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Array-to-Array Transfer of an Artificial Nose Classifier

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This paper describes the use of a microsphere sensor technology that allows simple fabrication of vapor sensor arrays with reproducible response patterns. Microsphere sensor fabrication protocols are uncomplicated and yield billions of highly reproducible sensors. Microsphere sensor arrays combined with a generalized Whitney−Mann−Wilcoxen (GWMW) classifier were used to discriminate between the presence and absence of nitroaromatic compounds in high background vapor mixtures. The classifier was trained on one sensor array and then used to obtain 98.2 and 93.7% correct classification rates with data collected using two subsequent arrays made up to six months after the initial training was performed. These results represent an advance in the ability to transfer training data between multiple sensor arrays with a fluorescence-based artificial nose.

Multiplexed sensor arrays have been the subject of burgeoning efforts in the sensor community, because they are capable of detecting a wide range of analytes with a limited number of sensing elements. An example is artificial or electronic noses, which are vapor detection systems that mimic aspects of mammalian olfaction by utilizing the response patterns from cross-reactive sensor arrays to discriminate odors.[1−3] Artificial nose arrays have been made with a variety of different sensor types, including surface acoustic wave devices,[4] conducting polymers,[5] metal oxides,[6,7] carbon black−polymer composite chemoresistors,[8,9] and fluorescent microspheres.[3,10] Ideally, every vapor presented to an artificial nose array causes some or all of the sensor elements to respond differentially, producing unique response patterns that encode each vapor.[11] Computational analysis of these patterns generates a classifier that correlates response patterns with specific vapors. The use of such response patterns provides a combinatorial advantage that allows the discrimination of more odors than there are types of sensors.[12]

An important issue for all artificial nose technologies is sensor-to-sensor reproducibility. Although some vapor sensor technologies have demonstrated reproducible sensor arrays,[2,13] the ability to fabricate reproducible sensors is typically reliant on stringent fabrication protocols, such as photolithography.[14,15] Techniques such as lithography allow precise control over fabrication conditions to ensure that like sensors have similar responses from batch to batch,[2,6] but these processes typically do not allow facile production of large quantities of sensors. Polymeric materials are notoriously difficult to fabricate reproducibly from batch to batch, especially among sensors with microscale features in which slight differences in polymer heterogeneity, porosity, or thickness can result in significant changes in sensor response. In our laboratory, we have moved from using irreproducible polymer sensors impregnated with a fluorescent dye[16] to fluorescent microspheres, which have good sensor-to-sensor reproducibility[10,17] and stability over time.[18] Unlike other fabrication techniques, microsphere sensors are made in large quantities through a simple process that requires soaking beads in a dye solution and then filtering. Just 1 g of 3-μm microspheres creates a stock containing ∼50 billion microsphere sensors, and this fabrication technique is easily scalable to trillions of sensors in one batch if desired. Conservatively, 1 g of microspheres can yield 10 000 sensor arrays, allowing us to avoid the issue of batch-to-batch sensor reproducibility.

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(1) Dickinson, T. A.; White, J.; Kauer, J. S.; Walt, D. R. *Trends Biotechnol.* **1998**, *16*, 250−258.
(2) Gardner, J.; Bartlett, P. *Electronic Noses Principles and Applications*; Oxford University Press: Oxford, 1999.
(3) Albert, K. J.; Lewis, N. S.; Schauer, C. L.; Sotzing, G. A.; Stitzel, S. E.; Vaid, T. P.; Walt, D. R. *Chem. Rev.* **2000**, *100*, 2592−2626.
(4) Grate, J. W. *Chem. Rev.* **2000**, *100*, 2627−2647.
(5) Freund, M. S.; Lewis, N. S. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 2652−2656.
(6) Gardner, J. W.; Shurmer, H. V.; Cocoran, P. *Sens. Actuators B* **1991**, *4*, 117−121.
(7) Gardner, J. W.; Craven, M.; Dow, C.; Hines, E. L. *Meas. Sci. Technol.* **1998**, *9*, 120−127.
(8) Lonergan, M. C.; Severin, E. J.; Doleman, B. J.; Beaber, S. A.; Grubb, R. H.; Lewis, N. S. *Chem. Mater.* **1996**, *8*, 2298−2312.
(9) Sotzing, G. A.; Briglin, S. M.; Grubbs, R. H.; Lewis, N. S. *Anal. Chem.* **2000**, *72*, 3181−3190.
(10) Dickinson, T. D.; Michael, K. L.; Kauer, J. S.; Walt, D. R. *Anal. Chem.* **1999**, *71*, 2192−2198.
(11) Jurs, P. C.; Bakken, G. A.; McClelland, H. E. *Chem. Rev.* **2000**, *100*, 2649−2678.
(12) Malnic, B.; Hirono, J.; Sato, T.; Buck, L. *Cell* **1999**, *96*, 713−723.
(13) Frank, M.; Ulmer, H.; Ruiz, J.; Visani, P.; Weimar, U. *Anal. Chim. Acta* **2001**, *431*, 11−29.
(14) Gardner, J. W.; Pike, A.; de Rooij, N. F.; Koudelka-Hep, M.; Clerc, P. A.; Hierlemann, A.; Gopel, W. *Sens. Actuators, B* **1995**, *26−27*, 135−139.
(15) Grate, J. W.; Patrash, S. J.; Kaganove, S. N.; Wise, B. M. *Anal. Chem.* **1999**, *71*, 1033−1040.
(16) Dickinson, T. A.; White, J.; Kauer, J. S.; Walt, D. R. *Nature* **1996**, *382*, 697−700.
(17) Albert, K. J.; Walt, D. R.; Gill, D. S.; Pearce, T. C. *Anal. Chem.* **2001**, *73*, 2501−2508.
(18) Albert, K. J.; Walt, D. R. *Anal. Chem.* **2000**, *72*, 1947−1955.

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Table 1. Microsphere Sensor Materials

sensor name	bead size (μm)	bead material	dye soln (mg dye/mL solvent)	fabrication date
IbsilC1	3	IB−Sil (methyl group)	0.5 mg/mL toluene	8/20/99
PhenosOH	3	Phenosphere (hydroxyl group)	0.5 mg/mL toluene	2/14/99
Selectosil	5	Selectosil (strong cation exchange)	0.5 mg/mL chloroform	2/14/99
Lun802/BMA	3	Luna (hydroxyl group), PS802, BMA	1.0 mg/mL toluene	6/21/99
55% DVB	3	polystyrene, divinylbenzene	1.0 mg/mL toluene	2/10/99

Because of the unprecedented numbers of sensors made at one time in a stock, we are able to fabricate new sensor arrays routinely, allowing us to avoid poisoning and sensor degradation exhibited by other sensor array types that use the same array over long periods of time. In this paper, we demonstrate the long-term *functional* stability of the microsphere sensor stock from which all sensor arrays are created, thereby obviating the need for long-term stability of an individual sensor array.

The central question posed in this work is whether sensor response patterns are reproducible enough from array to array over time to allow a classifier generated on one array to be applied to subsequent arrays made from the same sensor stock and still retain high classification fidelity. Although sensor uniformity is crucial to obtain reproducible responses from different arrays, changes in environmental conditions can also affect sensor response. Therefore, the classifier used would need to be flexible so that slight changes in sensor response would not make classification difficult. In the work reported here, the GWMW family of classifiers was employed because it is not likely to be unduly influenced by a sensor artifact in the training data, thus keeping it from correctly classifying responses from a different array.

A two-class problem was chosen to test if the response patterns from each array were reproducible enough to enable a trained classifier to be transferred between sensor arrays. The problem was to determine if explosives-like nitroaromatic compound (NAC) vapors were present or absent in a series of organic vapor samples. This problem is a straightforward yes-or-no classification with no attempt at analyte quantification, but it is still challenging as a result of the low NAC levels relative to the much higher VOC backgrounds. The ability to sense NACs in variable high backgrounds was investigated because of its importance in explosives detection, such as buried land mines,[19] but it should be noted that a different two-class problem could just as easily have been chosen to test the transferability of the classifier. Here we report that the microsphere sensor response patterns are stable over time, allowing array-to-array reproducibility and transfer of a trained classifier to multiple arrays.

EXPERIMENTAL SECTION

Materials. Acetone, benzene, chloroform, ethanol, methanol, toluene, and 22 × 30 mm glass coverslips were used as received from Fisher. Benzyl methacrylate, benzoin ethyl ether (BEE), 3-(trimethoxysilyl)propyl methacrylate, Nile Red, ethyl acetate, heptane, 1,3-dinitrobenzene (1,3-DNB), and 4-nitrotoluene (4-NT) were used as received from Aldrich. Ultrazero-grade air carrier gas was purchased from Northeast Airgas (Salem, NH). The following silica microspheres were removed from HPLC columns purchased from Phenomenex (Torrance, CA): 3-μm IB−Sil (C1), 3-μm Phenosphere (OH), 3-μm Luna (OH), and 5-μm Selectosil (SCX). Polymer beads of 3.12-μm P(S/55% DVB) were purchased from Bangs Laboratories, Inc. (Fishers, IN). PS802, a copolymer, was used as received from Gelest, Inc. (Tullytown, PA).

Microsensor Preparation. Microsensors were prepared by soaking silica or polymer beads in a fluorescent indicator, Nile Red. Each sensor type was dyed in a batch process that produced a stock of $\sim 5.0 \times 10^7$ microspheres/mg of microsensors. Once dyed, the sensors were placed on a vacuum filtration system and rinsed with toluene or chloroform to remove excess dye. The sensors were then dried in a 100 °C oven for approximately 1 h and stored in the dark until use. Table 1 shows the bead material and dye concentration for each sensor type. While four of the sensor types were made directly from commercially available beads, the Lun802/BMA beads were fabricated by silanizing 45 mg of 3-μm Luna (OH) microspheres using a 10% solution of 3-(trimethoxysilyl)propyl methacrylate in acetone for 2 h. The excess silane solution was removed via vacuum filtration, and the beads were allowed to cure overnight. In a colorless 4-mL dram, the silanized beads were combined with 60 mg of BEE and 1 mL of a toluene solution that was 0.5 vol % in both PS802 and BMA. The mixture was purged with N_2 for 15 min and allowed to photopolymerize for 1.5 h under UV light with constant stirring. Excess monomer solution was removed via vacuum filtration. These beads were then dyed as described above.

Sensor Array Fabrication. All tests employed a randomly distributed sensor array containing the five sensor types in Table 1 in which each array consists of the microsphere sensors smeared onto a glass coverslip. Three randomized sensor arrays were fabricated months apart, but all from the same sensor stock, to yield three arrays with hundreds of copies of each of the five sensor types.[18] The mixed sensor stock was made by combining equal portions of each of the five sensor types to create a dry slurry. The arrays were prepared by placing a small portion of the sensor mixture on a glass coverslip and then covering this with a second coverslip to create a sandwich. The coverslips were then rubbed together to smear the sensors over the glass surface, creating two randomized sensor arrays. This randomized dispersion of sensors simplifies array fabrication by eliminating the difficulty of positioning each sensor on a defined point within the array. In addition, a homogeneous array was made for each of the five sensor types, using an individual sensor type instead of the mixed sensor stock.

Instrumentation. A custom-built fluorescence imaging system described previously[18,20] with an inverted microscope attached to

(19) George, V.; Jenkins, T. F.; Leggett, D. C.; Cragin, J. H.; Phelan, J.; Oxley, J.; Pennington, J. *Proc. SPIE-Int. Soc. Opt. Eng.* **1999**; *3710*, 258−269.

(20) White, J.; Kauer, J. S.; Dickinson, T. A.; Walt, D. R. *Anal. Chem.* **1996**, *68*, 2191−2202.

Table 2. Concentration ± 15%[a] of the Pure Analytes

analyte	vap press @25 °C (mm Hg)	sample concn (ppm)
acetone	2.31×10^2	7.6×10^4
benzene	9.53×10^1	3.1×10^4
chloroform	1.97×10^2	6.5×10^4
ethanol	5.90×10^1	1.9×10^4
ethyl acetate	9.45×10^1	3.1×10^4
heptane	4.57×10^1	1.5×10^4
methanol	1.27×10^2	4.2×10^4
toluene	2.84×10^1	9.4×10^3
1,3-dinitrobenzene	9.00×10^{-4}	6.0×10^{-1}
4-nitrotoluene	1.64×10^{-1}	1.1×10^2

[a] The concentrations were calculated based on the literature values[25,26] for the analyte vapor pressures listed.

Table 3. Concentration ± 15% of the Binary Mixtures

		concn (ppm)	
analyte 1	analyte 2	analyte 1	analyte 2
benzene	methanol	3.1×10^4	4.2×10^4
benzene	4-nitrotoluene	3.1×10^4	5.5×10^1
benzene	4-nitrotoluene	3.1×10^4	1.1×10^2
ethyl acetate	heptane	3.1×10^4	1.5×10^4
ethyl acetate	1,3-dinitrotoluene	3.1×10^4	3.0×10^{-1}
ethyl acetate	1,3-dinitrotoluene	3.1×10^4	6.0×10^{-1}
heptane	1,3-dinitrotoluene	1.5×10^4	6.0×10^{-1}
heptane	4-nitrotoluene	1.5×10^4	1.1×10^2
methanol	4-nitrotoluene	4.2×10^4	5.5×10^1
methanol	4-nitrotoluene	4.2×10^4	1.1×10^2

a 640 × 480 pixel SensiCam high-performance charge-coupled device (CCD) camera (Cooke Corporation, Auburn Hills, MI) was used to detect sensor array responses. The imaging system was computer-controlled through IPLab imaging software (Scanalytics, Fairfax, VA). Vapor samples were delivered to the array in a pulsatile fashion via a previously described vacuum-controlled sparging apparatus.[20] Binary mixtures were produced in conjunction with a Tedlar bag gas dilution vapor delivery system.[18]

Sample Preparation. Volatile organic compounds (VOCs) and solid nitroaromatic compound (NAC) samples were placed in sealed Erlenmeyer flasks and delivered to the array in pure form at 25% and 50% saturated headspace vapor, respectively (Table 2). The analytes that were used were acetone, air carrier gas (control), benzene, chloroform, ethanol, ethyl acetate, heptane, methanol, toluene, and NACs, including 1,3-dinitrobenzene (1,3-DNB) and 4-nitrotoluene (4-NT). Binary mixtures of the VOCs and NACs were created using 50% saturated Tedlar bag samples of heptane, benzene, ethyl acetate, and methanol in combination with NAC flask samples. The relative concentration of the VOC ranged from 100 to 75 000 times higher than that of the NAC in a mixture (Table 3). Tedlar bag samples were prepared as previously described[18] by combining 3 L of ultrazero-grade air carrier gas with the following volumes of organic solvents (a) benzene (756 μL), (b) ethyl acetate (826 μL), (c) heptane (598 μL), and (d) methanol (458 μL). It should be noted that if quantification of analyte concentrations were desired, the above-described vapor delivery system would not be adequate. Because this paper only discusses a problem requiring a yes-or-no answer, this vapor delivery method is sufficient.

Data Acquisition. Fluorescence responses for all of the sensor elements in an array were recorded using a CCD camera by acquiring images before, during, and after vapor pulse delivery. The sensors were excited at 530 nm, and emission was monitored at 630 nm. For each vapor observation, a total of 60 images was collected in 4.12 s. First, registration pulses of 50% saturated ethanol and acetone were collected for each of five homogeneous arrays containing one of the five sensor types as well as the three randomized arrays. Then NACs and VOCs were presented in both pure form and as components of binary mixtures to the three randomized arrays. The training array and first testing array were each exposed to the 10 pure vapors and 10 binary mixtures listed in Tables 2 and 3. Each sample was tested five times, and 12 air responses were collected intermittently during the data set, giving a total of 112 vapor responses collected for each array. The sampling order for the training array was not randomized, but samples were partially randomized for the first testing array. These two sensor arrays were tested one month apart using new volatile organic samples each time and in a laboratory where temperature and humidity levels were not specifically controlled. A third sensor array was tested six months after the training array by collecting three replicates of the 10 pure analytes (Table 2) and four replicates of the binary mixtures (Table 3) except for the three mixtures containing methanol. Seven air samples were collected intermittently to give a total of 65 vapor responses that were collected in a partially randomized order. Approximately 400 microsphere sensors were monitored on each of the three arrays.

Sensor Registration. The sensors in the three randomized arrays had to be positionally registered as one of the five microsphere types. This task was accomplished by comparing the randomized sensor responses to the known response profiles of the five individual sensor types. Known response profiles were generated from the homogeneous array sensor responses to ethanol and acetone registration pulses by averaging the responses of 50 sensors over the 60 time points. These profiles were normalized to have the same amplitude and baseline. The ethanol and acetone responses from the randomized arrays were also normalized, and each sensor from the training and testing arrays was assigned to its closest microsphere type by comparing its response to the ethanol and acetone profile signals derived from the five homogeneous arrays. In each array, the 12 sensors that were closest to the known response profiles were chosen for each sensor type; the distance was measured with respect to the L1 norm taken over 60 discrete frame observations. The L1 norm is defined as $||(y_1, y_2, ..., y_n) - (x_1, x_2, ..., x_n)|| = |y_1 - x_1| + |y_2 - x_2| + ... + |y_n - x_n|$ where x and y are the two response curves that are being compared.

Data Analysis. First, air samples were identified by evaluating the raw fluorescence intensity of each sensor response. The difference between every sensor's raw maximum and minimum fluorescence intensity was measured for each vapor observation, and this intensity value was averaged over the ∼400 analyzed sensors in an array. If the average change in intensity was less than 40 fluorescence counts on the CCD camera, the observation was classified as air, because air had less intense response features than the other analytes. Observations with an average value of 40 or higher counts were passed on to a classifier composed of the simplest case of the generalized Whitney−Mann−Wilcoxon

classifier (with $k_1 = k_2 = 2$, henceforth called GWMW (2,2))[21] combined with an ordinary Whitney−Mann−Wilcoxon classifier (with $k_1 = k_2 = 1$, henceforth called GWMW (1,1)).

Data from the training array was used to define the classifier threshold values that are necessary to determine the presence or absence of NACs. Data from the testing arrays collected one and six months later were then analyzed using the same classifier. Prior to analysis by the classifier, the raw data from the training and testing arrays were preprocessed as follows. All responses from the 12 registered sensors of each of the five sensor types were normalized to have the same amplitude and baseline. Then each group of 12 responses was averaged to give one response per sensor type with 60 time points. Averaging the 12 responses eliminated differences between individual sensors and enhanced the signal-to-noise ratio by the $\sqrt{n}$ for each sensor type in the array, where n is the number of sensors averaged.[10,18] The five averaged responses from the sensor types were then concatenated to yield a 300-dimensional discrete vector for each vapor. Thus, the coordinates of the 300-dimensional vector would be expected to correspond for each array, even though the original arrays had different random mapping of sensor types. For each 300-dimensional test vector, the absolute value of its distance, coordinate-wise, to a training observation was computed and summed over all of the 300-dimensional training vectors. The GWMW (2,2) classifier assigned a weight to each vapor observation on the basis of its vector **v** as follows:

$$\mathrm{GWMW}(2,2)(\mathbf{v}) = \sum_{\mathrm{S}(2,2)} \begin{cases} 1, \text{ if the closest observation in S(2,2) to } \mathbf{v} \text{ is class 1} \\ 0, \text{ otherwise} \end{cases}$$

where class 1 is NAC-present observations, class 0 is NAC-absent observations, and S(2,2) is the collection of all 4-element subsets of the training data composed of exactly two observations of class 1 and two observations of class 0. The GWMW (1,1) classifier is similarly defined, where S(2,2) is replaced with S(1,1), and S(1,1) is defined as the collection of all 2-element subsets of the training data, composed of exactly one observation of class 1 and one observation of class 0. The larger the assigned weight, the more confidence that the observation is of class 1 and the lower the weight, the more confidence the observation is of class 0.[22]

RESULTS AND DISCUSSION

The response features from the microspheres result from the interaction between the analyte of interest, the sensor substrate, and the indicator Nile Red, a solvatochromic dye. Solvatochromic dyes are sensitive to changes in the polarity of their environment, which are reported as shifts in either or both of the dye's excitation and emission spectra.[23] Each sensor's temporal fluorescence change at a specific wavelength, therefore, gives rise to different response patterns based on how the vapor polarity and sensor surface functionality influence the dye's emission properties. Although other factors such as sorption of the vapor into the sensor material may influence the sensor response, the dominant influence is the polarity change of the dye. As can be seen in Figure 1, the data produced by these sensors are highly complex in shape, with some sensor types having nonlinear response features. As can also be seen in Figure 1, the presence of NAC in a sample leads to a decrease in the fluorescence intensity of all five sensor types. This quenching effect is seen even in binary mixtures that contain high concentrations of other organic vapors, helping to distinguish NAC-containing observations from the other observations.

In developing a classifier, we sought to use one that could deal directly with the high-dimensional sensor data, and avoid feature selection. We chose the GWMW family of classifiers, a nonparametric statistic that has the advantage of being *distribution-free*, meaning that it does not need to make any restrictive assumptions about the data produced. Priebe suggested specifically that the GWMW family of classifiers might be well-suited for high-dimensional classification problems in general, and artificial nose data analysis in particular.[24] An advantage of nonparametric statistics is that they produce a mathematically rigorous notion of "confidence" associated with the class label assigned to each observation. In addition, because the GWMW family of classifiers takes into account the relative distance of all training observations, it seemed particularly suited to the task at hand, because a sensor-specific artifact in data that was array-specific would not overly bias the classifier when tested on a new array. This insensitivity to artifacts is demonstrated in Figure 1, in which the fourth sensor response to ethanol varies from array to array. However, this sensor variation does not overly influence the global ethanol response over all five sensor types, so that ethanol was always correctly classified as not containing a NAC. In addition, instead of just looking at the *k*-nearest neighbor (KNN), the GWMW classifier family looks at inversions, counting when NAC-present observations are closer than NAC-absent observations across the entire training data set. Because the GWMW classifiers incorporate the relative distance order of all of the training observations, if there were some consistent drift in signal from one array to another that led the same set of training observations to be close to all the testing observations, this drift should not completely erode the discriminatory power of the classifiers.

In order for the two GWMW classifiers discussed above to be combined as one vapor discrimination model, thresholds were defined on the basis of the training data to interpret the weights of each observation as class assignments. For a randomly ordered sequence of 50 class 1 observations and 62 class 0 observations, a score of 1 158 237.5 would be expected. The lowest-scoring NAC-present example in the training data, on the basis of a leave-one-out cross validation, received a score of 855 114 (one instance of 1,3-DNB). Excluding air, the highest scoring NAC-absent observation was 1 435 625 (one observation of ethyl acetate at 25%). This result is almost exactly 25% above and below the mean value of the statistic. The GWMW (2,2) classifier was set to make three types of decisions: if GWMW (2,2) scores were under 750 000, the observation was classed NAC-absent; if GWMW (2,2) weight values were over 1 500 000, the class was assigned NAC-present;

(21) Priebe, C. E.; Cowen, L. *Communications in Statistics: Theory and Methods* **1999**, *28*, 2871−2878.
(22) Xie, J.; Priebe, C. E. *J. Nonparam. Stat.* **2000**, *12*, 661−682.
(23) Reichardt, C. *Chem. Rev.* **1994**, *94*, 2319−2358.
(24) Priebe, C. E. *IEEE Trans. Pattern Match Machine Intel.* ***2001***, *23*, 404−413.
(25) Lide, D. R.; CRC Press: Boca Raton, 1997; pp 15-14−15-18.
(26) Howard, P. H.; Meglan, W. M. *Handbook of Physical Properties of Organic Chemicals*; Lewis Publishers: New York, 1997.

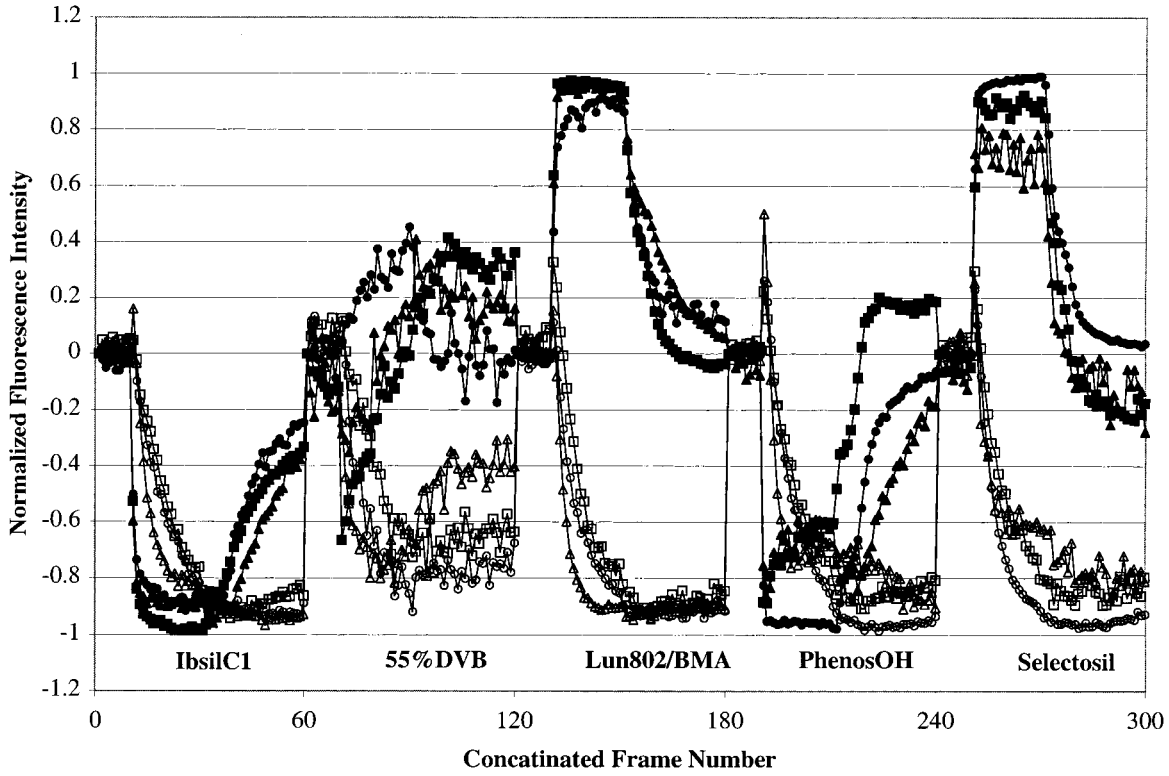

Figure 1. The concatinated 60-time-point (frame) responses of the five sensor types to 4-NT (open symbols) and ethanol (filled symbols) vapors are shown for the three arrays. These temporal response profiles demonstrate how a nitroaromatic compound can be distinguished from a non-nitroaromatic compound on the basis of different response features. Analytes are denoted by the following symbols. Ethanol: training array, ■; first testing array, ●; and second testing array, ▲. 4-NT: training array, □; first testing array, ○; and second testing array, △.

and for scores between 750 000 and 1 500 000, the decision was passed to the GWMW (1,1) classifier. For the GWMW (1,1) scores, excluding air, the highest-scoring NAC-absent example in a leave-one-out cross-validation of the training data had a score of 1325; therefore, scores above 1325 were classified as containing NAC vapor, and those below 1325 were classified as not containing NAC vapor. The classifier threshold values were defined to optimize the number of correctly assigned observations with the training data set. When the number of false positives or false negatives needs to be minimized, however, the threshold values can be adjusted to obtain acceptable levels of accuracy. Score levels were calibrated across training and testing arrays to a base response from an initial air observation from each array.

Thresholds for both classifiers were determined on the basis of the training data, and then the GWMW classifiers were used to analyze the observations from the two test data sets collected one and six months after the training data. The GWMW (2,2) classifier misidentified two observations on the first test data set containing 1,3-DNB as being NAC-absent. The GWMW (1,1) classifier made no additional errors. Figure 2 shows a plot of the GWMW (1,1) vs GWMW (2,2) scores for all 112 observations in the first test data set. The two false negatives obtained with the test data were both binary mixtures of 1,3-DNB and ethyl acetate. These errors are not surprising, given that the concentration of ethyl acetate in this mixture was approximately 75 000 times higher than that of 1,3-DNB. A 98.2% correct classification rate was achieved on this data set without any additional training.

The second test data set had two false positives and two false negatives (Figure 3). All four errors were made in the second

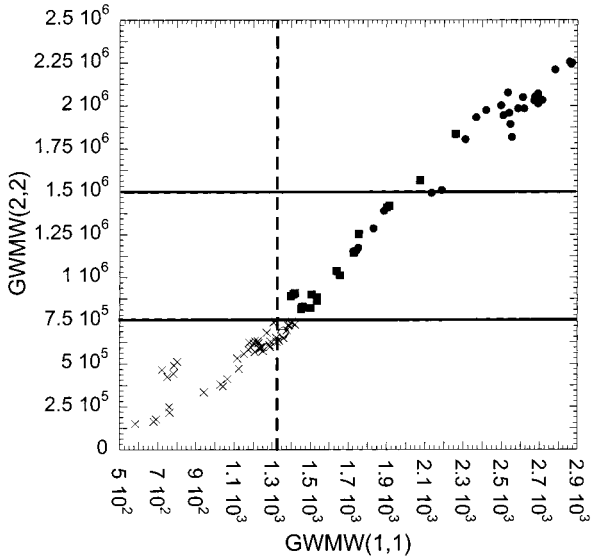

Figure 2. Graph of the GWMW (1,1) scores vs the GWMW (2,2) scores for the first test data set collected one month after the training data. Analytes are denoted with the following symbols: 4-NT, ●; 1,3-DNB, ■; all VOCs, ×; and false negative observations, ○. A 98.2% correct classification rate was achieved.

step of the classifier, with two chloroform responses being classed as containing a NAC, and two 1,3-DNB responses classed as not containing a NAC. Despite these errors, the second test data set achieved a 93.8% correct classification rate. This data set was collected six months after the training data, thus demonstrating the longevity of the classifier. The slight degradation in the classifier with time may be due to drift in the sensing chemistry

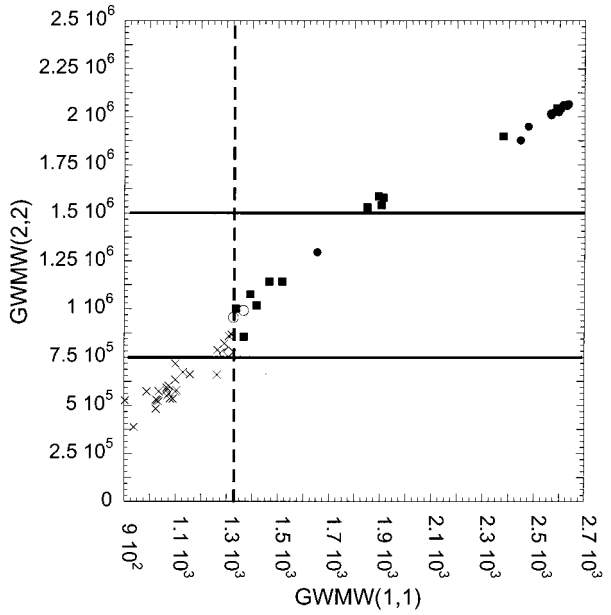

Figure 3. Graph of the GWMW (1,1) scores vs the GWMW (2,2) scores for the second test data set collected six months after the training data. Analytes are denoted with the following symbols: 4-NT, ●; 1,3-DNB, ■; all VOCs, ×; false negative observations, ○; and false positive observations, ◇. A 93.8% correct classification rate was achieved.

of the microspheres. It is important to note that although the GWMW (2,2) classifier could be used alone, the combination of the two GWMW classifiers improves the classification results. In addition, the GWMW classifiers outperform other classification methods, such as KNN, which obtained classification rates that were only 60−66% correct on the same data.

CONCLUSIONS

We have demonstrated an artificial nose technology that allows microsensors to be fabricated in unprecedented numbers, creating a sensor stock from which thousands of sensor arrays can be produced. This approach avoids the need to prepare different sensor batches with a high degree of reproducibility. The ease of the sensor and array fabrication protocols enables the microsphere sensor arrays to be disposable and, therefore, not subject to the degradation effects that other sensor array types experience over time. In addition, the stability of the sensor response patterns allows the trained GWMW classifier to maintain a high fidelity when applied to multiple sensor arrays. For practical applications, this result suggests that more efficient artificial noses can be developed, enabling sensor arrays to be replaced without retraining the classifier. More importantly, the ability to interchange sensor arrays allows a reference library of learned vapor response patterns to be generated over time. This library would represent the artificial nose's "odor memory" and should facilitate the investigation of complex problems, such as environmental monitoring or medical diagnostics for which large training sets may be required.

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