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Evaluation of Multitransducer Arrays for the Determination of Organic Vapor Mixtures

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A study of vapor recognition and quantification by polymer-coated multitransducer (MT) arrays is described. The primary data set consists of experimentally derived sensitivities for 11 organic vapors obtained from 15 microsensors comprising five cantilever, capacitor, and calorimeter devices coated with five different sorptive–polymer films. These are used in Monte Carlo simulations coupled with principal component regression models to assess expected performance. Recognition rates for individual vapors and for vapor mixtures of up to four components are estimated for single-transducer (ST) arrays of up to five sensors and MT arrays of up to 15 sensors. Recognition rates are not significantly improved by including more than five sensors in an MT array for any specific analysis, regardless of difficulty. Optimal MT arrays consistently outperform optimal ST arrays of similar size, and with judiciously selected 5-sensor MT arrays, one-third of all possible ternary vapor mixtures are reliably discriminated from their individual components and binary component mixtures, whereas none are reliably determined with any of the ST arrays. Quaternary mixtures could not be analyzed effectively with any of the arrays. A "universal" MT array consisting of eight sensors is defined, which provides the best possible performance for all analytical scenarios. Accurate quantification is predicted for correctly identified vapors.

In most reports on the application of microfabricated sensor arrays to multivapor analysis, the devices employed operate on the same transduction principle. Examples include surface acoustic wave (SAW) resonators,[1–3] cantilevers,[4,5] capacitors,[6–9] calorim-

eters,[10,11] and chemiresistors.[12–15] The sensors in such single-transducer (ST) arrays are typically coated with different sorptive–polymer interface layers. Reversible, partially selective responses to a given vapor can be obtained by virtue of differences in the magnitude of partitioning and the corresponding changes in the properties of the interface layer to which the underlying transducer is sensitive. Recognition (discrimination) of as many as 15–20 individual vapors is possible with ST arrays of just 2–6 sensors by use of statistical classification methods that compare each measured array response pattern to those stored in a calibration library.[1,3,15–20] Recognition of the components of mixtures contain-

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ing more than two vapors, on the other hand, has proven to be quite difficult with ST arrays.[2,17−22]

The difficulty in quantitatively analyzing vapor mixtures can be ascribed to (1) the limited range of nonbonding interactions that occur between vapors and polymers, which constrains the extent of differential partitioning, and (2) the limited range of properties probed by the sensors in an ST array. These two factors will dictate the diversity of responses achievable with such arrays, regardless of the transducer employed. It stands to reason that arrays incorporating sensors that operate on different transduction principles should enhance response diversity by probing different aspects of the vapor−interface interaction. This, in turn, should afford a greater amount of uncorrelated information about a set of vapors and, thereby, improve discrimination.

The notion of combining different microfabricated transducers in an array or operating a given transducer in different modes is not new; reports on multitransducer (MT) arrays of gas/vapor microsensors, often referred to as "hybrid arrays", date back to the mid-1980s.[23] Perhaps the most extensive effort to develop MT array technologies has been that of Göpel et al., who explored combinations of transducers (and interface materials) that probe changes in capacitance, heat flow, refractive index, thickness, mass, resistance, and electrochemical activity.[24] The MOSES II modular sensor system is a practical embodiment of the MT array concept.[25] In a parallel and similarly sustained effort, Baltes et al. have worked on integrating different vapor-sensitive transducers with on-chip circuitry to improve signal quality and reduce size.[26] A monolithic realization of such an MT array chip was reported in 2001[27] and characterized more recently.[28] A number of other reports on MT array performance have been published.[29−33]

Although it has been established that discrimination of vapor-phase analytes with an MT array can be superior to that with an ST array, comparative studies have been narrow in scope, generally relying on empirical data drawn from a few cases that afford little or no insight about the mechanistic features of the

discrimination or the ultimate boundaries on performance. Approaches to determining the optimal number of sensors to include in arrays for multivapor discriminations have been described in several reports,[3,20,29,30,34,35] but only one of these explores this topic for MT arrays.[30] The important question of whether MT arrays can provide quantitative analysis of multivapor mixtures of greater complexity than those that can be analyzed by ST arrays remains unanswered.

This article is a follow-up to a recent article by two of the authors (P. K. and A. H.) documenting that capacitive, calorimetric, and cantilever sensors provide responses that are generally consistent with their respective transduction mechanisms.[28] It was shown that the relative response patterns among a set of vapors varies with molecular mass for cantilevers, dielectric constant for capacitors, and heat of sorption for calorimeters after accounting for the degree of partitioning. Here, we use calibration data generated with the same set of MT chips as in that study. By use of various metrics of selectivity and Monte Carlo simulations coupled with pattern recognition algorithms, we evaluate the expected performance of such MT arrays and compare the performance of MT and ST arrays as a function of the size (i.e., the number of sensors) of the arrays. An emphasis is placed on determining the complexity of mixtures that can be quantitatively analyzed with such arrays.

EXPERIMENTAL SECTION

Data Set Description. The data set employed for this study consists of the slope sensitivities of 15 sensors to each of 11 organic vapors. Five sets of integrated 3-transducer chips were used to gather the data, each having a capacitor, cantilever, and calorimeter (referred to henceforth as CAP, CAN, and CAL, respectively). The three transducers on each chip were spray-coated simultaneously with one of the following polymers: ethyl cellulose (EC), poly(cyanopropylmethylsiloxane) (PCPMS, 10% cyano groups), poly(dimethylsiloxane) (PDMS), poly(epichloro-hydrin) (PECH), and poly(etherurethane) (PEUT). The 11 vapors included in this series of analyses are as follows: *n*-octane (OCT), *n*-heptane (HEP), toluene (TOL), methanol (MOH), ethanol (EOH), 1-propanol (POH), ethyl acetate (EAC), chloroform (CHL), carbon tetrachloride (CCL), trichloroethylene (TCE), and per-chloroethylene (PCE). Details of the devices, polymer structures, film deposition, vapor generation, and sensor calibration can be found in ref 28.

Most of the 165 sensitivity values included in the database were determined by linear regression of experimental sensor responses onto vapor concentration with a forced-zero intercept. For 12 of the vapor−sensor combinations, however, low signal-to-noise ratios in the target concentration range (methanol, ethanol) or other data acquisition difficulties precluded accurate determinations of sensitivity values. In order to have a coherent data set for this study, these 12 values were imputed using established response models. A summary of our use of these models for

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imputing missing values, the accuracies of the models for this data set, and tabulations of sensitivity values and the corresponding limits of detection are presented in the Supporting Information (SI) accompanying this article.

Monte Carlo Simulations and EDPCR Models. Although sensors were integrated in groups of three on each array chip, all five arrays (i.e., 15 sensors) were exposed simultaneously to all test atmospheres, and we have treated each sensor as an independent element for the purposes of exploring the various combinations of sensors that might be assembled into an ST or MT array for vapor analysis. To assess the performance of all possible combinations of sensors and vapors, we have employed Monte Carlo simulations in conjunction with classification models derived using extended disjoint principal components regression (EDPCR). Details of this approach to sensor array evaluation can be found in previous articles.[2,3,18]

For each simulated analysis, the slope sensitivity for each vapor−sensor pair is used as the starting point, and a response value is calculated from the regression equation for a vapor concentration randomly selected from within a predefined range (see below). Error is then superimposed on this response value as a way of simulating realistic variations in output signals during actual operation. Two sources of error were included in the error model employed: random slope variation and baseline noise. Both are assumed to be Gaussian and zero-centered. Estimates of the slope variation and baseline noise were obtained for each of the 15 sensors from experimental data and are summarized in Tables S-5 and S-6, respectively, in the SI. The average relative standard deviation of the slope sensitivity from the 11 calibrations generated for a given sensor was determined from the residual errors of the linear regression models. These ranged from 3.7 to 13.3% among all of the sensors. For simplicity, the grand average of these, 7%, was used as the basis for the error model in the Monte Carlo simulations. The average rms baseline noise values used are 2 Hz, 1 Hz, and 5.5 mV, respectively, for the CAP, CAN, and CAL sensors.

For each simulated exposure, an error-enhanced response is obtained independently for each sensor in the array under consideration (note: no preprocessing of the data was performed). This leads to an error-enhanced response pattern that is then classified via EDPCR by comparison with patterns constructed from the calibration slopes and stored in a library. By iteratively generating error-enhanced response patterns and classifying them via EDPCR, probabilistic estimates of recognition are obtained. Each test consisted of 500 simulations, and the recognition rate (RR) was used to assess performance.

For problems involving the discrimination of individual vapors, the 95% confidence interval (CI_{95}) calculated around each average RR reflects the distribution of individual vapor RR values for a given array, where the number of samples is equal to the number of vapors being discriminated. For problems involving the discrimination of mixtures from their components, the CI_{95} calculated around each average RR reflects the distribution of mixture RR values for a given array. In these cases, the number of samples is equal to the number of mixtures tested (note: for reference, there are 55 possible binary mixtures, 165 possible ternary mixtures, and 330 possible quaternary mixtures of the 11 vapors in the primary data set). This interval is used to assess the statistical significance of differences in RR among different arrays. The number and nature of recognition errors observed from a large sample set can be logged into a recognition matrix and evaluated with respect to the average or vapor-specific rates of recognition and the identities of any incorrect assignments. By repeating a given analysis several times, it is possible to derive estimates of the CI_{95} of the distribution of average RR values. This interval is used in this investigation to determine the statistical significance of differences in RR values obtained with arrays of different sizes performing the same analysis (e.g., discrimination of several individual vapors or a mixture from its components).

Previous studies of polymer-coated SAW sensors have shown that for individual vapor concentrations below ~5 times the LOD, the RR varies directly with the vapor concentration.[2,36] If the vapor concentration is >5×LOD, the RR becomes independent of concentration.[36] A similar threshold has been reported for binary and ternary mixture determinations.[2] This follows from the fact that at higher concentrations the predominant contributor to pattern variability is the slope error, which is presumed to be proportional to concentration. Note that the LOD is defined here in terms of the array as a whole such that it is determined by the highest LOD value among the individual sensors in that array.

Defining vapor concentrations on the basis of the LOD is useful for modeling, particularly in this case where transducers with different units of measure are employed. As part of our preliminary data screening, we performed Monte Carlo-EDPR analyses of each 5-sensor ST array for individual vapor recognition of the 11-vapor data set at discrete concentration intervals ranging from 1 to 20×LOD. Results (not shown) confirm that the average RR increases with the assumed vapor concentration up to ~5×LOD and then remains relatively constant at higher concentrations. Therefore, for this study, we have confined consideration to vapor concentrations in the range of 5−10×LOD. While this guarantees that there are measurable signals from all sensors in the array, this also means that tests within a given series of simulations are performed at different absolute concentrations and that for many tests the concentration is well above the 5−10×LOD range for the more sensitive sensors in the array under consideration.

Vapor mixtures of two, three, and four components were tested. For these analyses, each mixture was considered separately, and the RR was defined in terms of the ability to discriminate the mixture from its individual vapor components and any lower-order mixtures of those components. The composite response to a mixture was simulated by summing the modeled responses to the component vapors. Ample evidence to support the assumption of response additivity for resonant mass sensors (e.g., cantilevers, SAW sensors, TSMRs) can be found in the literature,[17,21,37] and although it is reasonable to assume, as we have done here, that composite responses to mixtures of vapors from polymer-coated capacitive and calorimetric sensors are also additive, experimental evidence was rather sparse.[38,39] Error was then superimposed on the composite response for each sensor in the array under consideration, and the response pattern was compared to the

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Table 1. Comparison of ST and MT Arrays of Different Sizes for Individual Vapor Recognition of 11 Vapors in Terms of Predicted Recognition Rates and Various Global Selectivity Metrics[a]

array size	array type	array composition					RR (CI$_{95}$)	CN	r_{rms}	SED
15	MT						93.0 (2.0)		0.61	424
5	ST	CAP-EC	CAP-PCPMS	CAP-PDMS	CAP-PECH	CAP-PEUT	91.0 (7.7)	740	0.67	26
5	ST	CAN-EC	CAN-PCPMS	CAN-PDMS	CAN-PECH	CAN-PEUT	82.9 (7.3)	1660	0.80	19
5	ST	CAL-EC	CAL-PCPMS	CAL-PDMS	CAL-PECH	CAL-PEUT	96.5 (1.6)	176	0.60	30
5	MT	CAP-PCPMS	CAP-PDMS	CAL-EC	CAL-PDMS	CAL-PEUT	98.8 (1.2)[b]	109	0.57	40
4	ST	CAP-EC	CAP-PCPMS	CAP-PDMS	CAP-PEUT		90.2 (4.0)	245	0.74	13
4	ST	CAN-PCPMS	CAN-PDMS	CAN-PECH	CAN-PEUT		78.9 (6.7)	247	0.78	12
4	ST	CAL-EC	CAL-PCPMS	CAL-PDMS	CAL-PEUT		93.3 (2.0)	123	0.69	15
4	MT	CAP-PCPMS	CAP-PDMS	CAL-EC	CAL-PEUT		98.2 (1.2)	70.4	0.52	21
3	ST	CAP-EC	CAP-PDMS	CAP-PEUT			89.5 (5.8)	11.7	0.65	8.0
3	ST	CAN-PDMS	CAN-PECH	CAN-PEUT			72.8 (7.0)	30.5	0.78	6.2
3	ST	CAL-EC	CAL-PDMS	CAL-PECH			91.3 (3.0)	10.1	0.57	8.9
3	MT	CAP-PCPMS	CAP-PDMS	CAL-PEUT			94.1 (2.2)	3.5	0.50	10
2	ST	CAP-PECH	CAP-PEUT				74.5 (7.0)	1.2	0.09	4.7
2	ST	CAN-PDMS	CAN-PEUT				53.0 (9.1)	6.5	0.73	2.3
2	ST	CAL-PDMS	CAL-PECH				68.6 (8.0)	2.3	0.39	3.5
2	MT	CAP-PDMS	CAL-PEUT				75.8 (6.8)	1.1	0.03	4.5

[a] For all ST arrays and all MT arrays containing <15 sensors, the array presented is that providing the highest recognition rate (RR, %) based on 500 trials; CI$_{95}$ is the width of the 95% confidence interval (%) around each RR value; r_{rms} is the rms average pairwise correlation coefficient for each array; SED is the sum of the Euclidean distances among the sensors in each array. [b] Two MT arrays give the same RR value of 98.8%; one yields a CN value of 109 and the other a CN value of 200 (see text).

previously defined EDPCR models for that mixture, its component vapors, and their lower-order mixtures (for ternary and quaternary mixtures). As with the individual vapor cases, 500 simulations were performed for each mixture.

It has been shown that the relative concentrations of the components of a mixture can have a dramatic effect on performance and that, in general, the capability to recognize the components of the mixture is never higher than when all the components are present at the same multiple of their respective LODs (i.e., at the same signal-to-noise ratio, S/N).[2] For this initial study of MT array performance, we consider mixtures where all components are present at the same S/N (i.e., the most favorable case).

For a representative subset of analyses, quantification accuracy is assessed by comparing concentration estimates for the correctly recognized cases to those derived from the calibration data using the corresponding EDPCR model.

Sensor Selection. For most of the cases considered here, all possible combinations of sensors were considered for each simulated analysis (exceptions noted). For the ST arrays, which are limited to a maximum of five sensors, this requires consideration of 5, 10, and 10 subsets, corresponding to arrays containing 4, 3, and 2 sensors, respectively. For the MT arrays, where up to 15 sensors could be included, the number of possible combinations is considerably larger. For example, 3003 different 5-sensor arrays can be selected from these 15 sensors. Although we consider MT arrays containing from 2 to 15 sensors for selected analyses, we have focused on MT arrays containing 5 sensors for comparison with the ST arrays and for additional reasons that will be explained below.

For each mixture, a separate determination of the best MT array of a given size is made on the basis of the highest RR. For the binary mixtures, this means that there could be as many as 55 different "optimal" 5-sensor MT arrays (MT-O). The average of the distribution of RR values obtained from these MT-O arrays has been used to represent the best possible 5-sensor MT array

performance. From a practical standpoint, it was also of interest to identify the single 5-sensor MT array that provides the best overall performance for a given set of analyses, that is, the highest average RR value among all the mixtures of a given complexity (i.e., binary, ternary, or quaternary). We refer to this as the "global" MT array (MT-G). Finally, we sought to determine the size and composition of the MT array that would provide optimal performance for all possible analyses, which we refer to as the "universal" MT array (MT-U). This was achieved through an assessment of the frequencies with which each of the 15 sensors appears in the 5-sensor MT-G and MT-O arrays and the dependence of performance on array size.

Monte Carlo simulations and EDPCR routines were performed in Excel using macros written in Visual Basic. Other computations were performed using Matlab 7 (MathWorks, Inc., Natick, MA).

RESULTS AND DISCUSSION

Individual Vapor Recognition and Array Size. Differentiating individual vapors in a data set is one of the simplest types of vapor recognition problems one can address because it does not consider the possibility of mixtures. Table 1 summarizes the results of attempting to discriminate among all 11 individual vapors with MT and ST arrays composed of different numbers of sensors. The average recognition rates provided by the three 5-sensor ST arrays are 91, 83, and 97% for the CAP, CAN, and CAL array, respectively (note: recognition matrixes for these analyses are presented in the SI and are discussed below).

The three alcohols are difficult to discriminate for all three ST arrays. Given the differences in dielectric constant, it is somewhat surprising that the CAP array does not provide better performance; however, the order of dielectric constant values tracks that of the vapor pressures, which determine (primarily) partition coefficients, and it appears that these two countervailing influences on the magnitude of responses with the CAP sensors effectively reduce the ability to discriminate among the alcohols. While recognition errors for the alcohols with the CAP array are
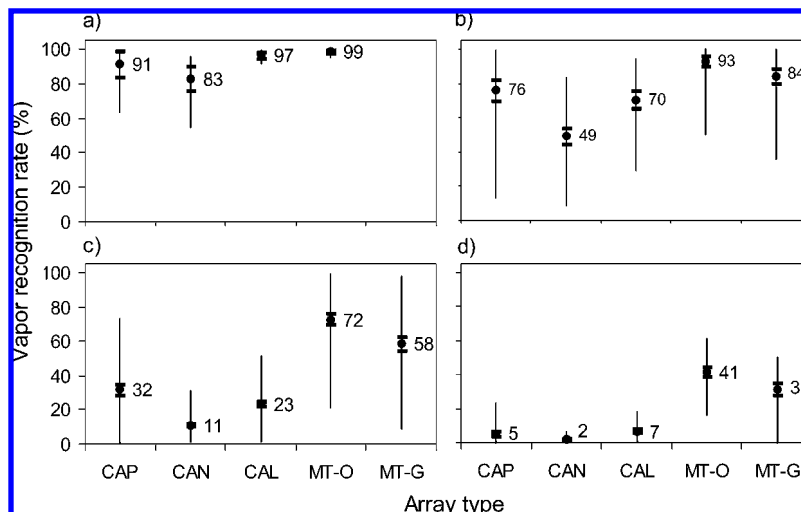
Figure 1. Comparison of 5-sensor ST arrays to 5-sensor global and optimal MT arrays (MT-G and MT-O, respectively; see text for explanation) for the recognition of (a) 11 individual vapors, (b) 55 binary mixtures, (c) 165 ternary mixtures, and (d) 330 quaternary mixtures. Confidence interval (95%) around mean recognition rate is shown for each array type, along with the range (minimum to maximum) of recognition rates calculated for each array type.

generally confined to other alcohols, recognition errors are more widely distributed with the other two arrays. The alkanes, *n*-heptane and *n*-octane, are consistently discriminated at a high rate, though there is persistent low-level confusion between these two vapors with all three types of arrays.

For the CAL array, RR values are uniformly high, with the only notable error arising in the confusion of PCE with toluene and vice versa. The average RR value for the CAN array is surprisingly low, and the nature of the errors is difficult to rationalize on the basis of physicochemical interactions. The electrothermal actuation mechanism used in these devices results in an elevation of the CAN temperature by up to 19 °C with respect to the ambient,[4c] which leads to some loss of sensitivity but should not affect response patterns greatly. Migration of the polymer films under the oscillatory motion of the cantilever might alter the mass sensitivity, which could be contributory. Although such phenomena would mitigate general conclusions about the contribution of mass-sensitive sensors to MT array discrimination, the data obtained here can still be considered typical of the cantilever technology, and analyses have been performed under that assumption.

Also shown in Table 1 are results of analyses with ST arrays containing fewer than five sensors. The arrays presented are those providing the highest 11-vapor average RR of all possible subsets of a given size. In all cases, as the number of sensors is reduced the RR also declines, but the dependence of the RR on array size is not particularly acute for $n = 3-5$ sensors, and the performance of the 3-sensor CAP and CAL arrays remains fairly good (i.e., RR > 89%). These data can be compared to those reported by Park using a polymer-coated SAW sensor array to analyze 16 vapors.[3] In that study, higher rates of recognition were generally observed and it was found that as few as two sensors could provide recognition rates as high as 95% for individual vapor recognition. The generally lower rates observed here can be ascribed to the higher slope error (i.e., 7% was used here whereas 3% was used in that study) as well as differences in the vapors and polymer interfaces. If the applied slope error is reduced to 3% for all three ST arrays, the RR values converge and approach those reported

for SAW sensors (i.e., >90% even for 2-sensor arrays, data not shown).[3] Thus, for individual vapor recognition, it appears that the type of transducer employed is not highly critical, provided that the variation in response is kept low. As variation increases, performance differences among the transducer types become apparent.

Considering the MT array data, Table 1 shows that the optimal MT array of any given size outperforms the corresponding optimal ST arrays in all cases. However, the margin of difference between the best MT array and the best ST array is not very large, consistent with the relatively facile discrimination problem being addressed. In fact, for arrays of two, three, or five sensors, the differences are not statistically significant (i.e., the 95% CIs overlap). A high RR value (i.e., >94%) is predicted even for the optimal 3-sensor MT array in spite of the high slope error assumed. It is worth noting that, while the optimal 5-sensor MT array provides an RR of 99%, there are 245 other 5-sensor MT arrays (out of 3003) that provide RR values of >95%. At the same time, the lowest RR value found among the 5-sensor MT arrays is 61% and there are 578 5-sensor MT arrays that provide RR values less than the RR provided by the 5-sensor CAN array (i.e., <83%). Thus, judicious sensor selection is essential for obtaining good performance from an MT array.

Figure 1a summarizes the individual vapor performance data by presenting the average RR, CI_{95} (error bars), and the range of RR values (vertical lines) for each type of 5-sensor array. There is considerable spread in the RR values. The RRs from the CAL and CAP arrays are not statistically significantly different, although the CAL array performs better on average.

Figure 2a presents the RR values obtained with optimal MT arrays of different sizes for individual vapor recognition of 3 sets of vapors: the entire 11-vapor set, a subset of 5 vapors from different functional group classes, which can be considered relatively easy to discriminate, and a 5-vapor subset comprising 2 alkanes and 3 alcohols, which contains the vapors that are the most difficult to discriminate. There are several noteworthy features to these plots. First, the performance improves fairly sharply as the number of sensors increases from two to four or
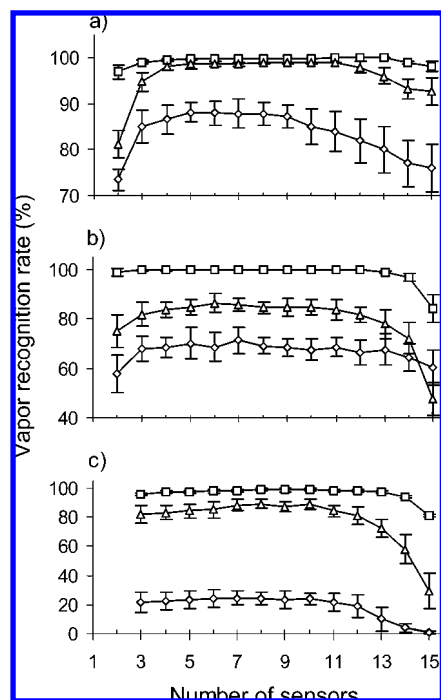
Figure 2. Effect of array size on performance for optimal MT arrays containing from 2 to 15 sensors for (a) individual vapor recognition of the entire 11-vapor set (triangles), a subset of five vapors of diverse structures considered to be relatively easy to discriminate (HEP, TOL, POH, EAC, CHL) (squares) and a subset of five vapors of similar chemical structure considered relatively difficult to discriminate (HEP, OCT, MOH, EOH, POH) (diamonds); (b) recognition of three binary mixtures, in order of increasing difficulty, HEP + MOH (squares), TOL + PCE (triangles), and HEP + OCT (diamonds); (c) recognition of three ternary mixtures, in order of increasing difficulty, OCT + EAC + CCL (squares), TOL + EOH + TCE (triangles), and MOH + EOH + POH (diamonds). Error bars represent the CI_{95} for each average RR value, determined on the basis of the number of vapors for the individual vapor cases and on the basis of five iterations for the binary and ternary cases.

five. It then shows little or no change until the number of sensors reaches somewhere between 9 and 13, depending on the difficulty of the analysis, at which point the performance starts to decline with additional sensors.

The CI_{95} values span a range of up to ±4%, and the difference of RR values on going from 5 to 11 sensors is ≤4%. Thus, including more than five sensors in the MT array provides no advantage for individual vapor recognition and eventually degrades performance due to the effects of redundancy and noise. As a result, the performance of the best 3-sensor MT array exceeds that of the entire 15-sensor MT array (RR = 93%, Table 1) for all three analyses considered here. The trends are similar for all three data sets, despite the difference in the maximum RR achievable, although the onset of the performance decline occurs at a smaller number of sensors with the more difficult analysis. The plateau in RR observed for >4 sensors is consistent with previous reports on polymer-coated acoustic wave and chemiresistor sensors.[3,16,20,35] The onset and extent of performance degradation for larger arrays will depend on the degree of collinearity (redundancy) among the sensors employed and the nature of the discrimination problem.

Local and Global Metrics of Selectivity. Although the approach used here of simulating exposures and estimating

recognition rates affords a detailed assessment of performance, it is computationally intensive and it would be useful to have summary measures of performance with which to prescreen arrays. Common metrics of discrimination or selectivity that can be derived for specific vapor pairs include the Euclidean distance, the pairwise correlation coefficient (r), and the so-called "resolution factor", which is the ratio of the average difference in responses between two vapors to the variations inherent in their individual responses.[16,35a,c]

Local selectivity metrics such as these, when determined with respect to the *vapors,* are problematic for comparison among different MT arrays because the component sensors have different units of response. Any sensor-wise normalization or autoscaling procedure used to address the discrepancy in sensor units will corrupt the inherent between-vapor correlations, leading to principal components models that are not meaningful for the purpose of comparing performance among different arrays. Local selectivity metrics can also be derived for the sensors in an array on the basis of their contribution to the differentiation of vapors in a data set. For the purposes of comparing the performance of various MT arrays, this approach is preferred; it is not subject to the problems arising from differences in the units of measure because between-sensor correlations are not affected by sensor-wise normalizations among different transducers. Therefore, we have restricted consideration to selectivity metrics derived from the correlations among the sensors.

Local selectivity metrics are constrained to vapor-specific analyses. To derive a global selectivity metric useful for summarizing array performance in multivapor discriminations, the most straightforward approach is to take the average or sum of the r values or Euclidean distances determined from all possible pairwise comparisons. Alternatively, one can calculate the condition number (CN) of the correlation matrix comprising the sensor pairwise correlation coefficients.[40] The CN is defined as the ratio of the maximum-to-minimum singular values (i.e., square root of the respective eigenvalues) of the data matrix and can be derived from principal components analysis (PCA). The CN can be calculated directly from the PCA of the sensitivity matrix. However, in this case, it reflects the composite influences of sensitivity and selectivity within the data matrix.[41] By calculating the CN from the sensorwise correlation matrix, it is strictly a function of selectivity (collinearity).[40]

Although the CN has been used in spectroscopic chemometrics to summarize collinearity among the spectral features associated with chemical species in mixtures,[41,42] we have found no prior reports on its application to sensor array data. In fact, we found only one report on vapor sensor arrays that employed any global selectivity metric at all.[34] In that study, the sum of the Euclidean distances (SED) was used as a guide for downselecting sensors into an optimal array, but its correlation with rates of misclassification was not explored.

The pairwise correlation matrix for the sensors comprising each of the three ST arrays as determined on the basis of their sensitivities to the 11 individual vapors in the data set is presented

(40) Meloun, M.; Militky, J.; Hill, M.; Brereton, R. G. *Analyst* **2002**, *127*, 433–450.
(41) Kalivas, J. H.; Lang, P. M. *Chemom. Intell. Lab. Syst.* **1996**, *32*, 135–149.
(42) Faber, N. M.; Ferré, J.; Boqué, R.; Kalivas, J. H. *Trends Anal. Chem.* **2003**, *22* (6), 352–361.

in Table S-7 (SI). The average (i.e., root-mean-square) r value (r_{rms}) for each ST array is presented in Table 1. The r_{rms} values are also presented for the MT arrays listed in Table 1. For each array, r_{rms} is a summary measure of correlation among the constituent sensors. The trend in r_{rms} values is consistent with the trend in RR values for the ST arrays and confirms that the CAL arrays are the most diverse, followed by the CAP and then the CAN arrays. The SED values are highly correlated with the r_{rms} values of the arrays, as expected, since they are similar measures of between-sensor vector separation.

The r_{rms} value between two arrays is calculated by averaging the individual pairwise r values determined among all sensor pairs in the two arrays (one from each different array, Table S-7, SI) and reflects the net (i.e., global) correlation between the two arrays. The interarray r_{rms} values found in this data set are 0.50, 0.72, and 0.49 for the cantilever–capacitor, cantilever–calorimeter, and capacitor–calorimeter pairs, respectively (note: correlations derived from a canonical analysis of the sensor pairs are consistent with these values). Ideally, these values would be close to zero. Thus, although each type of sensor measures a different property of the vapor-polymer interaction,[28] the responses provided are far from independent, most likely due to the direct or indirect influence of the extent of vapor–polymer partitioning on all sensor responses. The dominant influence of the nonspecific van der Waals dispersive interactions on vapor sorption in polymers has been described before.[1]

The CN values calculated from the 11-vapor data set for the 5-sensor CAP, CAN, and CAL arrays are 741, 1665, and 176, respectively. The lower value of the CN for the CAL array indicates a higher degree of selectivity. This is consistent with the other selectivity metrics and the high RR values presented in Table 1. The trend in CN values among the ST arrays of a given size is also consistent with the trend in RR values.[43]

The CN values for the optimal MT arrays in Table 1 follow the expected trends, in general. That is, for optimal MT arrays of four, three, and two sensors, the CN values shown in Table 1 are consistent with the RR values and are all lower than the corresponding CN values for the ST arrays of the same size. There are two 5-sensor MT arrays, however, that produce an RR value of 98.8%, with one yielding a CN value of 109 and the other a CN value of 200. The latter CN value is higher than that for the CAL array and is therefore inconsistent with the general correlation of RR and CN values.

In an attempt to extend the use of the CN as a tool for prescreening arrays, RR values were plotted against CN values for the 11-vapor individual vapor discrimination problem for all 3003 5-sensor MT arrays. Curiously, there was no significant correlation between RR and CN among these sensors (i.e., $r < 0.50$). A similar lack of correlation was found between RR and SED. Since the average RR value for this problem is generally inflated by (dominated by) the more successful recognitions, we also tried to correlate 1-RR with CN. However, a strong correlation still could not be found. Although we have no definitive explanation

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(43) Since the CN measures the magnitude of correlations among the sensors, the dimension of the correlation matrix directly affects the values of the CN, with more sensors corresponding to a higher range of CN values.This is evident in the CN values for the arrays of different sizes in Table 1—the relative order of the CN values among the ST arrays is maintained but the values decrease with the size of the array under consideration.

for the lack of correlations among these global metrics (note: the average RR value can also be considered a global selectivity metric), it appears as if the subtle differences in performance among this large group of arrays arise from a few vapor-specific (i.e., local) errors in recognition that are not effectively captured by the global metrics. The inherent insensitivity of global metrics to local selectivity changes has been noted.[41] Thus, while the data in Table 1 suggest that the CN provides an effective tool for ranking arrays, further study is warranted before an unconditional endorsement can be made of its use in this application.

Binary Mixture Recognition. The next series of analyses considered the problem of differentiating a mixture from its components and, in the case of ternary and quaternary mixtures, also from the lower-order mixtures of those components. The initial analyses considered MT arrays consisting of five sensors to facilitate comparisons with the ST arrays. Results for the three 5-sensor ST arrays are summarized in Figure 1b. As indicated by the maximum and minimum RR values, a considerable range in performance is exhibited by all three arrays. The best performance, on average, is obtained from the CAP array (RR = 76%), followed in order by the CAL array (RR = 70%) and CAN array (RR = 49%). The difference in performance between the CAP and CAL arrays is not statistically significant, but both of these arrays are significantly better than the CAN array. Still, only 11 out of the 55 binary mixtures (22%) could be analyzed with <5% error with the CAP (i.e., best ST) array.

According to the recognition matrices for the individual vapor discriminations (Tables S-8–S-11, SI), one would expect greatest difficulty in discriminating the alcohols with all three arrays. Indeed, the RR values for the binary mixtures of these three alcohols are quite low even for the CAP array (i.e., RR values of 17, 17, and 13% are obtained for mixtures of MOH + EOH, MOH + POH, and EOH + POH, respectively).

Analysis of the binary (and other) mixtures with the 5-sensor MT arrays took two forms. In one case, a new array was selected for each mixture and the RR values from the best array for each of the 55 mixtures were compiled. The distribution of RR values for this set of optimal MT arrays (MT-O) is presented in Figure 1b. Then, these data were analyzed to find the single best 5-sensor MT array. This is designated as "MT-G" in Figure 1b. The sensors comprising the MT-G array for the binary mixture case are presented, along with those of the MT-G array for the individual vapor analysis, in Table 2. The compositions of these two MT-G arrays are quite similar—they have four sensors in common.

With RR values of 84 and 93%, respectively, the MT-G and MT-O arrays outperform significantly all three of the ST arrays in recognizing binary mixtures. This is particularly evident for the problematic alcohol mixtures, for which the MT-O arrays provided an average RR value 3−5 times higher than those of the best ST array (i.e., RR values of 50, 66, and 68% for MOH + EOH, MOH + POH, and EOH + POH, respectively) and for which the MT-G array provided an RR value 2−4 times higher (i.e., 36.4, 50.2, and 56.0%, respectively). Overall, 32 of the 55 binary mixtures (60%) could be analyzed with <5% error with the analyte-specific MT-O arrays, and 25 of the 55 binary mixtures (45%) could be analyzed with <5% error with the MT-G array.

To explore the general question of how many sensors are required for effective binary mixture analyses with an MT array,

Table 2. Composition and Overall Performance of 5-Sensor Global MT Arrays (MT-G) Selected on the Basis of Performance in a Specific Type of Analysis

basis for sensor selection	array composition[a]					average recognition rate (%)			
						11 individual vapors	55 binary mixtures	165 ternary mixtures	330 quaternary mixtures
11 individual vapors	CAP-PCPMS	CAP-PDMS	CAL-EC	CAL-PDMS	CAL-PEUT	98.8	76.2	53.0	18.0
55 binary mixtures	CAP-PCPMS	CAP-PDMS	CAN-PEUT	CAL-EC	CAL-PEUT	98.2	84.3	52.8	27.4
165 ternary mixtures	CAP-PCPMS	CAP-PDMS	CAN-PEUT	CAL-PDMS	CAL-PEUT	95.6	77.9	58.4	23.9
330 quaternary mixtures	CAP-PDMS	CAP-PEUT	CAN-PEUT	CAL-PDMS	CAL-PECH	91.2	78.4	48.2	30.8

[a] These arrays are the 5-sensor MT-G arrays selected on the basis of the type of analysis in the first column. The performance (average recognition rate) of each array for each type of analysis is presented in the last four columns.

a subset of three binary mixtures was chosen: one each from the upper, middle, and lower quartiles of the RR distribution obtained for the recognition of the 55 binary mixtures with 5-sensor MT arrays. For each mixture, the optimal MT array was determined for array sizes of 2−15 sensors. The dependence of the RR on the number of sensors in the optimal MT array is plotted in Figure 2b. Trends similar to those found for the individual vapor recognition problems are observed. That is, a plateau is reached with a relatively small array, and the addition of sensors has little or no effect on performance up to ∼10−13 sensors, beyond which a significant decline in RR is observed. For the relatively easy mixture, only two sensors are required for an RR of >99%. For the moderately difficult mixture, the RR reaches a maximum value at ∼6 sensors, but the difference in RR between 4 and 11 sensors is not significant (see error bars in Figure 2b). For the most difficult mixture, the RR does not improve significantly beyond an MT array of three sensors. The trends are consistent regardless of the difficulty of the analysis. A typical binary mixture recognition matrix is presented in Table S-12.

Ternary and Quaternary Mixture Recognition. Ternary mixtures were then addressed. Results are summarized in Figure 1c. Of the 165 possible ternary mixtures, none could be analyzed at an RR > 90% with any of the 5-sensor ST arrays. In fact, the highest ST array RR value, obtained with the CAP array, is 73.4%. With 5-sensor MT-O arrays, RR values of >90% are achieved for 54 ternary mixtures, or one-third of the total. This capability for analysis of ternary organic vapor mixtures is unprecedented.[2,19] The single best MT array (MT-G) provides an average RR of 58.4% (range 8−98%), with RR values of >90% achieved for 14 ternary mixtures (∼8% of the total).

The composition of the MT-G array for the ternary mixtures is shown Table 2, and a recognition matrix obtained using the MT-O array for this mixture is presented in Table S-13 (SI). Figure 1c shows that, while the overall performance is rather low for all arrays, the ratio of average RR values for the MT and ST arrays increases compared to the individual vapor and binary mixture cases. This follows from the increased difficulty of ternary mixture determinations.

The question of how many sensors are required for ternary mixture analyses was also explored for a subset of three ternary mixtures, one each from the upper, middle, and lower quartiles of the RR distribution determined with the 5-sensor MT-O arrays. For each of these mixtures, the optimal MT array was determined for array sizes of 3−15 sensors. As shown in Figure 2c, the sensitivity to the number of sensors is similar to that for the individual vapor and binary mixture cases. That is, beyond a few sensors, there is little or no improvement in performance with increases in the number of sensors added to the array, regardless of the maximum RR value.

Results of analyses of quaternary vapor mixtures are summarized in Figure 2d, which shows that the best 5-sensor MT arrays outperform the 5-sensor ST arrays by a considerable margin, with an average RR of 41% for the MT-O arrays compared to 5, 2, and 7% for the 5-sensor CAP, CAN, and CAL arrays, respectively. The highest RR achievable with an ST array is 23% (CAL array). With 5-sensor MT arrays, the highest RR is only 62%. The single MT-G array provides an average RR of 31% and a maximum of 56%. The composition of the MT-G array for the quaternary mixtures is shown Table 2.

Constructing a Universal MT Array. The analyses described above beg the question of whether a universal MT array could be constructed—one that would provide optimal performance for any type of analysis. Certain sensors are selected repeatedly into the most effective 5-sensor MT arrays, while others are selected rarely. From Table 2, we see that all of the MT-G arrays can be constructed from eight sensors: the three CAP sensors coated with PCPMS, PDMS, and PEUT; the CAN sensor coated with PEUT; and the four CAL sensors coated with EC, PDMS, PEUT, and PECH. Consistent with the relative order of individual vapor ST array recognition rates (Table 1), the MT-G arrays contain more CAP and CAL sensors than CAN sensors.

The columns on the right-hand side of Table 2 show the RR values obtained with the MT-G arrays for each type of analysis, confirming that none of these arrays provides universally excellent performance for all types of analyses. That is, for example, the MT-G array selected on the basis of the binary mixture analyses gives an average RR value for the ternary analyses (52.8%) that is

Table 3. Performance of Universal MT Array (MT-U) Candidates Comprising from 5 to 11 Sensors Selected on the Basis of Their Ranking among All 5-Sensor Optimal MT Arrays (MT-O)

	average recognition rate (%)		
no. of sensors[a]	11 individual vapors	55 binary mixtures	165 ternary mixtures
5	95.8	86.2	51.7
6	98.8	85.6	50.0
7	98.9	86.9	52.5
8[b]	98.5	90.4	64.2
9	98.6	90.4	64.2
10	95.3	85.4	59.8
11	94.6	84.8	59.5

[a] Composition of each array is based on the rank of each sensor as determined by the frequency with which it was included in the 5-sensor optimal arrays (MT-O) for all analyses.[45] [b] This 8-sensor array provides the best overall performance as a universal MT array (MT-U).

significantly lower than that provided by the MT-G array selected on the basis of the ternary analyses (58.4%). It follows that an array of eight sensors from which all of the 5-sensor MT-G arrays could be constructed should provide the best overall performance for all possible analyses. This approach would ensure that the critical set of set of five sensors needed for a given recognition problem is available, and it assumes that including an additional set of three sensors will not degrade performance, as suggested by the trends shown for the representative cases in Figure 2a−c.

This 8-sensor MT-U array provides RR values of 99.6 ($CI_{95} = 0.2\%$), 85.1, ($CI_{95} = 4.4\%$), and 60.0% ($CI_{95} = 3.5\%$) for the 11 individual vapors, 55 binary mixtures, and 165 ternary mixtures, respectively. These RRs are slightly better than the corresponding values obtained from the 5-sensor MT-G arrays (98, 84, and 58%, respectively, Figure 1a−c), confirming that there is no cost to having additional "nonessential" sensors in the array beyond the five sensors comprising the MT-G array for any particular type of analysis and considerable benefit from being able to access those sensors required for any possible analysis.

At the same time, the MT-U RR values are considerably lower than those obtained from the 5-sensor MT-O arrays (Figure 1). Although this is expected because the MT-O arrays are selected on a case-by-case basis, it begs the question of whether an MT-U array could be constructed more effectively by consideration of the MT-O arrays. An alternative means of determining an MT-U array was therefore explored whereby the sensors were ranked according to their frequency of inclusion in the 5-sensor MT-O arrays whose RR distributions are shown in Figure 1a−d. Those sensors appearing most often in the MT-O arrays were culled out.[44] Arrays containing from 5 to 11 sensors were constructed in this manner, and their performance was assessed for the individual vapor, binary mixture, and ternary mixture analyses (note: given the low RR values for the quaternary mixture analyses, even with the MT-O arrays, they were not pursued further).

The results, summarized in Table 3, show that as the number of sensors in the array increases from five to eight there is a slight

Table 4. Accuracy of Quantification for Representative Individual Vapor, Binary Mixture, and Ternary Mixture Determinations[a]

		absolute error (%)	
vapors	RR (%)	avg[b]	max
Individual Vapors			
HEP	99.2	3.5 (2.7)	14
OCT	100	3.3 (2.4)	12
TOL	99.8	3.0 (2.2)	11
MOH	97.4	5.2 (3.9)	21
EOH	95.6	5.2 (3.8)	18
POH	96.4	4.7 (3.5)	19
EAC	98.8	3.8 (2.9)	16
CHL	99.6	4.2 (3.1)	19
CCL	100	3.3 (2.5)	13
TCE	99.8	2.8 (2.1)	12
PCE	99.8	3.0 (2.1)	11
Binary Mixture			
EAC	92.6	6.2 (4.4)	20
TCE	92.6	11 (7.6)	34
Ternary Mixture			
HEP	82.0	4.6 (3.6)	19
EOH	82.0	4.0 (3.0)	15
CCL	82.0	17 (13)	71

[a] Obtained with the corresponding 5-sensor MT-G arrays in Table 2. [b] Values in parentheses are standard deviations (%).

increase in RR across the board. The 9-sensor array provides the same performance as the 8-sensor array, and the 10-sensor and 11-sensor arrays show a decline in performance, most likely due to the negative influence of redundancy for certain discriminations outweighing the positive influence of added discrimination power for certain other discriminations. Thus, the 8-sensor MT-U array provides the best performance with the fewest possible sensors.[45] Not surprisingly, seven of the eight sensors selected by this approach coincide with those selected on the basis of the MT-G arrays. However, the one different sensor produces an incremental, if not statistically significant, improvement in the performance, i.e., RRs of 99.8 ($CI_{95} = 0.1\%$), 90.4 ($CI_{95} = 4.8\%$), and 64.2% ($CI_{95} = 4.6\%$), respectively, for analyses of the individual vapors, binary mixtures, and ternary mixtures, compared to the corresponding RRs of 99.6, 85, and 60% provided by the 8-sensor MT-U array constructed from the sensors in Table 2.

Quantification. Up to this point, we have considered only recognition. Although correct recognition generally leads to accurate quantification,[3,18,36,46] we set out to confirm this for the MT arrays considered here. Analyses were performed for three arbitrarily chosen problems, using the 5-sensor MT-O array in each case. Once the identity of the vapor or vapor mixture is established, the concentration of each vapor is determined by linear regression of the principal component score for that sample onto its concentration. For a vapor mixture, the composite response vector is decomposed into its constituent vectors prior to quantifying the contribution of each mixture component to the net response.

Table 4 presents the summary statistics. In all cases, the net bias is quite low (i.e., <1%, data not shown). For the 11 individual

(44) In order to eliminate the inherent bias arising from the fact that there are different numbers of binary, ternary, and quaternary mixtures, the frequency at which each sensor appeared in the MT-O arrays for a given type of analysis was converted to a percentage value, and then the percent frequencies were summed across all types of analyses.

(45) The component sensors and their frequency of occurrence in the 5-sensor MT-O arrays are: CAP-PDMS (16.7%), CAP-PCPMS (12.1%), CAN-PEUT (10.1%), CAL-PEUT (9.4%), CAL-PDMS (8.6%), CAL-EC (6.7%), CAN-EC (6.2%), and CAL-PECH (5.9%).

(46) Lu, C.-J.; Jin, C.; Zellers, E. T. *J. Environ. Monit.* **2006**, *8*, 270−278.

vapors, average absolute errors are consistently low, ranging from 2.8 to 5.2%, and the maximum errors are acceptable. Errors for the binary mixture of EAC and TCE, and the ternary mixture of HEP, EOH, and CCL are a bit higher (i.e., average errors are <17% and maximum errors are <72%), though still generally acceptable. There is always a tendency toward higher errors with more complex mixtures due to the inherent imprecision involved in decomposing the composite response pattern into its constituent vectors. Of course, the quantification accuracy is strongly influenced by the slope error assumed in the Monte Carlo simulations, and even better performance would be expected with sensors exhibiting lower noise and less slope variation.

CONCLUSIONS

On the basis of this assessment of MT arrays for multivapor determinations, it is clear that inclusion of judiciously selected sensors that operate by different transduction mechanisms in an array of vapor sensors enhances performance relative to arrays composed of sensors operating on a single transduction mechanism. MT arrays can provide recognition rates of >95% for problems involving the determination of individual vapors and numerous binary and ternary mixtures. The degree to which performance is improved over arrays employing sensors operating on the same transduction principle (ST arrays) increases with the complexity of the recognition problem.

This is the first report to compare the performance of ST arrays and MT arrays in a comprehensive and quantitative manner with respect to quantitative analysis of multivapor mixtures. The capability for accurately determining the composition of a fairly large number of ternary mixtures, in spite of a relatively large degree of variability assumed in the sensitivity values of the sensors in the arrays, is unprecedented. With better control on response variability, performance is expected to improve to some extent. However, it was also shown that quaternary mixtures could not be analyzed with acceptably low error rates, indicating that the improvement in performance afforded by combining sensors that operate on different principles is finite. Although the limitations on mixture complexity are related to the extent of correlation among the sensors, and there was significant correlation among these sensors, it seems highly unlikely that any array of sensors employing reversible, sorptive interface layers will be capable of consistently analyzing mixtures of more than three components. Thus, ternary mixture analysis would appear to be the upper boundary on performance with this class of sensor arrays.

These results add further support to the growing body of evidence that there is no advantage to including a large number of partially selective sensors in arrays of vapor sensors employing sorptive interface layers for any specific analysis. Furthermore, even for generalized applications, the advantage of adding sensors to address multiple discrimination problems is apparently quickly offset by the disadvantage associated with redundancy—in the series of cases studied here, a maximum of eight or nine sensors could be tolerated without a net loss in performance.

Several local and global selectivity metrics were examined as potential tools for summarizing or prescreening the performance of ST and MT arrays. Correlations with the recognition rates determined by Monte Carlo simulations coupled with EDPCR analysis were generally good. The condition number, which has apparently not been used before in the context of assessing sensor array performance, was one of the global metrics explored here for quantifying the selectivity of an array. If applied to the correlation matrix derived from a set of vapor response data, it is a pure measure of collinearity. Furthermore, it has the advantage of being applicable to underdetermined systems—i.e., where the number of sensors is less than the number of vapors under consideration. Analyses revealed that while the CN values generally correlated with RR values, there were exceptions. We speculate that local (i.e., vapor-specific) errors affect RR values to a greater extent than CN values, making the latter insensitive to important factors affecting array performance. However, further study is warranted.

For this initial study of MT array performance, we considered mixtures where all components are present at the same S/N and where all vapors are at a concentration of at least 5×LOD. Performance degrades as absolute concentrations (or sensor sensitivities) decrease and as the difference in concentrations (or, more accurately, relative S/N) among mixture components increases.[2] Although the most promising application of MT or ST arrays is in microsystems with upstream preconcentration (and separation) modules that can address the limited sensitivities of the sensors,[46–48] future studies should be directed at exploring the effects of absolute and relative vapor concentrations on MT array performance.

Finally, a limited study of previously published response models of polymer-coated CAP, CAN, and CAL arrays (see Supporting Information) yielded mixed results. While model performance was quite good for some transducer—polymer combinations, for several it was only fair and for some it was not acceptable. Cases of poor performance were confined to CAP sensors and could be ascribed to properties of the polymer coatings that violate assumptions about free volume inherent in the models[28] or to data sets with a preponderance of low responses.

SUPPORTING INFORMATION AVAILABLE

Information related to the use and comparison of ST and MT arrays for multivapor recognition. This material is available free of charge via the Internet at http://pubs.acs.org.