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Limits of Recognition for Simple Vapor Mixtures Determined with a Microsensor Array

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The “limit of recognition” (LOR) has been defined as the minimum concentration at which reliable individual vapor recognition can be achieved with a multisensor array, and methodology for determining the LORs of individual vapors probabilistically on the basis of sensor array response patterns has been reported. This article explores the problems of defining and evaluating LORs for vapor mixtures in terms of the absolute and relative component vapor concentrations, where the mixture must be discriminated from those component vapors and from the subset of possible lower-order component mixtures. Monte Carlo simulations and principal components regression analyses of an extant database of calibrated responses to a set of 16 vapors from an array of 6 diverse polymer-coated surface acoustic wave sensors are used to illustrate the approach and to examine trends in LOR values among the 120 possible binary mixtures and 560 possible ternary mixtures in the data set. At concentrations exceeding the LOD, 89% of the binary mixtures could be reliably recognized ($<5\%$ error) over some composite concentration range, while only 3% of the ternary mixtures could be recognized. Most binary mixtures could be recognized only if the constituent vapor relative concentration ratio, defined in terms of multiples of the LOD for each vapor, was ≤ 20. Correlations with the Euclidean distance(s) separating the normalized constituent vapor response vectors allow reasonably accurate predictions of the limiting recognizable mixture composition ranges for binary and ternary cases. Results are considered in the context of using microsensor arrays for vapor detection and recognition in microanalytical systems.

Arrays of partially selective vapor microsensors have been the focus of extensive research over the past three decades because of their potential for widespread application in ambient air monitoring, occupational health and safety, biomedical diagnostics, industrial process control, and military and civilian counterterrorism. Sorptive-polymer interface layers are often used to temporarily concentrate the vapors near the sensor surface and to facilitate detection by whatever transduction mechanism is employed in the sensing devices.[1−4] Differential sorption among the set of polymer layers in the array produces response patterns that can be correlated with the identities, or at least the functional group classes, of the analyte vapors.[1−7] Although often referred to as electronic noses, it is perhaps more accurate to refer to such arrays as “sorption spectrometers” since the responses from the sensors are associated with structural features that govern the extent of vapor sorption akin to the association of structural features with resonant modes excited at characteristic electromagnetic frequencies in vibrational spectroscopy.

It is now generally accepted that the nonbonding vapor−polymer sorption interactions in such arrays do not afford sufficient collective selectivity for quantitative determinations of more than a few vapors simultaneously regardless of the number of sensors or the sensor technology employed.[7−12] Furthermore, the limits of detection (LODs) achievable for volatile organic compounds with vapor pressures of >1 Torr are typically >1 part-per-million (ppm) by volume, again, regardless of the sensor technology.[12−18] As a result, stand-alone sensor arrays may have difficulty meeting the performance requirements of many potential applications.

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Recognition of these inherent limitations has spawned efforts to couple microsensor arrays with preconcentration[10,18−22] and separation stages[22−25] in order to increase sensitivity and to constrain the number of vapors presented to the array at a given point in time. Separation stages with tunable retention offer an additional degree of control over both the nature and number of coeluting vapors reaching the sensor array; [24,25] the tolerance for incomplete separations afforded by the array reduces the required column length and time of analysis while the adjustment of relative retention afforded by the separation stage tuning helps to ensure that the discriminating power of the array is not exceeded. Initial reports on microanalytical systems that combine integrated microsensor arrays with micromachined-Si preconcentrators and separation columns, as well as other important components, have appeared recently.[3a,26−29] Proposed microsystem designs that couple high-performance, low-power analytical and control modules with wireless networking capabilities show promise for effective field determinations of complex environmental vapor mixtures once thought to be addressable by microsensor arrays alone.[30]

In such microanalytical systems, it is important to assess the range of absolute and relative concentrations over which reliable discrimination of resolved or coeluting analytes is possible via statistical pattern recognition or neural network analysis. Although it is known that response patterns will degrade at low concentrations due to a reduction in signal-to-noise ratios, relatively few studies have addressed the dependence of vapor recognition on concentration[3c,6,8,31] and none has characterized the recognition of vapor mixtures as a function of the relative concentrations of the mixture components.[32]

Building on statistical approaches reported by Carey and Kowalski,[6] Zellers et al. recently coined the phrase “limit of recognition” (LOR) and presented methodology for establishing and evaluating LORs for individual vapors on the basis of the output from a vapor sensor array.[31] The LOR was defined as the lowest concentration at which a vapor could be reliably recognized and discriminated from other vapors on the basis of its sensor array response pattern. In that study, the threshold for reliable recognition was set at 95% and Monte Carlo simulations were used in conjunction with standard pattern recognition analyses of an array of four polymer-coated SAW sensors to evaluate the LOR probabilistically for each of a set of 16 vapors under the constraint that only a single vapor could be presented to the array at one time. It was found that for many vapors the LOR was greater than the LOD.

In this article, we explore for the first time the problems of defining and evaluating the LOR for a vapor mixture. Key assumptions associated with operating the sensor array within a microanalytical system are discussed first, followed by a proposed definition of the LOR for mixtures. The graphical determination of LORs for representative binary and ternary vapor mixtures is then described and general trends of how the LOR varies with the relative and absolute concentrations of the constituent vapors are presented. Attempts are then made to correlate the LORs with more accessible measures of the relative similarities and sensitivities of the component vapor responses from the array. The binary-mixture LORs are compared to the LODs for the mixture components, as well, to stress the need for considering recognition in assessing sensor array performance at low concentrations. Constraints on mixture analyses with sensor arrays in microanalytical systems are delineated.

Defining the LOR for a Mixture. As for the individual vapor problem, the recognition of a mixture will depend on the number of sensors in the array and the range of sensitivities they exhibit for the vapors being analyzed. The latter will be determined by the analyte vapor pressures,[15,35,36] the diversity of structures

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(32) Recognition and discrimination capabilities are typically assessed with respect to individual vapors well above their LODs, for example, by matching to calibrated response patterns stored in a library. Pairwise discriminations have been espoused by certain researchers as indicators of the resolving power of an array where the response from each individual vapor in the data set is serially compared to that of another vapor until all possible pairs are made (e.g. refs 33 and 34). Such analyses are of limited value in forecasting performance for practical vapor determination problems because they neglect both the need to recognize the vapors and the possibility that both components are present simultaneously.

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represented in the (typically polymeric) interface materials coated on the sensors,[1] and the consequent uniqueness of response patterns obtained. For generalized organic vapor analyses, an array of sensors having coatings that span as much of the range of interaction forces known to govern sorption as possible will afford the broadest potential utility. Guidance in coating selection can be obtained from models based on linear solvation energy relationships.[1,15,37−39]

For a specific sensor array, discriminating a mixture from its components will depend on the number of vapors in the mixture, their structural similarity (or more accurately, the similarity of their interactions with the interface layers on the array sensors), and their absolute and relative air concentrations. Of course, the noise levels and reproducibility of the array sensors are important as well,[8] but are assumed to be independent of the vapors and therefore not central to this discussion. Assuming the sensor array is part of a microsystem with an upstream separation column, differential retention can be used to reduce the number of possible vapors simultaneously passing across the sensor array, as mentioned above, and the retention time can be used to identify a priori the subset of possible analytes encountered at a given point in the analysis.[25] In this context, it is feasible to constrain the mixture analysis problem to one where, say, one to three vapors *could be present* simultaneously and the identity and concentration of those that *are actually present* needs to be determined. For a ternary mixture, there are only seven possible combinations of vapors to discriminate (i.e., the entire mixture, three binary mixtures, and three individual vapors), and for a binary mixture, there are only three (i.e., the mixture and the two individual constituent vapors), which are tractable though not necessarily facile discrimination problems for a sensor array.[8]

Figure 1 presents a principal components (PC) plot derived from concentration-normalized response data for three vapors obtained from the six-sensor array studied here. The mixture responses were synthesized as described below. The individual vapor response patterns appear unique enough to permit their recognition and discrimination relatively easily. The composite responses from the binary mixtures span the regions between those of the respective component vapors, and it is evident that the mixture pattern will increasingly resemble that of the predominant component in the mixture as the relative concentration of the latter increases. This implies that discrimination should be maximal for the 1:1 mixture (see “X” marks in Figure 1). Note, however, that the vector for the 1:1 mixture may be offset from the midpoint between the component vapor vectors, despite the assumption of response additivity for such mixtures (vide infra).

Similar behavior is expected in attempting to recognize the ternary mixture and to discriminate it from the binary mixtures and the individual vapors. Regions of overlap within the plot in Figure 1 indicate mixture compositions where discrimination may not be possible and quantitative analysis is thereby precluded. If two (or three) of the vapors were to have more similar response patterns, then the range over which the mixtures would be differentiable from the individual components or lower-order-mixture subset would logically contract, and in the worst cases, it may not be possible to differentiate the vapors from each other or from any of their mixtures. Not reflected in Figure 1 is the effect of absolute concentration on differentiation. Since the influence of response variability on the response patterns invariably increases as the absolute concentrations decrease, the domains in the PC plot associated with the projected eigen vectors of the different vapors and mixtures will expand, reducing the ability to discriminate one pattern from another.

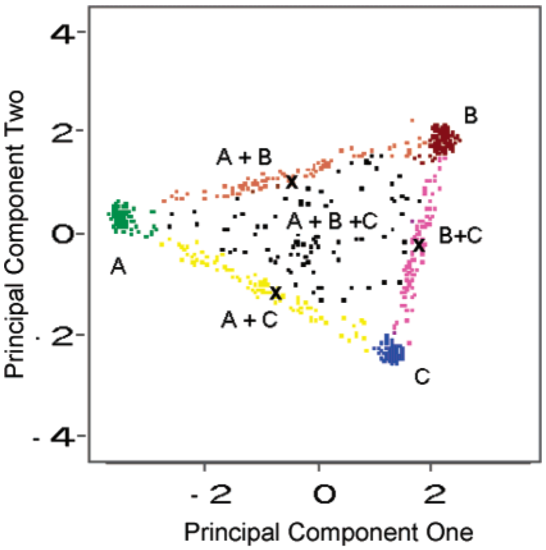

Figure 1. Principal components plot of sensor array responses to three vapors (A = toluene, B = hexane, C = 2-methoxyethanol) and their binary and ternary mixtures. Individual vapor responses were generated experimentally and mixture responses were synthesized by Monte Carlo simulation (see text). Each “X” indicates the binary mixture at a 1:1 (*x*LOD) component relative concentration ratio. Sensor array responses were normalized by dividing each response by the sum of the responses from all sensors for a given vapor or vapor mixture.

This brings us to the problem of how to define an LOR for a mixture. Unlike the individual vapor case, the LOR for a mixture cannot be defined as a single concentration or even as a set of m specific concentrations, where m is the number of mixture components. Since mixture recognition is expected to vary as a function of both the absolute and relative concentrations of the components, it must be defined as the boundary of an m-dimensional region: a surface or plane, in the case of a binary mixture, a volume in the case of a ternary mixture, and a hypervolume in the case of higher-order mixtures. The boundary of the region corresponds to the constellation of “isorecognition” points and should represent the threshold between recognizable and unrecognizable mixtures based on some predetermined level of acceptable recognition error. The magnitude of the area, volume, or hypervolume should then provide a way of ranking mixtures in terms of relative ease of discrimination and to identify mixtures where discrimination is not possible.

The LOR of a mixture can thus be defined, in the most general terms, as the *range of absolute and relative constituent concentra-*

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Table 1. Calibration Data for the 16 Vapors and Six Polymer-Coated SAW Sensors[10]

vapors (abbr)	calib range[a]	sensitivity, Hz/ppm (LOD[a])						LOD ratio	
		PIB	PECH	FPOL	PDPP	OV-25	OV-275	intra-vapor[b]	inter-vapor[c]
dichloromethane (DCL)	20−400	2.68 (6.54)	4.73 (8.97)	0.89 (46.8)	2.85 (3.97)	4.70 (6.18)	3.81 (9.99)	11.8	32.0
trichloroethylene (TCE)	10−250	31.2 (0.52)	18.1 (2.21)	4.88 (5.98)	13.0 (0.84)	22.0 (2.71)	9.11 (5.42)	11.5	4.1
perchloroethylene (PCE)	2.5−125	95.2 (0.24)	32.4 (1.41)	9.37 (3.89)	27.2 (0.46)	43.3 (1.22)	14.7 (4.12)	17.2	2.8
acetone (ACE)	50−2500	1.19 (11.7)	4.64 (8.27)	9.80 (3.52)	1.52 (7.44)	3.01 (14.3)	3.06 (11.3)	4.1	9.8
2-butanone (MEK)	20−1000	4.70 (2.95)	14.1 (2.76)	25.6 (1.03)	5.07 (1.97)	9.18 (4.89)	7.34 (5.89)	5.7	4.0
2-methoxyethanol (2ME)	2−50	14.3 (1.18)	60.1 (0.70)	206 (0.15)	20.3 (0.61)	29.5 (1.46)	57.1 (0.91)	9.7	1.0
2-propanol (IPA)	40−2000	2.75 (5.04)	7.09 (5.42)	25.7 (1.35)	2.93 (3.86)	3.73 (11.5)	7.67 (4.53)	8.5	7.9
1,4-dioxane (DOX)	20−1000	15.0 (1.32)	41.4 (1.04)	66.2 (0.52)	15.0 (0.89)	23.0 (1.88)	19.7 (2.88)	5.5	2.0
tetrahydrofuran (THF)	2.5−125	6.86 (2.12)	10.1 (3.97)	26.3 (1.01)	4.79 (2.18)	8.93 (5.90)	4.41 (10.7)	10.6	7.3
n-hexane (HEX)	5−400	10.3 (1.21)	1.63 (22.7)	0.87 (30.7)	1.63 (6.23)	2.69 (18.6)	1.31 (30.2)	25.3	21.0
isooctane (IOC)	30−1500	23.5 (0.79)	2.72 (15.9)	1.48 (21.4)	2.97 (4.16)	6.35 (7.53)	2.80 (19.5)	27.1	14.6
isoamyl acetate (IAA)	10−500	104 (0.27)	114 (0.47)	241 (0.17)	48.8 (0.45)	97.4 (0.50)	33.2 (2.03)	11.9	1.4
n-butyl acetate (BAC)	15−750	58.5 (0.48)	78.6 (0.68)	155 (0.26)	34.3 (0.63)	69.3 (0.71)	24.1 (2.79)	10.7	1.9
benzene (BEN)	4−120	13.5 (1.26)	12.8 (3.27)	3.95 (7.72)	6.79 (1.80)	15.0 (2.87)	5.57 (9.29)	7.4	6.4
toluene (TOL)	10−250	40.0 (0.52)	31.4 (1.37)	9.25 (3.77)	17.7 (0.75)	34.7 (1.90)	12.4 (4.69)	9.0	3.2
m-xylene (XYL)	10−200	89.2 (0.32)	54.4 (0.99)	16.2 (2.49)	31.0 (0.70)	59.9 (0.82)	20.9 (3.21)	10.0	2.2

[a] Quantities are in units of ppm by volume. [b] The LOD of the most sensitive sensor divided by the LOD of least sensitive sensor for each vapor. [c] The LOD of the least sensitive sensor for each vapor divided by the LOD of least sensitive sensor for 2-ME.

tions over which a mixture can be reliably recognized. Graphically, it is a region bound by a set of limiting absolute and relative concentrations of the mixture components. Given that random and systematic errors in responses will cause fluctuations in the response pattern used in the recognition analysis, it is appropriate, if not necessary, to evaluate the LOR probabilistically. Following conventional practice and retaining consistency with the definition of acceptable error adopted previously,[31] a default threshold of 5% recognition error is adopted here and the associated boundaries are referred to as LOR_{95}. Of course, other threshold recognition levels could be used and would be designated accordingly (e.g., LOR_{90} for ≥90% recognition). Furthermore, assuming Gaussian fluctuations in responses, it also would be possible to assign a confidence interval around this boundary, which is often desirable where critical decisions rest on the analytical findings.

For LOR evaluations, the range of possible absolute and relative concentrations spanned by the mixture components must be specified. Although the dynamic range of the sensor array in a microanalytical system will be affected by a number of factors (e.g., sample volume, preconcentrator adsorption capacity, separation column loading capacity, analyte vapor pressures, and sensor coating−film sorption rates or capacities), it is certainly conceivable to have situations where absolute vapor concentrations and relative vapor concentration ratios might range over 2, or perhaps, 3 orders of magnitude. But they are not likely to exceed this range and still be amenable to *simultaneous, quantitative determination* in a practical microsystem.

EXPERIMENTAL SECTION

Data Set Description. The database used for the analyses presented here was collected in conjunction with another study, and details of the instrumentation and measurement methodology are described elsewhere.[8] Only a brief summary is provided here. Response data were collected from six polymer-coated SAW resonators operating at 250 MHz and configured in sets of three as the detectors in two small prototype instruments. Calibrations were performed for each of 16 individual solvent vapors (Table 1) representing seven functional group classes, with at least two members of each class included to assess intraclass discrimination. Selected binary and ternary mixture calibrations were performed to confirm that mixture responses are equivalent to the sum of the individual vapor responses.[8,10] Sensor coatings of polyisobutylene (PIB), poly(diphenoxyphosphazine) (PDPP), polyepichlorohydrin (PECH), fluoropolyol (FPOL), triphenylmethyl polysiloxane (OV-25), and bis(cyanoallyl) polysiloxane (OV-275) were applied by airbrush in a volatile solvent to give net frequency shifts ranging from 370 to 470 kHz, which correspond to coating thicknesses of approximately 30−65 nm. Test atmospheres were generated in air at 50% relative humidity. The instruments used adsorbent preconcentrators to collect a fixed volume of air containing the test vapor at a given concentration. The vapors were quantitatively trapped by the preconcentrator, and the majority of the coadsorbed water vapor was stripped with a stream of backflushed clean, dry air at ambient temperature. Thermal desorption yielded an enriched vapor pulse that was drawn past the sensor arrays on a background of clean, dry air. Due to relatively slow heating, the desorbed peaks were rather broad and the maximums are assumed to reflect equilibrium or near-equilibrium sorption conditions in the thin polymeric sensor coatings.

Response maximums determined from the shifts in sensor frequencies (in Hz) were measured for each of the 16 vapors tested over a 20−80-fold range of concentrations. All calibration curves were linear ($r^2 \geq 0.99$), and the sensitivity for each vapor−sensor pair was defined as the slope of the curve obtained from linear regression analysis with forced zero. Table 1 presents the sensitivity and LOD for each sensor−vapor combination as well as the ratio of the highest-to-lowest LOD among the six sensors for each vapor. Also presented are the ratios of array LODs among the different vapors, based on the least-sensitive sensor for each vapor and normalized to the vapor with the lowest array LOD (i.e., 2-methoxyethanol). This array provides a fairly high degree of diversity as expected from the range of chemical structures spanned among the polymer coatings on the sensors and as evidenced by correlation analysis.[8]

EDPCR−Monte Carlo Simulation Model. The extended disjoint principal components regression (EDPCR) pattern recognition analysis method employed here is well suited for arrays of polymer-coated SAW sensors where the responses to individual vapors are linear and responses to mixtures of vapors are additive. It has been described elsewhere[9,40] and used in numerous subsequent studies.[8,10,13,31,35] With EDPCR, SAW sensor responses to each vapor challenge are summed to yield a vector in six-dimensional space. Regression is used to model the first eigen vector (i.e., principal component) of the mean-centered response vectors for each tested vapor over a range of concentrations. One regression model is created for each vapor and is used as the basis of EDPCR vapor recognition. The response vectors of vapor mixtures are synthesized from those of the component individual vapors under the assumption of additivity of responses, which has been verified for polymer-coated SAW sensors in several studies,[7−10,15] including those of the instruments generating the data used here.[8,10] Regression models are then created for all possible mixtures under this assumption.

Coupling EDPCR analysis with Monte Carlo simulations provides a means for testing the performance of any sensor array for a wide range of possible exposure scenarios. It is the only feasible way of assessing the LOR for a large data set. The Monte Carlo process generates simulated responses from each sensor in the array by randomly selecting a point along the regression line (calibration curve) for a given vapor and applying a combination of random and systematic errors to the corresponding calibrated sensor response by assuming the errors follow a Gaussian distribution. Simulated responses from all of the sensors in the array are then summed to create a vector that is treated as an "unknown" or "test" sample, which is then assigned an identity using the EDPCR models established from the calibration data. The EDPCR decision rule is simply based on proximity: the test sample is assigned the identity of the vapor whose stored calibration vector falls closest to that of the test sample, as determined by the Euclidean distance. By iteratively simulating such error-enhanced test samples and comparing their true identities to those determined by EDPCR recognition, the nature and statistical likelihood of expected recognition errors can be evaluated.

The error model used for the Monte Carlo simulations has also been described and validated previously.[8,10,31] It accounts for systematic variations in sample collection, delivery, response, residual humidity, and random variations in baseline noise and slope sensitivity. For mixture simulations, the responses for each component are generated separately and then summed. EDPCR classification routines and Monte Carlo simulations were performed on a laptop computer using in-house software written in Visual Basic (Version 7.0, Microsoft Corp.) and output to Excel (Version 7.0, Microsoft Corp). Additional statistical analyses were performed using standard commercial packages.

Recognition Rate Determinations. Recognition rates were estimated for each of the 120 possible binary mixture combinations of the 16 test vapors on the basis of 500 Monte Carlo−EDPCR analyses at each of 136 concentration combinations spanning an absolute concentration range of 0.1−1500 × LOD for each vapor and relative concentration ratio (RCR), expressed as multiples of the array LOD for each vapor, ranging from 1:75 to 75:1 for each pair of vapors. For modeling purposes, it is assumed that sensor responses remain linear and additive at concentrations exceeding those examined during calibration, despite expected deviations at the higher concentrations examined (for the vapors tested here, a concentration of 1500LOD corresponds to from 8 to 59% of the saturation vapor concentration). Each analysis was performed by simulating error-enhanced responses around a fixed combination of vapor concentrations and entailed discriminating the response pattern of the mixture from those of the constituent vapors. LORs were determined from these data as described in the next section. Quantification accuracy was not assessed in this study.

For the ternary cases, each analysis entailed discriminating the response pattern of the mixture from those of the constituent vapors and their binary mixtures**.** Each set of three vapors was analyzed ($n = 500$) at 567 combinations of component vapor concentrations: the concentration of one vapor at a time was varied from 1LOD to 30LOD in seven discrete increments while the relative concentrations of the second and third vapors were varied up to a ratio of 75:1 (in terms of the LOD of each vapor) with respect to the first vapor in nine discrete increments. These data were used to construct three-dimensional recognition contours from which the LOR could be derived.

Recognition matrices are presented in Tables S-1 and S-2 of the Supporting Information for this article for a representative binary and ternary mixture, respectively, and illustrate the type of output obtained from these analyses. As shown, differentiating the highest-order mixture from the individual vapors and lower-order mixtures (ternary case only) is the most difficult problem.

The analyses performed in this study address the following questions: to what extent do the absolute and relative vapor concentrations affect the recognition of vapor mixtures? What is the maximum RCR that can be tolerated without losing the ability to recognize the minority component and does this vary as a function of which vapor is in excess? Which vapor mixtures will be the most difficult to differentiate and can we predict the LOR using simpler metrics of pattern similarity or relative vapor sensitivity? How does the LOR compare to the LOD?

RESULTS AND DISCUSSION

Recognition Contours and LORs for Binary and Ternary Mixtures. Figure 2 shows three representative examples of the simulated binary-mixture recognition rate contours generated from the data set. In each of the panels the *x*-axis is the RCR of the component vapors, the vertical (*y*) axis is the calculated recognition rate, and the *z*-axis is the absolute concentration of the lower-concentration component. Absolute concentrations are presented on the *z*-axis in multiples of the LOD of the minority mixture component, spanning a range of 0.1−20 × LOD. Specifying the absolute and relative concentrations as multiples or fractions of the vapor LODs facilitates comparisons across all vapor mixtures in terms of signal-to-noise ratio. The LOD is defined with respect to the array as a whole, corresponding to the highest individual sensor LOD for a given vapor. Recognition was assessed at seven arbitrarily chosen absolute concentration values (0.1−20LOD), and the plotted range was terminated at a minority component

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(40) Zellers, E. T.; Pan, T. S.; Patrash, S. J.; Han, M. W.; Batterman, S. A. *Sens. Actuators, B* **1993**, *12*, 123−33.

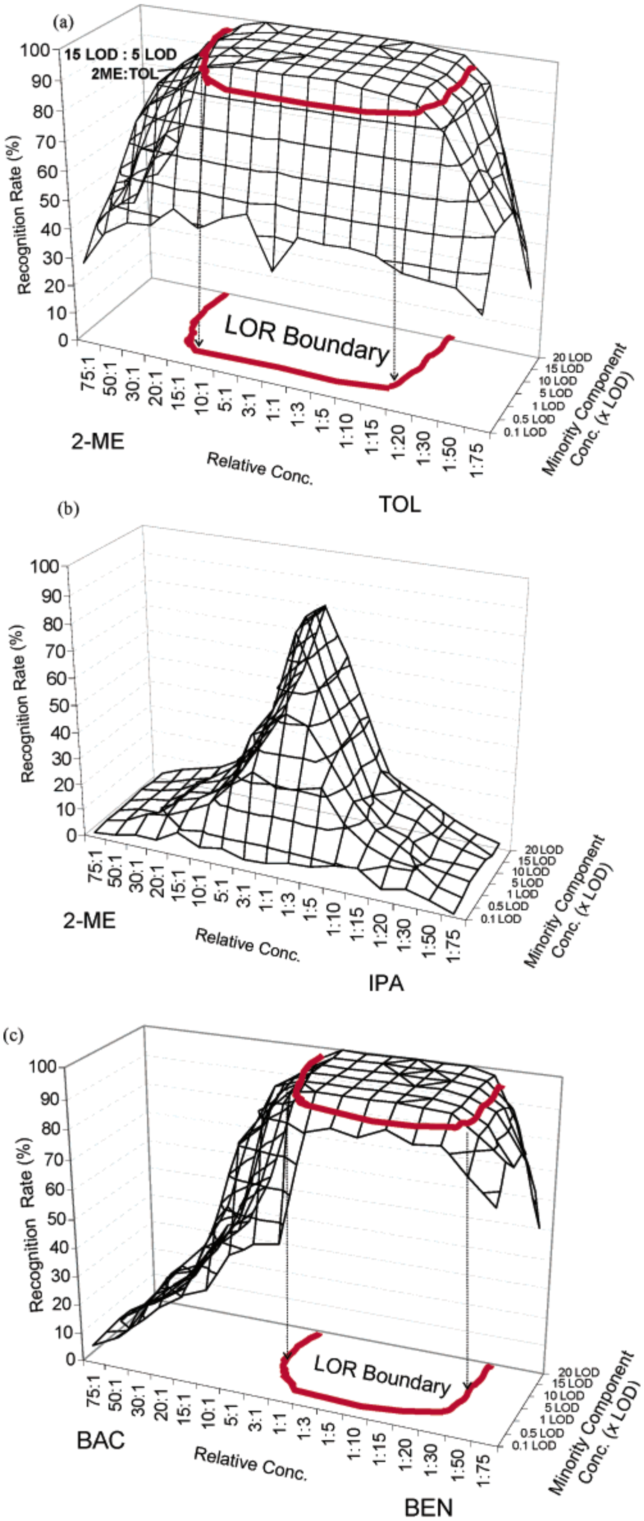

Figure 2. Recognition contours for binary mixtures of (a) 2-methoxyethanol (2ME) + toluene (TOL), (b) 2ME + 2-propanol (IPA), and (c) *n*-butyl acetate (BAC) + benzene (BEN). In each plot, the x-axis is the relative concentration ratio (in multiples of the LOD), the y-axis is the mixture recognition rate, and the z-axis is the minority component absolute concentration (in multiples of the LOD). The LOR$_{95}$ boundary is defined by the projection onto the $x-z$ plane.

(absolute) concentration of 20LOD to improve readability and because the shapes of the recognition contours at higher absolute concentrations did not differ significantly from those in the vicinity of 20LOD. Note that for the left-most half of the plots (i.e., RCRs of 1:1−75:1), the absolute concentrations on the z-axis correspond to one of the mixture components and for the right-most half (i.e., RCRs of 1:1−1:75) they correspond to the other component. Each contour consists of 136 coordinate points that define the absolute and relative concentrations of the components over the range of greatest interest (i.e., 0.1−1500LOD).

Figure 2a shows the recognition contour for the mixture of 2-methoxyethanol + toluene (2ME+TOL), which represents a relatively easy discrimination problem due to the differences in the vapor structures and sorption properties. The arrow in Figure 2a specifies the coordinate ⟨3:1, 100%, 5LOD⟩ and corresponds to a mixture containing 2ME at a concentration of 15LOD (21.9 ppm, see Table 1) and TOL at a concentration of 5LOD (i.e., 23.5 ppm) for which the simulated recognition rate is 100%. The plot is symmetric about the 1:1 RCR line, and the recognition rates for the 2ME+TOL mixture remain uniformly high at intermediate RCRs and absolute concentrations of >0.5LOD, dropping off to lower values quite rapidly as the RCR exceeds 20 (i.e., 20:1 or 1:20) and the absolute concentration of the minority component falls below 0.5LOD. The absolute concentration axis is extended below the LOD to determine whether reliable recognition is achievable with fewer than six sensors,[8,31] which happens to be the case for this mixture.

By connecting the coordinates where the contour crosses the plane corresponding to 95% recognition on the y-axis, a surface is defined corresponding to the LOR$_{95}$ boundary compositions for the mixture. This bounded region can be projected onto the $x-z$ plane as indicated in Figure 2a and its area calculated as discussed below.

The recognition contour shown in Figure 2b is for the mixture of 2ME + 2-propanol (2ME+IPA), which is representative of the more difficult, intraclass discriminations in the data set. The shape of the contour for the 2ME+IPA mixture is quite different from that of the 2ME+TOL mixture, showing a sharp recognition rate peak at the 1:1 ratio that drops off rapidly as the absolute concentration drops below 5LOD and the RCR extends beyond 1 in either direction along the x-axis. Since the maximum rate of recognition is <95%, the LOR$_{95}$ cannot be specified and is assigned a value of zero. That is, it is not possible to adequately (as defined here) discriminate this mixture of alcohols from either of its components at any concentration. Note the symmetry of both of the surfaces in Figure 2a and b, which indicates that the component vapors have similar effects on recognition as their respective concentrations change.

Figure 2c presents the recognition contour for the mixture of *n*-butyl acetate and benzene (BAC+BEN), which is decidedly unsymmetric with respect to the relative concentration ratio. In this case, the collective sensitivities of the array sensors to butyl acetate are much greater than they are to benzene (see individual sensor LODs in Table 1). As a consequence, despite normalizing the comparison to the LOD for the least sensitive sensor in the array for each vapor, when the concentration of benzene is reduced, its contribution to the composite response pattern is less readily discerned and the mixture is confused for *n*-butyl acetate alone even at modest relative concentration ratios.

The projected area in the $x-z$ plane bound by the 95% recognition rate coordinates provides a convenient means of summarizing the LOR$_{95}$ values of binary mixtures. It is defined

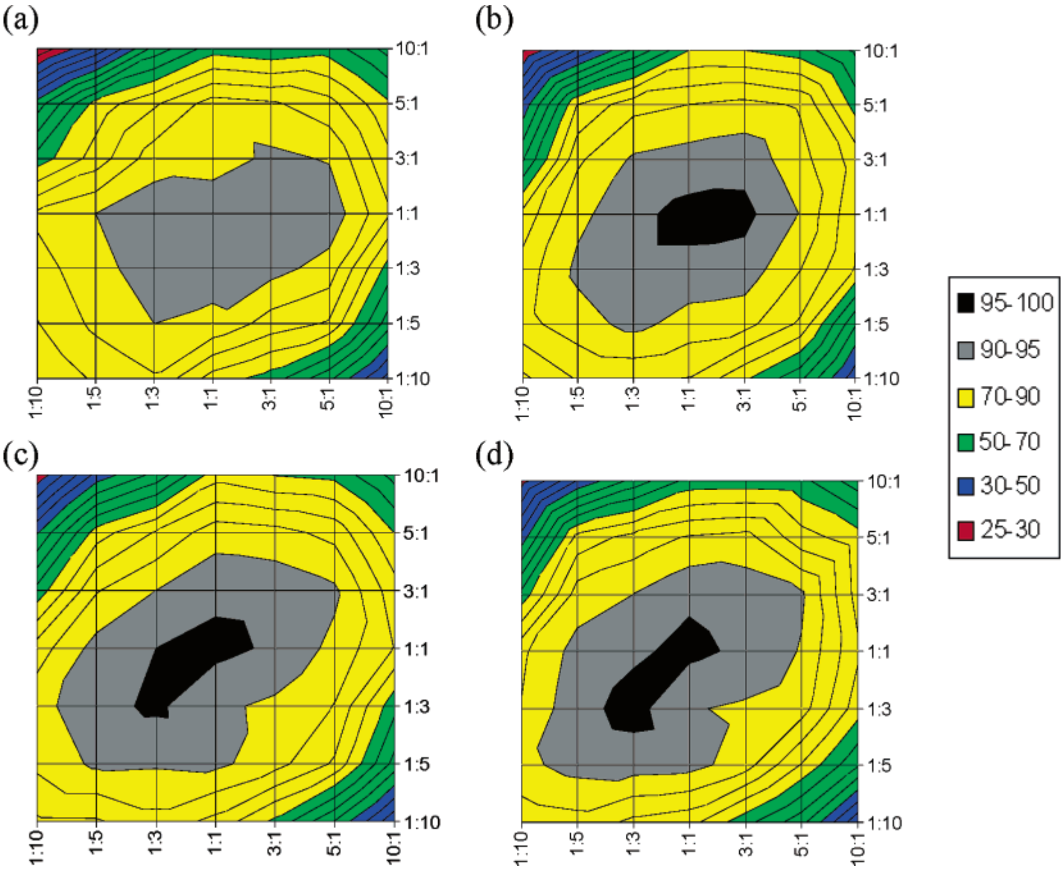

Figure 3. Recognition contour sections for the ternary mixture of DCL + 2-ME + HEX at DCL concentrations of (a) 5LOD, (b) 10LOD, (c) 20LOD, and (d) 30LOD and RCRs ranging from 10:1 to 1:10 for 2-ME and HEX with respect to DCL. The *x*-axis is the DCL/2-ME concentration ratio (LOD) and the *y*-axis is the DCL/HEX concentration ratio (LOD). Legend indicates recognition rate corresponding to each color.

on two sides by the relative concentration range boundaries determined analytically. The LOD establishes the lower bound on the absolute concentration axis. Setting the upper bound on the absolute concentration axis is somewhat arbitrary. We observe generally for those mixtures where an LOR_{95} can be defined at all, that above ~5LOD for the minority component there is little or no variation in recognition rate. We have elected to truncate these projections at 20LOD with the rationale that this captures roughly equal contributions from an area of potential variability in the LOR_{95} (i.e., 1−5LOD for the minority component) and an area of relative constancy in the LOR_{95} (i.e., 5−20LOD for the minority component) for most vapors. Since the "depth" of the LOR_{95} area is fixed at 20, differences among the mixture LOR_{95} values will depend on the collective "widths" defined by the limiting RCRs. To quantify these widths, the two sections of the projected area on either side of the 1:1 ratio were divided (e.g., 5:1/1:3 = 15, for the case where the LOR_{95} has RCR boundaries at 5LOD:1LOD and 1LOD:3LOD) and then averaged over the absolute concentration range of 1−20LOD.

For a ternary mixture, it is not possible to capture all of the variables affecting recognition in a single contour map because four dimensions are required. If only the points corresponding to the LOR threshold recognition rate are plotted (e.g., 95%), then one axis specifying the absolute concentration of one constituent and two axes specifying the RCRs of the other two constituents relative to the first yield the LOR_{95} polyhedron. The volume of the polyhedron should vary in proportion to the range of mixture compositions that can be differentiated from the constituents. Alternatively, two-dimensional sections at discrete levels of absolute concentration for the first component can be created and then stacked to allow visualization of the recognition contours.

Figure 3 presents a series of such recognition contour sections for a mixture of dichloromethane, *n*-hexane, and 2ME. As with all recognizable ternary mixtures, the RCR over which recognition is reliable is ≤5 among the three components, and although the recognition rate increases with increasing absolute concentration, above a minority component concentration of 5−10LOD there is little variation in the cross sectional area of the contours defining either the LOR_{95} (black) or LOR_{90} (gray).

In lieu of integrating the resulting irregular polyhedron, a simpler means of estimating the volume was used and a scoring system was developed for ranking the various ternary mixtures. At each absolute concentration specified for vapor A, the RCRs for B:A and C:A that define each coordinate point on the LOR_{95} or LOR_{90} boundary were multiplied to give the largest possible integer product. For example, for the coordinate on the 20LOD plane for vapor A corresponding to a C:A ratio of 1:3 and a B:A ratio of 1:5, the "score" would be 15. Averaging these scores over the seven discrete absolute concentration increments in vapor A that were analyzed from 1 to 30LOD gives a total score for the mixture that varies in proportion to the total range of reliably analyzable concentrations.

Dependence of Recognition Rate and LOR_x on Absolute and Relative Concentrations. Overall, 91% (109/120) of the

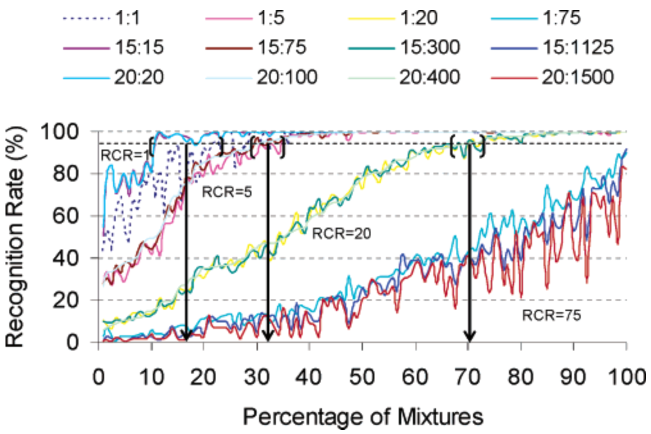

Figure 4. Binary mixture recognition rates as a function of absolute and relative component concentrations, illustrating the importance of the relative concentration ratio (RCR). Four sets of three curves are presented, each set at a constant RCR that spans a 20-fold range of absolute concentration among the three curves. The mixtures are plotted in ascending order of the Euclidean distance between the components, and the *x*-axis is the (cumulative) percentage of mixtures (out of 120) that correspond to a given recognition rate. Arrows indicate where the average recognition rate of a group of curves crosses the 95% point (i.e., LOR_{95}).

binary mixtures had LOR_{95} areas spanning some finite concentration range. In contrast only 3% (16/560) of the ternary mixtures had LOR_{95} scores greater than zero. Relaxing the criterion for reliable recognition to 90% yielded 74 ternary mixtures (13%) with nonzero LOR_{90} scores. None of the remaining ternary mixtures could be recognized at any composite concentration with this diverse polymer-coated sensor array. All of the 74 ternary mixtures with nonzero LOR_{90} scores contained at least one of the following vapors as mixture components: DCL, HEX, or IOC. All 16 ternary mixtures with nonzero LOR_{95} scores contained DCL. This is consistent with PC analysis indicating that DCL has a unique response pattern compared to all of the vapors in the data set.

The binary mixture recognition rates were then examined to determine separately the strength of their dependence on the absolute and relative concentrations of the components. Figure 4 presents four sets of curves, with three curves in each set. Each curve is a plot of the recognition rates of all 120 mixtures at a specific absolute and relative concentration in ascending order of the Euclidean distance between the components. The horizontal axis is the cumulative percentage of mixtures. All the curves within a set represent mixtures where the RCR of the vapors, again in terms of multiples of their respective array LOD, are the same but the absolute concentration varies by 20-fold. The plots in Figure 4 are for half of the total range of RCRs (i.e., 1:1−75:1). Similar plots are obtained for the complementary cases where the majority component was the other vapor within a given pair (note: the unsymmetric cases are fairly evenly distributed between these two data groups).

As shown, differences between sets are much larger than those within a set, illustrating that when all vapors are present at concentrations equal to or greater than the LOD, recognition is affected more by the relative concentration than by the absolute concentration. Across sets, recognition rates decrease as the RCR increases. The vertical arrows superimposed on the plots show the percentages of all mixtures falling below the 95% recognition level. So, for RCRs of >75, fewer than 1% of the mixtures can be reliably recognized. For the intermediate RCR of 20, ∼30% of the mixtures can be reliably recognized, and for RCRs of <5, the majority of vapors can be recognized. Note that when both constituents are at their respective LODs, there is a significant decline in performance most likely due to distortions in the response patterns from increased noise and to the loss of one or more sensors from the patterns of both vapors, since the Monte Carlo simulation generates a portion of the concentrations below the LOD for at least one sensor in the array. However, the data show that the recognition rate of any mixture is never greater than it is at an RCR of 1. The larger fluctuations observed at high absolute and relative concentrations are not fully understood but apparently arise from the large proportional slope error term in the Monte Carlo error model producing very large changes in response patterns.

The reader is reminded that all absolute and relative vapor concentrations are expressed relative to the individual vapor LODs. This means that for analyses performed at a 1:1 RCR the S/N ratios are the same for both vapors and for analyses performed at other RCRs the S/N ratios vary accordingly for each vapor. This convention was adopted to permit generalized analyses to be performed. The differences in LODs among the vapors must be considered in order to assess performance in terms of more standard units of air concentration such as ppm by volume. For example, when benzene and *n*-butyl acetate are present at their respective LODs, the RCR as expressed here is 1 but the RCR in terms of ppm is 9.3 ppm/2.8 ppm = 3.3 (refer to Table 1). In contrast, the RCRs for MEK and TCE are nearly the same regardless of whether they are expressed in terms of S/N ratio or ppm because their LODs are nearly identical.

Table 2 presents a matrix of the overall distribution of binary LOR_{95} values. As expected, as the absolute concentration of the minority component increases, the percentage of mixtures with no LOD_{95} decreases, reaching a limiting value of ∼11% above 5LOD. The data in the remaining columns are the percentages of mixtures whose limiting (i.e., maximum) RCRs are as indicated in the column heading. The larger the maximum RCR, the wider the tolerable differential concentration before losing the ability to recognize the mixture. Although the percentage of mixtures within a given RCR increases with increasing absolute concentration, above 5LOD, the increase is marginal. Above the LOD, 11−14% of the mixtures have maximum RCRs of ≤5 (i.e., 5:1−1:5) while a consistently larger fraction (i.e., 19−24%) could be recognized out to a maximum RCR of 30. Only one mixture could be recognized above an RCR of 50: acetone + isooctane. This mixture had a highly unsymmetric recognition profile and was recognizable out to 75:1 (acetone/isooctane) but was not recognizable at 100:1.

Correlations with Euclidean Distance. By definition, the similarity in the response patterns of the mixture components varies inversely with their Euclidean distance measured in six-dimensional space. Accordingly, we generally observe smaller Euclidean distances between vapors from similar functional groups or with similar sorption properties. It follows that there should be a correlation between the LOR_{95} area of a binary mixture and the component Euclidean distances determined from concentration-normalized vectors. Figure 5 shows the strength of that

Table 2. Percentages ($n = 120$) of Binary Mixtures without LOR_{95} Values and Percentages of Remaining Mixtures Having the Limiting LOR_{95} Relative Concentration Ratios (in Multiples of the LOD) Indicated (Columns) for Minority Component Absolute Concentrations of 1–20LOD (Rows)[a]

absolute concn of minority component	no LOR	limiting relative concentration ratio (RCR)							
		3:1–1:3	5:1–1:5	10:1–1:10	15:1–1:15	20:1–1:20	30:1–1:30	50:1–1:50	75:1–1:75
1LOD	18	6	11	8	8	23	22	4	1
5LOD	12	11	14	3	9	21	23	6	1
10LOD	11	13	12	6	11	21	24	3	1
15LOD	11	12	13	4	16	21	19	5	1
20LOD	11	11	13	5	13	23	22	3	1

[a] Mixtures exhibiting unsymmetric limiting RCRs were assigned to the category corresponding to the largest of the two limiting RCR values.

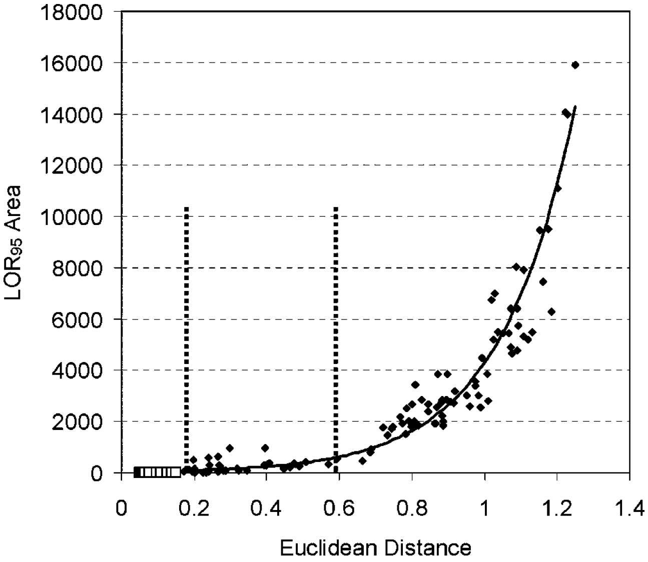

Figure 5. Correlation of LOR_{95} area with Euclidean distance for 120 binary vapor mixtures. Hollow symbols indicate vapor mixtures with no LOR_{95}. Dashed lines delineate groups of vapors with no LOR (left), LOR_{95} areas having narrow RCRs (center), and LOR_{95} areas with broader RCRs (right). Solid curve is from regression equation: $y = 34.7e^{4.82x}$ ($r^2 = 0.942$). Euclidean distances were calculated using normalized sensor response patterns whereby each sensor response was divided by the root sum of squares of the responses from all sensors for each vapor.

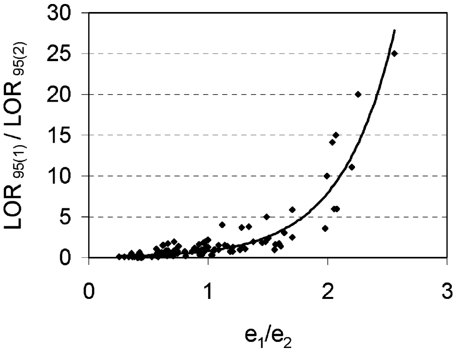

Figure 6. Correlation of $LOR_{95(1)}/LOR_{95(2)}$ with e_1/e_2, where $LOR_{95(1)}$ is the portion of the LOR_{95} area corresponding to one side of the 1:1 composition line, $LOR_{95(2)}$ is the LOR_{95} area corresponding to the other side, and e_1 and e_2 are the Euclidean distances between the 1:1 mixture vector and the vectors for components 1 and 2, respectively Euclidean distances were determined on the basis of normalized patterns whereby each sensor response was divided by the sum of all sensor responses to the vapor or vapor mixture. Solid curve is from regression equation: $y = 0.0908e^{2.23x}$ ($r^2 = 0.91$).

correlation. Those mixtures having no LOR_{95} were assigned a zero value in the plot. Regression analysis of the remaining mixtures revealed a linear correlation between the logarithm of the LOR_{95} area and the Euclidean distance ($r^2 = 0.941$) strong enough to predict the former from the latter with reasonable accuracy.

The vertical dashed lines in Figure 5 parse out three regions. Below a Euclidean distance of 0.2, there is no LOR_{95}. Between 0.2 and 0.6, the LOR_{95} area is finite but is constrained to a relatively small RCR range (i.e., <7-fold excess in either component by assuming a symmetric recognition profile such as shown in Figure 2a). Above 0.6, recognition is possible over an increasingly wide range of RCR values.

Among the 120 binary mixtures, 30 gave recognition profiles that were significantly unsymmetric, that is, where the projected areas on either side of the 1:1 mixture differed by ≥5-fold. Although this behavior was observed predominantly with vapor pairs having large differences in array LODs, there were numerous exceptions and the latter was not a strong predictor of recognition profile asymmetry because it is based only on the least sensitive sensor in the array. A lack of symmetry is expected for cases where one vapor response pattern dominates over the other such that the 1:1 mixture vector is located closer to that of the pattern-dominant individual vapor in hyperspace (unlike the cases illustrated in Figure 1). In such cases, even small increases in the relative concentration of the dominant vapor results in the loss of contribution of the minority component to the composite pattern.

To explore this, the Euclidean distance between the two component vapors was partitioned into the distances between the component vapor vectors and the vector for the 1:1 mixture (e_1 and e_2, respectively). The difference between these vectors should reflect the lack of symmetry observed in the recognition plots. Figure 6 plots the e_1/e_2 ratio to the corresponding ratio of LOR_{95} areas on either side of the 1:1 composition line. A strong correlation is observed ($r^2 = 0.91$) as expected.

Correlations between Euclidean distances and LOR areas were then explored for the ternary mixtures. Since there are three distances involved, as a first approach we employed a similarity metric that we have not seen reported before in the literature: the area of the triangular plane created by the three individual vapor vectors in hyperspace. Logically, the area of such a "Euclidean triangle" should be related to the LOR score. The area, A, of a triangle can be related to the perimeter, P, and the lengths of each of the three sides (a, b, c) as follows:

$$A = \sqrt{\frac{P}{2}\left(\frac{P}{2} - a\right)\left(\frac{P}{2} - b\right)\left(\frac{P}{2} - c\right)}. \qquad (1)$$

where $P = a + b + c$.

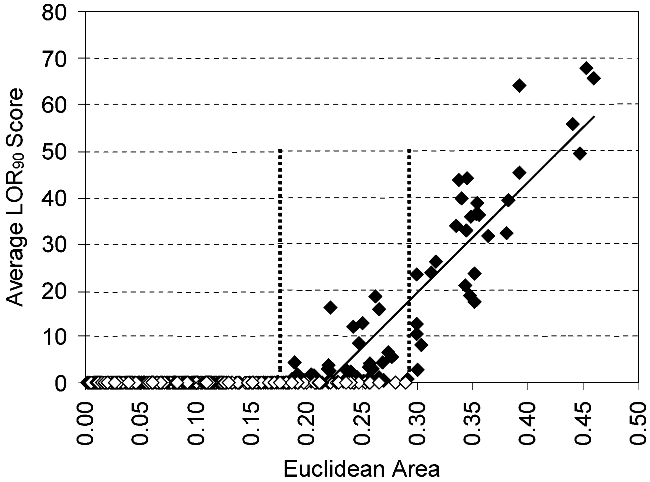

Figure 7. Correlation of ternary mixture Euclidean area with average LOR$_{90}$ score from 1 to 30LOD (see text). Open symbols are for ternary mixtures without LOR$_{90}$ scores. Solid curve is from linear regression ($r^2 = 0.792$). Dashed lines establish three regions: recognition is not possible (left); recognition is uncertain and limiting RCR is narrow (center); and recognition is assured and RCR is broader (right).

Figure 7 show the relationship between the 74 LOR$_{90}$ scores and their corresponding Euclidean areas (filled symbols). The remaining 486 mixtures with no definable LOR$_{90}$ scores are represented by open symbols. The correlation is only fair ($r^2 = 0.79$) but does permit rough estimates of whether the mixtures can be recognized and over what range of RCRs. The correlation is not expected to be perfect because the calculation of Euclidean area does not account for differently shaped triangular planes; a ternary mixture with equal component-vapor Euclidean distances (e.g., Figure 1) would be easier to recognize than one having unequal Euclidean distances. Including weighting factors to account for this would likely improve the predictive power of this metric. The vertical dashed lines provide reference points for decision making: below a Euclidean area of 0.18, recognition is not possible at <10% error, and above an area of 0.29, recognition is assured over some finite range of composition. In the region between these values, the outcome is uncertain and the limiting RCRs of any recognizable mixtures will be constrained to compositions where the magnitudes of the sensor responses from each component are similar.

LOR versus LOD. As the vapor concentrations are progressively reduced below the LOD for the array, fewer sensors will contribute to the composite response pattern. At a given sub-LOD concentration, the number of contributing sensors will vary with each vapor because of differences in sensitivity. The range of LODs among the sensors in the array for a given vapor can be as high as 30-fold but is typically 10-fold or less (Table 1). Therefore, running simulations down to a concentration of 0.1LOD will result in at least five sensors being lost from the response pattern for any vapor. This also allows an examination of how the LOR compares to the LOD.[31]

We find that as the minority component concentration decreases below the array LOD an increasing number of mixtures cannot be recognized. At 0.5LOD, 0.3LOD, and 0.1LOD, the fraction of unrecognizable vapors is 25, 32, and 78%, respectively. However, while 22% of the mixtures remained recognizable at a minority component concentration of 0.1LOD, all of these mixtures exhibited unsymmetric recognition profiles similar to that illustrated in Figure 2c, and the majority component was always ≥0.5LOD. The number of sensors contributing to the response patterns of the components for these mixtures was typically four to six for the majority component but typically only one for the minority component. The minority component contribution was apparently just sufficient to perturb the response pattern of the majority component enough to cause the EDPCR routine to classify it as a mixture.

CONCLUDING REMARKS

The definition of the limit of recognition proposed here for binary, ternary, and higher-order vapor mixtures can be generalized to arrays employing any sensor technology and any class of sensor interface materials. However, since the LOR is a function of the similarity of response patterns, it will depend on the specific array employed and the specific vapor set considered and therefore must be determined on a case-by-case basis. The approaches developed here for determining and evaluating the LOR boundaries are sufficiently rigorous to permit effective assessments of array performance as a function of all relevant variables. They are conceptually straightforward and analytically accessible provided that the sensor responses and their expected variations can be modeled and simulated. This is facilitated by having individual vapor responses that are linear with concentration and mixture responses that are equivalent to the sum of the component vapor responses. The magnitude of the LOR area, volume, or hypervolume provides a way of ranking mixtures in terms of the ease with which they can be recognized and differentiated from their constituents and to identify mixtures where such discriminations are not possible. Such information could be used, for example, to guide retention tuning strategies in microanalytical systems with such capabilities.

Results obtained with the diverse six-sensor array used here indicate that while most binary mixtures can be recognized, very few ternary mixtures can be recognized at acceptable error levels. For all mixtures, the ratio of vapor concentrations is a much more important determinant of performance than are their absolute concentrations, and for binary mixtures, the relative concentration range over which components can be recognized will typically be <20-fold, where relative concentrations are defined in terms of multiples or fractions of the component vapor LODs. When the determination of all vapors in a complex mixture is desired, this establishes a significant constraint on trace analysis, since (chromatographically) unresolved binary mixture components at low relative concentrations cannot be detected reliably. However, in situations where targeted vapor analysis is desired, this factor can be used to advantage. That is, when the determination of one vapor or one class of vapors among many is desired, if selective preconcentration or judicious sensor interface material selection can be used to enhance the response of the vapor(s) of interest by 20-fold or more, then the likelihood of significant interference, or false positives, will be greatly reduced. This type of information should be useful in setting design and operating criteria for microanalytical system components.

Correlations with simpler measures of response pattern similarity were established that facilitate decisions about expected performance. The new metric presented here for ternary mixtures based on the Euclidean area defined by the eigen vectors of the three components of the mixture performed reasonably well but would be improved by applying weighting factors to account for asymmetry in the triangular region.

Although from 11 to 18% of the binary mixtures considered were unrecognizable above the LOD for the sensor array, numerous binary mixtures could be recognized at sub-LOD concentrations. That is, in many cases, not all of the sensors in an array were necessary to effect a particular recognition or discrimination.[8,11] Reducing the dimension of the array offers the advantages of reducing computational complexity, increasing data acquisition rates, and reducing the size of the detector, all of which become increasingly important in microanalytical systems attempting to perform high-speed analyses.

The results from this systematic study of mixture recognition support earlier assertions made in the context of individual vapor analysis[31] that recognition must be incorporated into the repertoire of standard criteria by which array performance is evaluated. The concepts and approaches presented here could, and perhaps should, be adopted as part of routine assessments.

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SUPPORTING INFORMATION AVAILABLE

Typical examples of recognition matrices for binary and ternary mixtures. This material is available free of charge via the Internet at http://pubs.acs.org.

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