically. By including indicator Drierite®, which turns from blue to pink upon saturation, the change-out schedule can be verified (Groves and Zellers, 1996b; Groves *et al.*, 1998).

Calibration

The instrument was calibrated with the 16 individual solvents vapors listed in Table 1. Test atmospheres were prepared by first collecting a volume of breath in a 1-l. Tedlar® bag, then injecting a known volume of liquid solvent, and gently massaging the bag to effect complete mixing of the evaporated solvent. Samples were allowed to cool to room temperature (~20–24°C) prior to analysis. Solvents were all > 98% pure and were used as received (Aldrich Chemical, Milwaukee, WI). Calibrations were performed at six concentrations, which bracketed the American Conference of Governmental Industrial Hygienists' Threshold Limit Value (ACGIH–TLV) for each vapor. The actual concentration range used for a specific vapor was determined by the lowest concentration needed to produce a detectable response in one of the sensors and then approximately doubling this concentration five times to yield a total of six calibration concentrations. The concentrations of the test atmospheres were determined using GC–FID by making 1-ml injections using a gas-tight syringe and comparing the resulting peak areas to those of daily liquid calibration standards for the solvent of interest.

Test atmospheres containing only breath or dry N_2 gas were used as baseline samples (i.e. blanks). From three to five blank analyses were performed for each calibration series and the average was subtracted from responses for calibration standards to yield a net response profile for each sensor. Comparison of baselines for 'blank' breath samples and nitrogen samples spiked with water to the point of saturation showed no significant difference thus confirming that the prototype instrument's baseline is essentially defined by the response of the sensors to residual water on the PCT tube and that endogenous vapors in breath are not detectable. Calibration curves were prepared by plotting the response maximum from each coated sensor (Hz) versus concentration (mg/m^3). The sensitivity of each sensor was determined from the slope of the calibration curves for each polymer-solvent vapor combination by linear regression with a forced zero intercept. Additional calibrations were performed for selected solvent test atmospheres prepared in dry N_2 for comparison to the results for the breath samples.

Pattern recognition

The EDPCR algorithm is based on the comparison of the mean-centered response vector for an unknown sample to the modeled vectors derived from the calibrated responses to a set of known vapors (Zellers *et al.*, 1993, 1995). With EDPCR, modeled vectors are established by principal component regression of the vector sum of the responses of the sensors in the array to each calibration vapor. The distance between the response vector of any subsequent 'unknown' test vapor and each modeled vector is calculated and the identity of the test vapor is assigned on the basis of the shortest distance, or 'error', between model and response vectors. Once the vapor is recognized, its concentration is determined by projecting the response vector onto the model *vector*, in the case of individual vapors, or onto the model *plane*, in the case of a binary vapor mixture. The components of any mixtures are quantified by projecting the response vector onto the model vectors defining the plane for the mixture. The approach is easily extended to ternary or more complex mixtures (Park *et al.*, 1999, 2000; Park and Zellers, 2000a,b; Cai *et al.*, 2000).

A probabilistic ANN was also used to interpret response patterns, but analyses were restricted to the recognition of individual vapors. A commercial software package (Neuroshell 2, Ward Systems Group, Frederick, MD) was used to develop and train the ANN. The default settings for activation functions, number of hidden neurons, and internal architecture were used. Absolute sensor responses (Hz), relative responses, and elution times were all used as inputs for the classification networks, yielding a total of 12 input variables (4 sensors × 3 parameters/sensor). A training set was developed from the calibration data for each vapor to yield a set of 'correct' outputs for the network in a spreadsheet format. The training set consisted of 89 patterns derived from the 5–6 calibration concentrations analyzed for each individual vapor. The number of outputs is equal to the number of possible classifications, e.g., if it is stipulated for a given application scenario that only one of 16 possible vapors can be present at a time, there would be 16 outputs or classifications — one for each vapor. Once trained, the ANN is applied by entering values for the 12 input variables for a sample and the vapor identity is assigned on the basis of the output with the highest probability. An ANN for the classification of vapors that might be present in mixtures could be constructed in the same fashion with one output for every possible classification, but this was not explored in this study. An example of the probabilistic neural network architecture used for vapor identification is shown in Fig. 2 for the case where an unknown response is to be classified as one of the 16 possible individual solvent vapors.

Table 1. Calibration results for the 16 solvents examined

Chemical (ID)	2000 TLV (mg/m^3)	Range (mg/m^3)	B.P. (°C)	PW^c (s)	ET^a (s)	Sensitivity Hz/mg/m^3 (LOD, mg/m^3)^{4d}			
						PECH	PIB	OV275	PDPP
Benzene (BEN)	1.60	4–200	80.1	20	22–24	3.40 (22)	3.28 (4.2)	2.05 (23)	2.52 (5.2)
Toluene (TOL)	188	5–1000	111	27	26–28	6.98 (2.3)	8.75 (1.1)	3.54 (9.0)	5.17 (3.7)
Ethylbenzene (EBE)	434	6–1800	136	45	32–38	8.94 (6.3)	14.8 (0.88)	4.15 (9.4)	7.76 (2.8)
m-Xylene (XYL)	434	4–1600	139	52	34–40	8.93 (3.1)	15.5 (0.64)	3.80 (5.5)	6.73 (4.5)
Dichloromethane (DCM)	174	10–730	40.0	14	22–24	1.72 (17)	0.950 (10)	1.86 (21)	1.15 (11)
Halothane (HAL)	404	30–1700	50.2	26	26–28	0.610 (51)	0.691 (43)	0.800 (37)	0.536 (43)
1,1,1-Trichloroethane (TCA)	1910	20–1300	74.1	28	26–28	1.29 (7.7)	1.79 (5.6)	0.721 (38)	1.25 (8.8)
Trichloroethylene (TCE)	269	9–1300	87.0	22	24	2.62 (9.2)	4.61 (2.1)	1.59 (25)	2.56 (3.9)
Perchloroethylene (PRC)	170	10–630	121	32	28–30	3.14 (23)	10.5 (0.95)	1.41 (29)	3.80 (3.2)
Tetrahydrofuran (THF)	590	14–2800	67	23	22–24	4.23 (13)	2.89 (11)	2.07 (43)	2.18 (10)
1,4-Dioxane (DXN)	72.1	10–740	101	28	26–28	9.68 (9.7)	3.59 (18)	6.14 (20)	3.56 (22)
Methoxyflurane (MXY)	13.5^b	10–1700	104	32	28–30	3.57 (7.6)	2.39 (6.3)	3.42 (19)	2.72 (5.5)
Acetone (ACE)	1187	35–1900	56.2	17	22–24	3.60 (11)	0.977 (62)	3.47 (12)	1.29 (7.8)
2-Butanone (MEK)	590	14–1500	79.6	21	22–24	6.33 (4.2)	2.28 (13)	4.87 (20)	2.52 (9.5)
2-Propanol (IPA)	983	25–3800	82.4	22	22–24	2.84 (14)	1.27 (10)	3.44 (28)	1.04 (26)
n-Butanol (BUT)	152^c	6–730	117	27	24–28	11.9 (3.6)	5.10 (4.7)	12.1 (4.2)	4.31 (12)

[a] Elution time — time of maximum net response after heat is applied in thermal desorption mode.
[b] NIOSH Recommended Exposure Level — Ceiling Limit (Anon, 1997).
[c] PW=peak width at half-height.
[d] Based on a 250 ml sample volume.

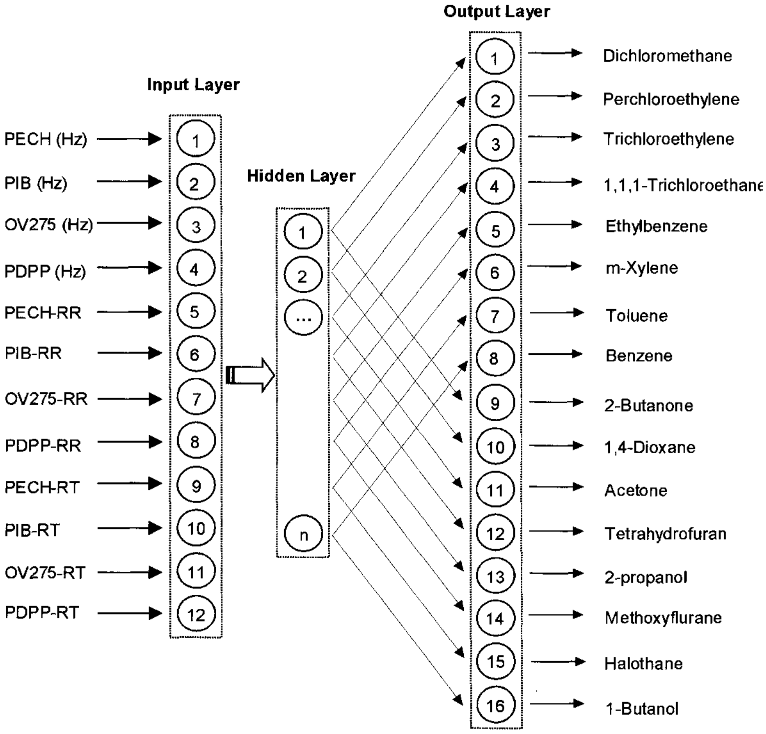

Fig. 2. Simplified schematic for probabilistic neural net classification architecture — example shown is for individual vapor classification (16 outputs) using peak height (Hz), relative response (RR), and retention time (RT) as the 12 inputs.

RESULTS AND DISCUSSION

Response profiles

Representative response profiles for a spiked breath sample containing 25 ppm of perchloroethylene are presented in Fig. 3. The sequence of operating modes is indicated below the timeline. The sample and purge modes span the interval from 0 to 300 s and are followed by the analysis and recovery (warm-up) modes from 300 to 450 s. The response profiles resemble peaks seen with many separation-based analytical techniques such as GC or HPLC. There is a correlation between the solvent boiling points and the vapor elution times, ET, (Table 1) that reflects a crude chromatographic separation of the vapors in the PCT

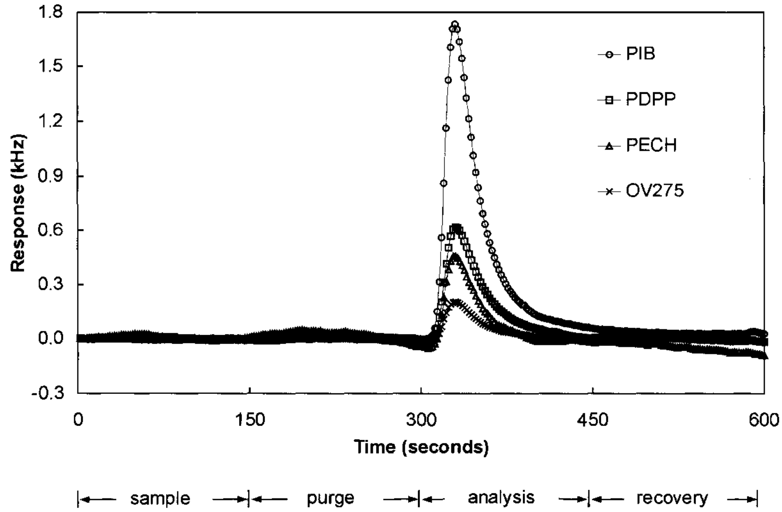

Fig. 3. Representative sample timeline for calibrations: 25 ppm perchloroethylene; 100% RH; 250 ml preconcentrated sample volume; sample/purge flow rate=100 ml/min; array flow rate=40 ml/min; desorption temp.=170°C; temperature ramp ~12°C/s starting at $t = 300$ s.

based on volatility. However the peaks are relatively broad as indicated by the peak width at half height, PW (Table 1), such that there is generally only partial resolution among the different vapor response profiles. Complete resolution of the solvent vapors is not necessary since recognition relies on the response patterns from the array, although the elution time does comprise additional information that was incorporated into the ANN pattern recognition algorithm (Shaffer *et al.*, 1998).

Calibrations

Calibration curves were linear in all cases ($r^2 \geq 0.99$) indicating that PCT capacity was adequate for the conditions examined. Although a systematic evaluation of linear dynamic range was not conducted in this study, responses were linear for all vapors over a range of approximately two orders of magnitude and linearity is expected to extend much further for less volatile vapors such as ethylbenzene, m-xylene, and perchloroethylene, due to the higher adsorption capacity of the PCT for these vapors. Sample carry-over was found to be less than 1% based on an examination of blank samples run immediately following a spiked breath sample.

The LOD was defined as the concentration producing a response equal to three times the standard deviation of the baseline response. Based on the lowest LOD value of the four sensors, LODs ranged from 0.6 to 37 mg/m^3 and were less than 0.25×TLV for all solvents examined except benzene (2.6×TLV). The LOD for methoxyflurane was 0.4 times the NIOSH Recommended Exposure Limit (Anon, 1997) (there is no TLV for this compound). If it is assumed that a response is needed from all four sensors in order to recognize and quantify a given vapor, the minimum concentration required should be that corresponding to the LOD for the least sensitive sensor (i.e., the sensor with the highest individual LOD value) (Zellers *et al.*, 1998). Using this more conservative approach, LODs ranged from 5.5 to 62 mg/m^3, and 14 of the 16 solvents were detectable at concentrations less than 0.3×TLV. For the two vapors which currently have ACGIH BEIs for breath, perchloroethylene (34 mg/m^3) and 1,1,1-trichloroethane (218 mg/m^3), the LODs were 29 and 38 mg/m^3, respectively, thus further supporting the applicability of this instrument to workplace breath monitoring (American Conference of Governmental Industrial Hygienists, 1996; Groves and Zellers, 1996a). Sample volumes could most likely be doubled to improve LODs for many less volatile vapors without a significant redesign of the PCT. However, for benzene and methoxyflurane which have a relatively low occupational exposure limits and for which SAW device sensitivity is also low, breath monitoring would not be feasible with the current instrument design.

Relative response patterns for the 16 solvents are shown in Fig. 4. The relative response of a coating is equal to the sensitivity of the coating divided by the sum of the sensitivities for all four coatings. The sum of these scaled sensitivities is unity for each vapor, which facilitates comparisons. Figure 4 provides a visual (i.e., qualitative) indication of the discriminating capability of the sensor array for the various solvents. Some similarities can be seen among the patterns of vapors from the same chemical class. For example, response patterns for the aromatic solvents (i.e., benzene, toluene, ethylbenzene, and m-xylene) are similarly dominated by the response from the PIB and PECH sensors. A casual inspection of the response patterns also quickly leads to an appreciation for the problems of recognizing and discriminating among more than a few vapors.

Humidity effects

Although breath samples invariably contain background water vapor concentrations near saturation, the possibility of using this instrument for both breath and ambient air monitoring prompted an examination of the effect of humidity on instrument performance. Calibrations were performed for the following subset of solvents in test atmospheres prepared in dry nitrogen: benzene, dichloromethane, halothane, 1,1,1-trichloroethane, trichloroethylene, tetrahydrofuran, and acetone. The sensitivities and relative responses to these vapors are compared to those for the same vapors in spiked breath samples in Table 2. Differences in sensitivities ranged from 2.5% (trichloroethylene) to −19% (halothane) and were consistently either positive or negative across all sensors for a given vapor, indicating a systematic error in test-atmosphere generation or, possibly, that water vapor is affecting the response profiles by altering the vapor desorption dynamics. Neither the sign nor magnitude of the errors showed trends that could be related to the physical properties of the solvents (i.e., boiling point, polarity, functionality). The mean absolute difference between sensitivities for all vapors/sensors was 10%. The differences between *relative responses* at 0% and 100% RH are small in all cases, with the average differences ranging from −2.1% to 1.5% (mean absolute difference =1.1%). A paired *t*-test showed that these differences are not significant ($P = 1.000$).

These results indicate that the instrument response is effectively independent of sample humidity, which is not only important for breath analysis, but also for ambient air monitoring applications where prevailing humidity levels can vary over a wide range. Differences in absolute responses will increase quantification error, but the magnitude of this error is on the order of the expected day to day variability in sensitivities (~10%). Thus, calibrations performed at one humidity level can be applied to conditions of more extreme RH without significant errors in vapor recognition or quantification, which is consistent with find-

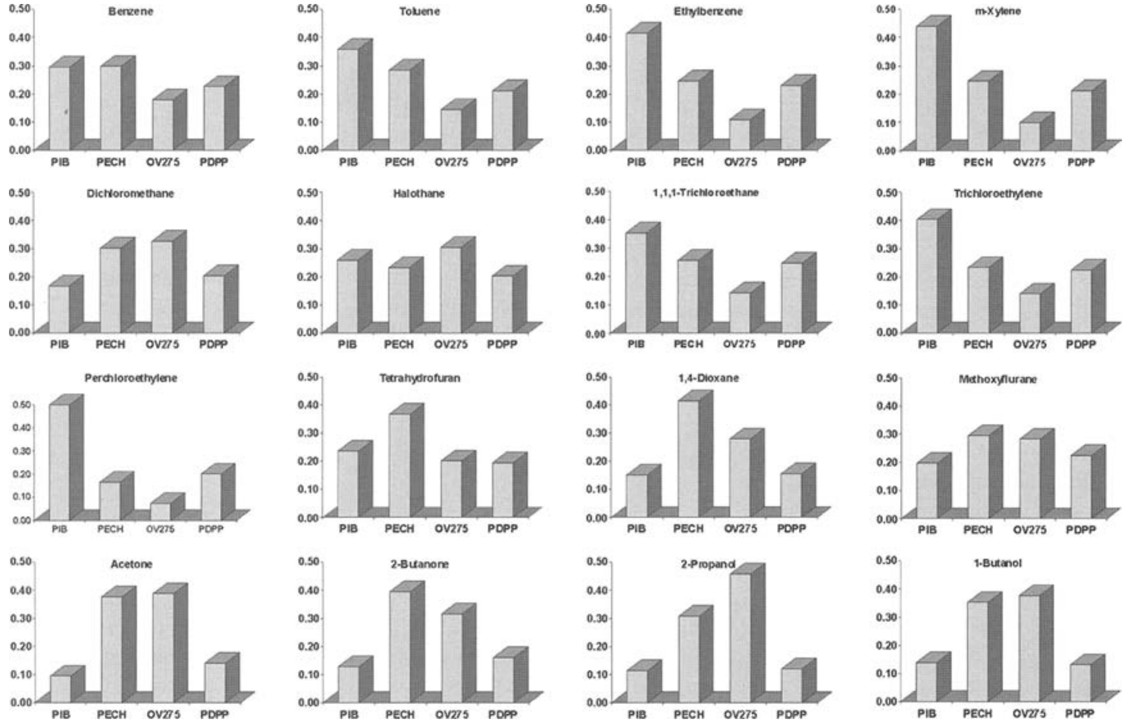

Fig. 4. Relative response patterns for 16 vapors.

ings reported recently from a separate study (Park and Zellers, 2000a,b).

Vapor mixture responses

It has been shown that the responses of polymer-coated SAW sensors to binary and ternary mixtures of vapors are additive, but that account must be taken of possible differences in elution times from any upstream PCT used (Zellers *et al.*, 1995; Cai *et al.*, 2000; Park *et al.*, 1999, 2000; Park and Zellers, 2000a,b). To the extent that the component vapor response maxima are temporally resolved, the mixture maximum will be reduced even for cases where the component peaks are not evident. In such cases one would expect that, after the pattern recognition analysis reveals the presence of two vapors, a point-by-point analysis must be performed to locate the maxima of each component for accurate quantification. Regardless, where responses are additive, calibrations are only needed for the individual components, since responses for all possible mixtures can be synthesized from the individual component responses.

To explore this issue, calibrations were performed for the following four binary mixtures: 1,1,1-trichloroethane+acetone, perchloroethylene+benzene, dichloromethane+perchloroethylene, and 2-propanol+1-butanol in spiked breath samples. These vapors span a range of differences in volatility, polarity, hydrogen-bonding strength, individual elution times, and peak width at half-height (see Table 1) all of which are expected to affect mixture response profiles. For each mixture, responses were measured for from four to seven test atmospheres covering a response ratio range of up to 9:1.

Figure 5 shows representative response profiles from two sensors for a mixture of perchloroethylene (68.3 mg/m^3) and dichloromethane (696 mg/m^3). Response profiles for the individual vapors are superimposed on those for the mixture. The profile that would result if the responses were additive is designated as the 'sum' in each panel in Fig. 5, and the linear combination of the individual maxima (i.e., ignoring elution time differences) is denoted by the symbol X placed at the time corresponding to the mixture maximum. The response of the PECH-coated sensor is dominated by dichloromethane because the dichloromethane concentration is higher and the sensitivities of this sensor to perchloroethylene and dichloromethane are similar. In contrast, the response for the PIB-coated sensor comprises nearly equal contributions from each vapor because this sensor is much more sensitive to perchloroethylene (see Table 1).

It was expected that actual mixture responses would be less than or equal to the responses predicted assuming linear additivity, with the negative bias increasing for vapor pairs with larger differences in elution time (ΔET). However, referring to Table 3 it can be seen that although the actual responses are lower than the predicted results for the dichloromethane+perchloroethylene mixture which has one of the largest ΔETs, this is not the case for

Table 2. Calibration results for samples prepared in breath (100% RH) and dry nitrogen (0% RH)

Chemical	PIB		PECH		OV275		PDPP		% diff.[a]
	100%RH	0% RH	100%RH	0% RH	100%RH	0% RH	100%RH	0% RH	
Sensitivity Hz/(mg/m^3)									
Benzene	3.09	3.62	3.22	3.83	1.93	2.35	2.38	2.79	16
Dichloromethane	0.965	1.17	1.73	2.11	1.87	2.32	1.16	1.43	18
Halothane	0.871	0.743	0.783	0.649	1.02	0.850	0.683	0.578	−19
1,1,1-Trichloroethane	1.83	1.92	1.33	1.40	0.732	0.783	1.28	1.35	5.4
Trichloroethylene	4.72	4.79	2.74	2.83	1.64	1.68	2.63	2.71	2.5
Tetrahydrofuran	2.46	2.26	3.69	3.44	1.91	1.84	1.96	1.86	−6.3
Acetone	0.842	0.880	3.35	3.50	3.45	3.60	1.25	1.31	4.4
									MAD[c] =10%
Relative response[b]									
Benzene	0.291	0.288	0.303	0.304	0.182	0.187	0.224	0.222	−1.2
Dichloromethane	0.169	0.166	0.302	0.300	0.327	0.330	0.203	0.203	−1.3
Halothane	0.259	0.263	0.233	0.230	0.304	0.301	0.203	0.205	1.5
1,1,1-Trichloroethane	0.354	0.352	0.257	0.257	0.142	0.144	0.247	0.248	−0.49
Trichloroethylene	0.402	0.399	0.234	0.236	0.140	0.140	0.224	0.226	−0.89
Tetrahydrofuran	0.246	0.240	0.368	0.366	0.191	0.196	0.196	0.198	−2.1
Acetone	0.095	0.095	0.377	0.377	0.388	0.388	0.141	0.141	0.035
									MAD[c] =1.1%

[a] Difference between 100% and 0% RH values relative to 0% RH value — averaged across four sensors.

[b] Relative response=sensitivity/(sum of sensitivities for all four sensors).

[c] Mean absolute difference (MAD)=mean of the absolute value of the % differences.

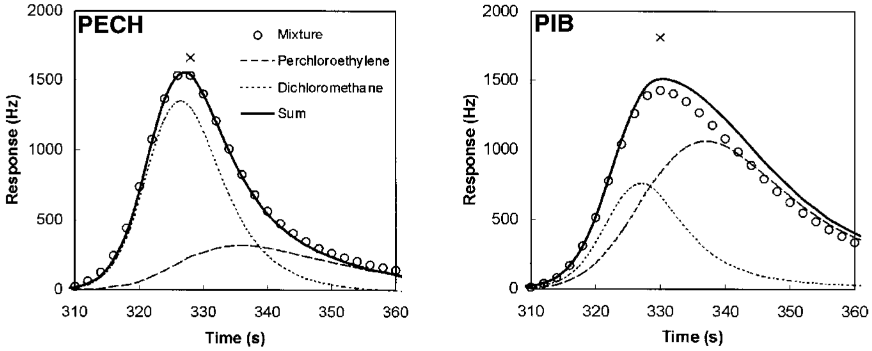

Fig. 5. Experimental mixture response profile compared with sum of individual vapor component responses and linear maxima (denoted by ×)-dichloromethane (696±5 mg/m^3) and perchloroethylene (68.3±5 mg/m^3).

all the mixtures. The 1,1,1-trichloroethane+acetone mixture experimental results were higher than predicted with the linearly additive model in all cases. A pair-wise comparison of actual mixture responses versus responses predicted assuming linear additivity of individual vapors did not detect a significant difference between the two ($P = 0.459$, Wilcoxon Signed Rank Test). This suggests that other factors such as changes in vapor desorption dynamics for mixtures, or normal variability due to environmental factors may offset expected departures from linear additivity. Peak width may also minimize departures from linear additivity that occur as a result of differences in elution time — the later eluting vapors have broader peaks which tends to reduce the negative bias caused by partial resolution. This has important implications for classification algorithms since it suggests that complicated models accounting for the departures from linear additivity may not be necessary if normal variability in responses is on the same order.

A mixture of dichloromethane and m-xylene would represent the worst case scenario based on its having the largest ΔET for this set of vapors. This mixture was not examined due to difficulties in establishing GC conditions that permitted rapid analysis of both components simultaneously (overlap of dichloromethane with the CS_2 solvent used in calibrations occurred at higher temperatures). Instead, the problem was explored by simulation using normalized peak profiles for the individual solvents over a range of concentrations. As expected, dichloromethane and m-xylene were correctly recognized and discriminated. However, using the composite response peak for quantification can introduce significant error. Thus, for ΔET values >10 s, quantification requires analyzing mixture component responses at their respective elution times once they are identified (Park *et al.*, 2000).

Test set data — classification and quantification

To examine individual-vapor recognition, an independent test set of 31 samples was compiled by recording response data for one additional sample each time a calibration was performed. These data were not used to calculate the sensitivities reported in Table 1. The test set consisted of single or duplicate responses for each of the 16 vapors in breath and an additional series of eight responses collected in a matrix of dry N_2 for a subset of vapors.

Table 4 shows the results of attempts to recognize the test-set vapors by EDPCR and the trained ANN for a subset of five samples. The best three matches by EDPCR are listed along with the residual error, ε, associated with each assigned identity. A small ε value indicates a better correlation with a given response pattern in the calibration library. The best three matches by the ANN are also listed along with the probability associated with each assigned identity. The probabilities range from 0 to 1 with a value of 1 indicating the highest possible correlation with a library response pattern. The last column in Table 4 shows the results of quantification using principal components regression (PCR) for a correctly classified response. Percent error is calculated relative to the concentration determined by GC–FID ('true' concentration in Table 4).

The EDPCR ε values and ANN probabilities provide a relative measure of confidence in the assigned vapor identities. For example, for the sample of perchloroethylene, which was correctly identified by both methods, the EDPCR residual error for perchloroethylene ($\varepsilon = 12$) is nearly 50 times smaller than that for m-xylene ($\varepsilon = 594$) which had the next closest pattern match. Similarly, the ANN probability value for perchloroethylene (0.50) is more than 60 times greater than for toluene (0.008), which was the next closest pattern match as determined by this method. In contrast, the EDPCR residual error and ANN probability for m-xylene are only slightly better than those for ethylbenzene, indicating a lower level of confidence in the assignments. This is not surprising given the similarity in the response patterns for these structurally homologous aromatic vapors (see Fig. 4). It is important to note that large values for ε and very low ANN probabilities may also indicate that an unknown sample, i.e., a sample that was not included in the

Table 3. Comparison of actual mixture responses (Hz) to predicted responses assuming a linearly additive model[a]

Concentration (mg/m^3)			PECH			PIB			OV275			PDPP	
Component 1	Component 2	Actual	Predicted	%Diff[c]	Actual	Predicted	%Diff	Actual	Predicted	% Diff	Actual	Predicted	%Diff
1,1,1 Trichloroethane	Acetone												
63.6	168	387	367	5.2	174	168	3.4	347	320	7.8	172	170	1.2
70.3	95.5	257	233	9.3	142	130	8.4	224	195	13	126	121	4.0
171	26.6	194	171	12	214	190	11	109	111	−1.8	152	140	7.9
473	235	830	784	5.5	651	624	4.1	649	593	8.6	531	508	4.3
908	137	964	902	6.4	1077	1004	6.8	612	585	4.4	786	740	5.8
ΔET[b] = 4s				**Avg.=7.7**			**6.7**			**6.4**			**4.6**
Perchloroethylene	Benzene												
28.5	91.0	309	310	−0.2	510	466	8.7	148	170	−15	279	260	6.7
35.3	136	463	442	4.6	703	632	10	235	246	−4.6	400	365	8.8
37.7	179	571	556	2.6	801	754	5.9	300	314	−4.5	479	451	5.8
48.7	34.8	208	227	−9.3	515	512	0.6	95	107	−13	222	225	−1.4
95.0	65.8	430	438	−1.9	1023	994	2.9	193	206	−7.0	444	435	1.9
278	191	1295	1278	1.3	3057	2905	5.0	599	602	−0.5	1327	1271	4.2
407	306	1852	1937	−4.6	4271	4314	−1.0	871	921	−5.7	1865	1909	−2.4
ΔET = 6s				**Avg.=−1.1**			**4.6**			**−7.2**			**3.4**
Dichloromethane	Perchloroethylene												
75.0	34.3	254	286	−12	521	561	−7.7	201	196	2.5	238	268	−13
224	19.8	482	512	−6.3	447	518	−16	461	470	−1.9	358	387	−8.1
235	107	730	893	−22	1512	1751	−16	556	613	−10	675	838	−24
691	63.3	1533	1590	−3.7	1426	1630	−14	1426	1452	−1.8	1123	1205	−7.3
ΔET = 6s				**Avg.=−11**			**−13**			**−2.9**			**−13**
2-Propanol	1-Butanol												
105	47.0	811	864	−6.5	414	448	−8.2	739	825	−12	329	331	−0.5
131	30.0	751	771	−2.7	377	386	−2.4	740	801	−8.2	289	293	−1.5
176	71.8	1349	1373	−1.8	648	709	−9.3	1354	1328	1.9	522	525	−0.6
501	55.1	2322	2312	0.4	1014	1117	−10	2816	2586	8.2	883	874	1.0
ΔET = 3s				**Avg.=−2.6**			**−7.5**			**−2.4**			**−0.4**

[a] Predicted mixture response=the sum of individual vapor maximum responses.
[b] Difference in elution times for individual vapors.
[c] Relative to actual values.

Table 4. Selected results for recognition and quantification of individual vapor test-set data

Sample			Recognition				Quantification Conc. (mg/m^3)		
#	Chemical (ID)	RH (%)	EDPCR		ANN				
			Class.	ε[a]	Class.	Prob.	True	Pred.[b]	% Err
1	Dichloromethane	100	**DCM**	**20**	**DCM**	**0.41**	160	148	−7.4
	(DCM)		MXY	38	MXY	0.14			
			BUT	90	TOL	0.08			
2	Perchloroethylene	0	**PRC**	**12**	**PRC**	**0.50**	234	226	−3.4
	(PRC)		XYL	594	TOL	0.008			
			EBE	683	EBE	0.005			
3	Ethylbenzene	100	**EBE**	**42**	**EBE**	**0.58**	132	116	−12.2
	(EBE)		TCE	121	XYL	0.16			
			XYL	192	PRC	0.001			
4	m-Xylene	100	**XYL**	**43**	**XYL**	**0.43**	65.9	59.5	−9.7
	(XYL)		EBE	54	EBE	0.16			
			TCE	103	PRC	0.001			
5	2-Propanol	100	**BUT**	**52**	**IPA**	**0.44**	354	381	7.6
	(IPA)		IPA	118	ACE	0.30			
			ACE	221	BUT	0.27			

[a] ε — residual error from EDPCR assignment.

[b] Quantified using principal components regression (PCR).

calibration library, has been detected which emphasizes the need for careful selection and evaluation of the calibration set for a given application.

Overall, recognition rates are very high by EDPCR (30/31, 97%) and by ANN (31/31, 100%). Quantification errors averaged −2.7% with a standard deviation of 11% ($N = 31$), which is considered acceptable by most standards. These results are consistent with those reported previously using arrays of SAW or related AW sensors in similar configurations (Park *et al.*, 1999, 2000; Cai *et al.*, 2000), and verify the independence from humidity effects attributable to the dry-air purge step over the entire range of possible humidity encountered in breath and ambient air monitoring. As noted above, there were no apparent interferences from endogenous vapors in breath, most likely due to their presence at very low concentrations. The similarity in performance between the EDPCR and ANN methods suggests that the additional inputs to the ANN (e.g., elution time) do not appear to be necessary in most cases in order to recognize and discriminate among a set of individual vapors.

An independent set of 20 binary vapor mixture responses was also analyzed by EDPCR. ANN analyses were not performed because of the relatively large number of training patterns needed to establish the network for all possible mixtures. This highlights an advantage of more conventional statistical pattern recognition methods, such as EDPCR, over ANNs — in the former, mixture patterns can be established on the basis of individual-vapor calibrations provided that mixture responses are linear combinations of the component vapors responses.

Results from the mixture analyses are summarized in Table 5. As in Table 4, the top three pattern matches are listed along with the residual error. There are 21 possible binary combinations of the seven mixture test-set vapors which when added to the seven individual vapors makes a total of 28 possible outcomes for each pattern recognition analysis. EDPCR correctly recognized both components in 15 of the 20 samples (75%) and recognized both components as one of the top two possibilities in 18 of the 20 samples (90%). In all 20 samples, the correct mixture was among the top three possibilities. Also, in all 20 samples at least one of the mixture components was correctly recognized. Note that both within-class and between-class discrimination is achieved.

Although it is likely that more complex mixtures would be encountered in actual occupational air and breath monitoring scenarios, the results of this preliminary study establish the capability of the prototype instrument to perform mixture analyses. Subsequent work has shown that mixtures of up to four vapors can be analyzed with polymer-coated sensor arrays (Park *et al.*, 1999). Beyond this, the selectivity provided even by a diverse set of sensors is not sufficient to resolve the mixture components (note: for a subset of five vapors and allowing mixtures with up to four components there are 30 possible combinations of the component vapors). Thus, complex mixtures cannot be analyzed effectively without employing some sort of chromatographic separation prior to analysis (Grall *et al.*, 2000; Lu and Zellers, 2000).

One of the challenges in performing mixture analyses is the recognition of component(s) present at relatively low concentrations. In many cases the component with the dominant response will be correctly

Table 5. Results for EDPCR recognition and quantification of binary mixture test-set data

Sample			Recognized as ID(ε[a])			True		Concentration Predicted[b]		%Error	
#	ID	ΔET	1st	2nd	3rd	1	2	1	2	1	2
1	ACE+TCA	4s	ACE+TCA (7.9)	ACE+BEN (12)	ACE+BUT (23)	168	63.6	182	57.4	8.3	−9.7
2	ACE+TCA		BUT+DCM (4.9)	ACE+TCA (8.1)	ACE+BEN (13)	95.5	70.3	110	69.4	15	−1.3
3	ACE+TCA		BEN+TCA (6.3)	BUT+TCA (8.3)	ACE+TCA (13)	26.6	171	24.1	197	−9.4	15
4	ACE+TCA		ACE+TCA (13)	BEN+IPA (18)	BEN+DCM (48)	235	473	260	481	11	1.7
5	ACE+TCA		ACE+TCA (9.6)	BUT+TCA (37)	BEN+TCA (42)	137	908	141	976	2.9	7.5
											Avg=4.1 SD=9.06
6	BEN+PRC	6s	BEN+PRC (19)	PRC+TCA (27)	DCM+PRC (60)	91.0	28.5	80.0	35.7	−12	25
7	BEN+PRC		BEN+PRC (19)	PRC+TCA (51)	TCA (73)	136	35.3	132	43.4	−2.9	23
8	BEN+PRC		BEN+PRC (20)	BUT+TCA (65)	BEN+TCA (69)	179	37.7	176	42.9	−1.7	14
9	BEN+PRC		BEN+PRC (5.8)	PRC+TCA (6.7)	DCM+PRC (15)	34.8	48.7	25.2	50.1	−28	2.9
10	BEN+PRC		BEN+PRC (8.3)	PRC+TCA (19)	DCM+PRC (36)	65.8	95.0	56.9	97.7	−13	2.8
11	BEN+PRC		BEN+PRC (14)	PRC+TCA (70)	DCM+PRC (100)	191	278	179	289	−6.3	4.0
12	BEN+PRC		BEN+PRC (10)	PRC+TCA (120)	DCM+PRC (145)	306	407	274	398	−10	−2.2
											Avg.=−0.31 SD=14
13	DCM+PRC	6s	IPA+PRC (22)	DCM+PRC (26)	ACE+PRC (38)	75.0	34.3	64.7	48.8	−14	42
14	DCM+PRC		DCM+PRC (25)	DCM+TCA (38)	IPA+TCA (54)	224	19.8	220	23.5	−1.8	19
15	DCM+PRC		IPA+PRC (49)	DCM+PRC (70)	ACE+PRC (95)	235	107	176	143	−25	34
16	DCM+PRC		DCM+PRC (9.9)	IPA+TCA (80)	DCM+TCA (153)	691	63.3	678	76.1	−1.9	20
											Avg.=9.0 SD=23
17	BUT+IPA	3s	BUT+IPA (22)	ACE+PRC (34)	BUT+ACE (62)	47.0	105	50.1	79.6	6.6	−24
18	BUT+IPA		BUT+IPA (6.9)	BEN+IPA (68)	ACE+PRC (72)	30.0	131	35.9	106	20	−19
19	BUT+IPA		BUT+IPA (33)	BEN+IPA (120)	ACE+PRC (135)	71.8	176	57.0	211	−21	20
20	BUT+IPA		ACE+IPA (15)	DCM+IPA (52)	BUT+IPA (53)	55.1	501	7.50	646	−86	29
											Avg.=−9.3 SD=37
											Overall average % error=0.86 SD=22

[a] ε — residual error from EDPCR assignment.

[b] Quantified using principal components regression (PCR).

recognized but the other component(s) may not be recognized at all or may be confused with some other vapor, despite being present at concentrations greater than the LOD. An example of this can be seen for dichloromethane+perchloroethylene in Table 5. In all cases perchloroethylene is correctly identified as one of the components of the mixture, while dichloromethane is not recognized in two of the four samples. This effect has led to the development of an additional performance metric called the limit of recognition (LOR) which can be used to evaluate the performance of multisensor arrays (Zellers *et al.*, 1998). LORs for this set of vapors ranged from 0.5 to 2.5 × the LOD.

The last column of Table 5 presents the quantification errors for the mixture components, assuming they were both recognized. The concentrations were evaluated at the point in time corresponding to the maximum of the composite response profile regardless of the difference in elution times observed in the individual component calibrations. The average error is 0.86% with a standard deviation of 22%. No relationship between ΔET and quantification error is apparent which again suggests that for this set of vapors, factors other than partial component resolution contribute to the error. Collinearity of the response vectors for the mixture components will be contributory to quantitative error (Carey *et al.*, 1987) and will occur in all practical sensor arrays because of the inherent partial selectivity. It is minimized by choosing a diverse set of sensor coatings as was done here (Grate and Abraham, 1991; Zellers *et al.*, 1995).

CONCLUSIONS

This study has demonstrated that accurate recognition and quantification of vapors in breath, alone or in simple mixtures, is possible at concentrations $\leq 0.3\times$TLV using this instrumentation. The LODs achieved here assume a sample volume of 0.25 l., which is a reasonable volume expected from a single end-tidal expiration of breath. Improvements can be expected merely by increasing the sample volume: for breath analysis, this would require either collection of a second end-tidal exhalation or the use of a sampling protocol that allowed for collection of the larger expiratory reserve volume, while for air sampling this would require either increasing the duration of the sampling or increasing the flow rate of the pump within the instrument.

Immunity from humidity effects was demonstrated here and is consistent with previous studies of this issue with SAW sensor arrays conducted over more limited ranges of RH (Park and Zellers, 2000a,b; Zellers and Han, 1996). This was accomplished by using a drying agent (Drierite®) to condition purge and sensor array air streams, and a specially selected adsorbent that permits purging of water vapor with retention of organic vapors in the preconcentration unit prior to thermal desorption.

The two pattern recognition methods employed in this study, EDPCR and a probabilistic ANN, performed similarly well, and served to illustrate the advantages of the SAW sensor array technology: individual vapors can be recognized from among a large set of possibilities using an array of only four sensors with little or no error. Binary mixture analyses, performed with EDPCR, were prone to greater errors in recognition, but the performance is still considered sufficiently accurate for many occupational health applications. The use of sensor arrays with pattern recognition analysis is very powerful tool that provides analytical capabilities not currently present in low-cost field-deployable occupational hygiene monitoring instrumentation.

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REFERENCES

Anon. Perchloroethylene (portable GC) in exhaled breath and air (method 3704), In: NIOSH manual of analytical methods (NMAM). 4th ed. Cincinnati, OH: DHHS; 1994..

Anon. NIOSH pocket guide to chemical hazards. Cincinnati, OH: US Dept. of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, 1997.

American Conference of Governmental Industrial Hygienists. TLVs and BEIs threshold limit values for chemical substances and physical agents; biological exposure indices. ACGIH Worldwide. Cincinnati, OH, 1996.

Ballantine DS. Acoustic wave sensors theory, design, and physico-chemical applications. San Diego, CA: Academic Press, 1997.

Benoit FM, Davidson WR, Lovett AM, Nacson S, Ngo A. Breath analysis by API/MS — human exposure to volatile organic solvents. Int. Arch. Occup. Envir. Health 1985;55:113–20.

Cai QY, Park J, Heldsinger D, Hsieh MD, Zellers ET. Vapor recognition with an integrated array of polymer-coated flexural plate wave sensors. Sensors Actuat. B-Chem. 2000;62:121–30.

Carey WP, Beebe KR, Kowalski BR. Multicomponent analysis using an array of piezoelectric crystal sensors. Anal. Chem. 1987;59:1529–34.

Carey WP, Beebe KR, Sanchez E, Geladi P, Kowalski BR. Chemometric analysis of multisensor arrays. Sensors Actuat. 1986;9:223–34.

Carey WP, Kowalski BR. Chemical piezoelectric sensor and sensor array characterization. Anal. Chem. 1986;58:3077–84.

Dickinson TA, White J, Kauer JS, Walt DR. A chemical-detecting system based on a cross-reactive optical sensor array. Nature 1996;382:697–700.

Droz PO, Guillemin MP. Occupational exposure monitoring using breath analysis. J. Occup. Envir. Med. 1986;28:593–602.

Eklov T, Lundstrom I. Gas mixture analysis using a distributed chemical sensor system. Sensors Actuat. B-Chem. 1999;57:274–82.

Ewers L, Petersen M, Ruder A, Burroughs GE, Sweet N. A field evaluation of a new end-exhaled breath method to evaluate solvent exposure in dry-cleaning shops. Paper presented at the American Industrial Hygiene Conference and Exposition, Orlando, FL, 2000.

Franzblau A, Levine SP, Burgess LA et al.. The use of a transportable Fourier-transform infrared (Ftir) spectrometer for the direct measurement of solvents in breath and ambient air. 1. Methanol. Am. Ind. Hyg. Assoc. J. 1992;53:221–7.

Gardner JW. Detection of vapors and odors from a multisensor array using pattern-recognition. 1. Principal component and cluster-analysis. Sensors Actuat. B-Chem. 1991;4:109–15.

Gardner JW, Hines EL, Tang HC. Detection of vapors and odors form a multisensor array using pattern-recognition techniques. 2. Artificial neural networks. Sensors Actuat. B-Chem. 1992;9:9–15.

Gardner JW, Hines EL, Wilkinson M. Application of artificial neural networks to an electronic olfactory system. Meas. Sci. Technol. 1990;1:446–51.

Grall AJ, Zellers ET, Sacks RD. High-speed analysis of indoor VOCs using vacuum-outlet GC with ambient air carrier gas and programmable column selectivity. Envir Sci Technol 2000 (in press).

Grate JW. Acoustic wave microsensor arrays for vapor sensing. Chem. Rev. 2000;100:2627–48.

Grate JW, Abraham MH. Solubility Interactions and the design of chemically selective sorbent coatings for chemical sensors and arrays. Sensors Actuat. B-Chem. 1991;3:85–111.

Grate JW, Klusty M. Surface acoustic-wave vapor sensors based on resonator devices. Anal. Chem. 1991;63:1719–27.

Grate JW, Zellers ET. The fractional free volume of the sorbed vapor in modeling the viscoelastic contribution to polymer-coated surface acoustic wave vapor sensor responses. Anal. Chem. 2000;72:2861–8.

Grate JW, Martin SJ, White RM. Acoustic-wave microsensors. 1. Anal. Chem. 1993;65:A940–8.

Groves WA, Zellers ET. Investigation of organic vapor losses to condensed water vapor in Tedlar(R) bags used for exhaled-breath sampling. Am. Ind. Hyg. Assoc. J. 1996;57:257–63.

Groves WA, Zellers ET. Prototype instrument employing a microsensor array for the analysis of organic vapors in exhaled breath. Am. Ind. Hyg. Assoc. J. 1996;57:1103–8.

Groves WA, Zellers ET, Frye GC. Analyzing organic vapors in exhaled breath using a surface acoustic wave sensor array with preconcentration: selection and characterization of the preconcentrator adsorbent. Anal. Chim. Acta 1998;371:131–43.

Hierlemann A, Weimar U, Kraus G, Gauglitz G, Gopel W. Environmental chemical sensing using quartz microbalance sensor arrays: application of multicomponent analysis techniques. Sensors Mater. 1995;7:179–89.

Ho MH, Dillon HK. Biological monitoring of exposure to chemicals organic compounds. New York: Wiley, 1987.

Jurs PC, Bakken GA, McClelland HE. Computational methods for the analysis of chemical sensor array data from volatile analytes. Chem. Rev. 2000;100:2649–78.

Lu CJ, Zellers ET. A dual-stage preconcentrator for an indoor-VOC microanalytical system. Anal. Chem. 2000 (in press).

Manolis A. The diagnostic potential of breath analysis. Clin. Chem. 1983;29:5–15.

Martin SJ, Frye GC, Senturia SD. Dynamics and response of polymer-coated surface-acoustic-wave devices — effect of viscoelastic properties and film resonance. Anal. Chem. 1994;66:2201–19.

Massart DL. Chemometrics a textbook. Amsterdan: Elsevier, 1988.

Park J, Zellers ET. Determination of solvents permeating through chemical protective clothing with a microsensor. J. Envir. Monit. 2000a;2:300–6.

Park J, Zellers ET. Temperature and humidity compensation in the determination of solvent vapors with a microsensor system. The Analyst, 2000b;125(10):1775–82.

Park J, Groves WA, Zellers ET. Vapor recognition with small arrays of polymer-coated microsensors. A comprehensive analysis. Anal. Chem. 1999;71:3877–86.

Park J, Zhang GZ, Zellers ET. Personal monitoring instrument for the selective measurement of multiple organic vapors. Am. Ind. Hyg. Assoc. J. 2000;61:192–204.

Patrash SJ, Zellers ET. Characterization of polymeric surface-acoustic-wave sensor coatings and semiempirical models of sensor responses to organic vapors. Anal. Chem. 1993;65:2055–66.

Pleil JD, Fisher JW, Lindstrom AB. Trichloroethene levels in human blood and exhaled breath from controlled inhalation exposure. Envir. Hlth Perspect. 1998;106:573–80.

Rose-Pehrsson SL, Grate JW, Ballantine DS, Jurs PC. Detection of hazardous vapors including mixtures using pattern-recognition analysis of responses from surface acoustic-wave devices. Anal. Chem. 1988;60:2801–11.

Shaffer RE, Rose-Pehrsson SL. Improved probabilistic neural network algorithm for chemical sensor array pattern recognition. Anal. Chem. 1999;71:4263–71.

Shaffer RE, Rose-Pehrsson SL, Mcgill RA. Multiway analysis of preconcentrator-sampled surface acoustic wave chemical sensor array data. Field Anal. Chem. Technol. 1998;2:179–92.

Shaffer RE, Rose-Pehrsson SL, Mcgill RA. A comparison study of chemical sensor array pattern recognition algorithms. Anal. Chim. Acta 1999;384:305–17.

Stetter JR, Jurs PC, Rose SL. Detection of hazardous gases and vapors — pattern-recognition analysis of data from an electrochemical sensor array. Anal. Chem. 1986;58:860–6.

Sundgren H, Lundstrom I, Winquist F et al.. Evaluation of a multiple gas-mixture with a simple Mosfet gas sensor array and pattern-recognition. Sensors Actuat. B-Chem. 1990;2:115–23.

Sutter JM, Jurs PC. Neural network classification and quantification of organic vapors based on fluorescence data from a fiber optic sensor array. Anal. Chem. 1997;69:856–62.

Wallace L, Buckley T, Pellizzari E, Gordon S. Breath measurements as volatile organic compound biomarkers. Envir. Hlth Perspect. 1996;104:861–9.

White J, Kauer JS, Dickinson TA, Walt DR. Rapid analyte recognition in a device based on optical sensors and the olfactory system. Anal. Chem. 1996;68:2191–202.

Wilson HK. Breath analysis — physiological-basis and sampling techniques. Scand. J. Work Envir. Hlth 1986;12:174–92.

Wohltjen H. Mechanism of operation and design considerations for surface acoustic wave device vapour sensors. Sensors Actuat. 1984;5:307–25.

Zellers ET, Han MW. Effects of temperature and humidity on the performance of polymer-coated surface acoustic wave vapor sensor arrays. Anal. Chem. 1996;68:2409–18.

Zellers ET, Pan TS, Patrash SJ, Han MW, Batterman SA. Extended disjoint principal-components regression-analysis of SAW vapor sensor-array responses. Sensors Actuat. B-Chem. 1993;12:123–33.

Zellers ET, Batterman SA, Han MW, Patrash SJ. Optimal coating selection for the analysis of organic vapor mixtures with polymer-coated surface-acoustic-wave sensor arrays. Anal. Chem. 1995;67:1092–106.

Zellers ET, Park J, Hsu T, Groves WA. Establishing a limit of recognition for a vapor sensor array. Anal. Chem. 1998;70:4191–201.