

# Comparisons between Mammalian and Artificial Olfaction Based on Arrays of Carbon Black–Polymer Composite Vapor Detectors

NATHAN S. LEWIS

*Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California 91125*

Received November 19, 2003

## ABSTRACT

Arrays of broadly cross-reactive vapor sensors provide a man-made implementation of an olfactory system, in which an analyte elicits a response from many receptors and each receptor responds to a variety of analytes. Pattern recognition methods are then used to detect analytes based on the collective response of the sensor array. With the use of this architecture, arrays of chemically sensitive resistors made from composites of conductors and insulating organic polymers have been shown to robustly classify, identify, and quantify a diverse collection of organic vapors, even though no individual sensor responds selectively to a particular analyte. The properties and functioning of these arrays are inspired by advances in the understanding of biological olfaction, and in turn, evaluation of the performance of the man-made array provides suggestions regarding some of the fundamental odor detection principles of the mammalian olfactory system.

## 1. Introduction

No known man-made sensor system combines the sensitivity, low-power, rapid response, selectivity, generalizability, and ability to track analytes to their source that is characteristic of a canine's olfactory system. The mechanism by which humans assign different odor qualities (sweet, fruity, musty, etc.) to various chemicals is also not well-understood. The potential to understand, and possibly even replicate, these features is the primary motivation behind our efforts to construct an artificial olfactory system, that is, an "electronic nose".

The immune system uses a traditional "lock and key" approach to chemical sensing in which each receptor responds specifically to a particular analyte of interest. This approach works well when one knows in advance which molecules are to be detected so that specific receptors can be constructed. In contrast, the mammalian olfactory system uses an array of broadly cross-reactive receptors, in which each analyte elicits a response from an array of receptors and, in turn, each receptor responds to a collection of odorants.<sup>1,2</sup> The response pattern

produced upon exposure to an odorant is then sent to the olfactory bulb and subsequently is transmitted to the brain, where pattern recognition methods are used to identify, classify, and quantify the odor of interest.

Bioinspired, artificial olfactory systems, often called "electronic noses", also perform odor detection through use of an array of broadly cross-reactive sensors in conjunction with pattern recognition methods (Figure 1).<sup>3</sup> Such systems gained increased attention in the early 1990s, when advances in computational capability added significant performance potential to pattern-recognition-based sensing architectures.<sup>3–5</sup> The various implementations of "electronic noses" differ in the specifics of how the signal transduction is performed and in the nature of the algorithms that are used to analyze the sensor array data. Sensor modalities include surface acoustic wave and bulk resonating quartz crystal devices, micromachined cantilevers, conducting polymers, polymeric dielectric capacitors, dye-impregnated polymeric films coated on optical beads or fibers, semiconducting metal oxide resistors, chemically sensitive field effect transistors, and vapochromic inorganic and porphyrinic metal complexes.<sup>6,7</sup> Pattern recognition algorithms include statistically based methods, such as principal components analysis or partial least-squares regression analysis, and neural network-based methods, such as self-organizing maps and Kohonen maps.<sup>3</sup> In this article, we discuss the progress and insights that have arisen from recent work in our laboratory based on investigation of one such "electronic nose" system. Additionally, we discuss how these observations have produced insight into the performance of sensor arrays for odor detection and have provided suggestions regarding some of the fundamental odor detection principles of the mammalian olfactory system.

Our approach utilizes composites comprised of regions of conductors interspersed in regions of insulating organic polymers.<sup>8,9</sup> The polymer is typically a low glass transition temperature, organic polymer,<sup>10</sup> and the conducting phase can be either a conducting organic polymer or an inorganic or organic conductor, such as colloidal Ag, colloidal Au, carbon black, or doped polypyrrole. When a volatile organic vapor is exposed to the composite, the vapor is readily sorbed into the polymer and produces a swelling of the polymer film. This sorption-induced swelling increases the dc electrical resistance of the composite, providing a simple, low-power method for transducing the presence of an analyte into a readily detectable electrical signal (Figure 2). An array of such sensors, each containing a chemically distinct polymer and a common conducting phase, thereby produces pattern-based signatures for the detection, classification, and analysis of various analytes.<sup>8,9</sup> In a sufficiently diverse sensor array, even subtle differences between analytes, such as their molecular shape, size, volume, dipole moment, and hydrogen bonding capacity, produce differentiable response signatures for different analytes.<sup>11,12</sup>

N. S. Lewis received his Ph.D. in chemistry in 1981 from MIT, served on the Stanford faculty from 1981 to 1988, moved to Caltech in 1988, and is currently the George L. Argyros Professor of Chemistry and Principal Investigator of the Materials Resource Center of the Beckman Institute at Caltech. Among his honors are the ACS Pure Chemistry Award and the Fresenius Award. His current research activities include semiconductor photoelectrochemistry, scanning tunneling microscopy, and artificial olfaction.

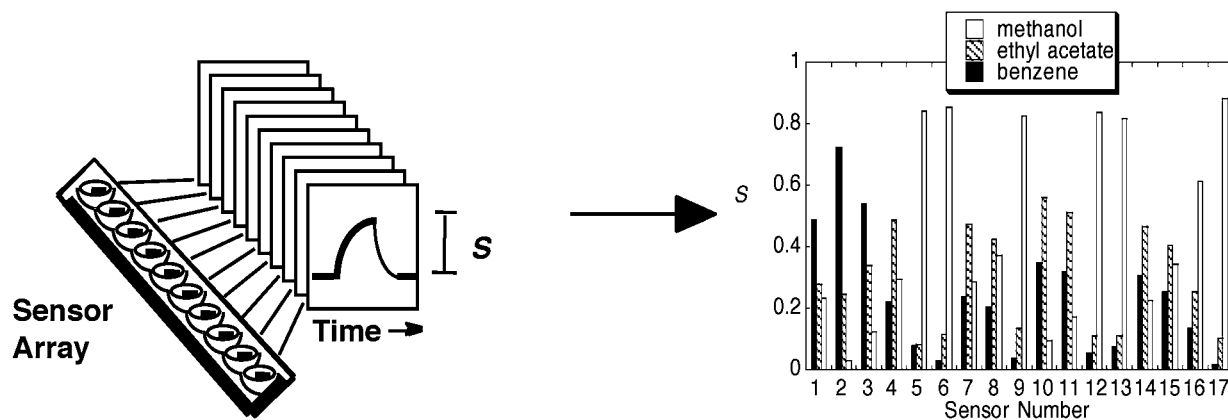


FIGURE 1. Differentiation between odorants through use of combinatorially encoded response patterns from a broadly cross-reactive sensor array.

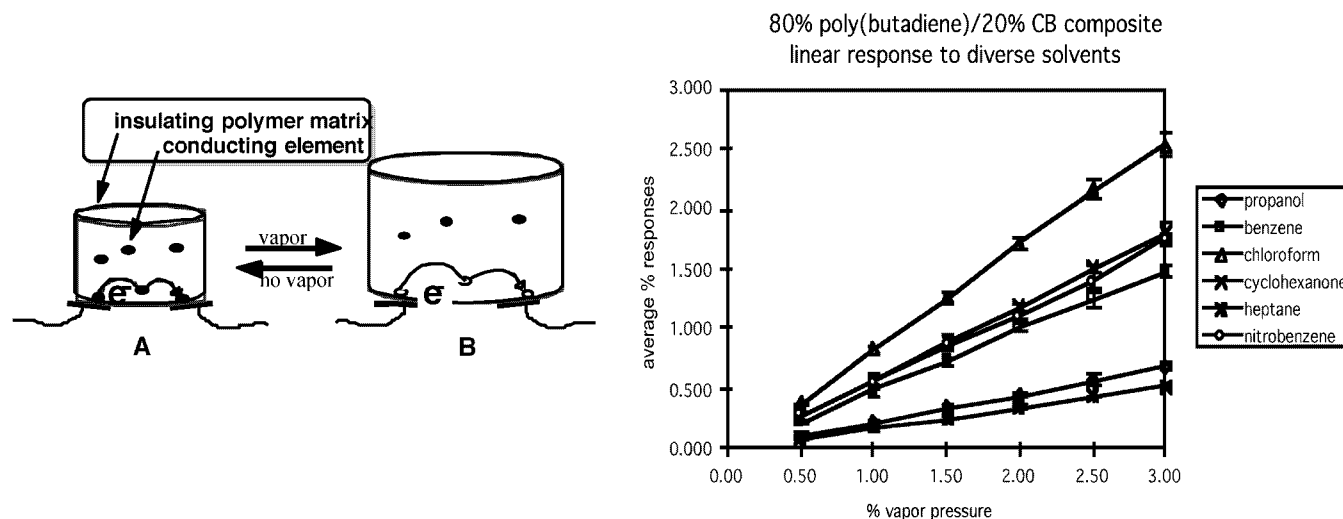


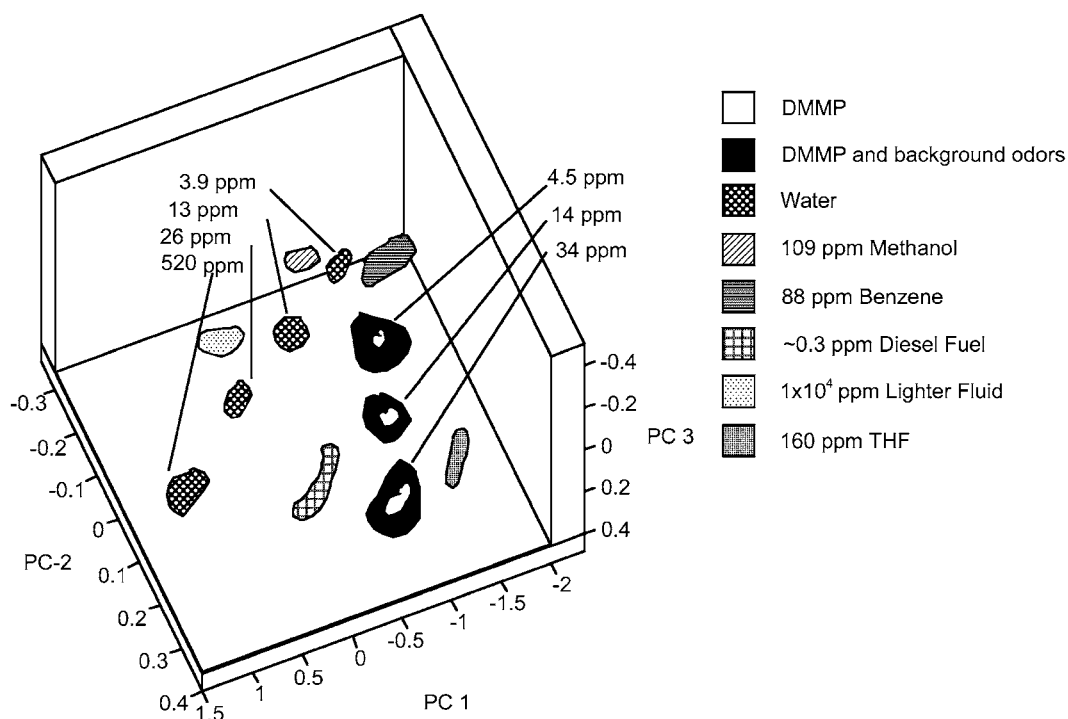
FIGURE 2. Swelling-induced resistance changes (a) of polymer composite vapor sensors and (b) linearity of response vs analyte concentration.

## II. Properties of Individual Polymer—Conductor Composite Chemiresistor Vapor Sensors

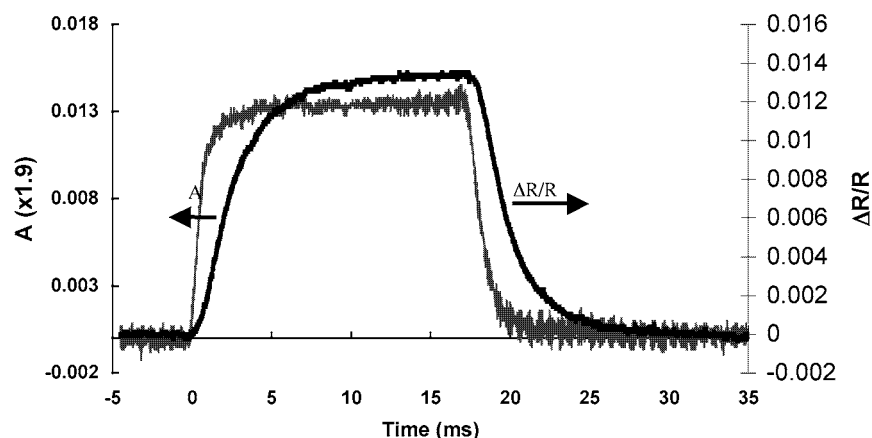
**1. Basic Sensing Characteristics.** We first consider the response properties of the individual sensors. The relative differential resistance response,  $\Delta R/R_b$ , where  $R_b$  is the baseline resistance of the sensor before exposure to the analyte and  $\Delta R$  is the steady-state change in resistance upon exposure to the analyte, is a useful response descriptor (Figure 2a) because it is largely independent of the amount of carbon black loaded into the film, the thickness of the film, the time response of the sensor, and other process-related variables.<sup>9</sup> The ability to adjust the amount of the conductor in the insulating polymer allows for operation of the sensors in a highly desirable regime in which  $\Delta R/R_b$  is a linear function of the concentration of analyte in the vapor phase (Figure 2b).<sup>13,14</sup> This linearity of the sensor response greatly simplifies the signal processing of the response patterns produced by the sensor array because the pattern type identifies the analyte and the pattern amplitude is linearly related to the concentration of the analyte in the vapor phase.<sup>13,14</sup> Hence, the response of a sensor array can be described by a feature vector that is associated with that particular analyte.

**2. Response to Binary and Complex Mixtures of Analytes.** The response of the chemiresistive composite sensors to two analytes is generally a linear combination, weighted by the mole fraction sorbed into the polymer, of the response of the individual analytes. Hence, binary mixtures of analytes can be readily analyzed to yield the mole fraction and identity of the components of the mixture.<sup>9,13</sup> Additionally, the array response to a particular analyte is largely independent of the background in which the response is measured.<sup>13</sup> Hence, exposures to the nerve agent simulant dimethylmethylphosphonate, DMMP, even at concentrations of 10 ppb, produced the same response pattern whether the DMMP was exposed to the array in an air ambient or in the presence of a background that contained a high concentration of diesel fuel, lighter fluid, humidity, or other vapor combinations of interest (Figure 3).<sup>14</sup>

Like the human nose, the electronic nose devices are change-detection systems and cannot readily break down a complex mixture (i.e., wine) into its hundreds of different chemical components. However, arrays of broadly cross-reactive sensors can readily probe changes in complex analyte mixtures either over time or over a collection of samples. Accordingly, such sensor arrays are well-mated



**FIGURE 3.** Principal components plot showing that the response to DMMP (white ellipses) is different than that of other odorants and showing that DMMP produces the same response pattern in the presence of backgrounds of these other odorants (black ellipses).



**FIGURE 4.** Time response of a PEVA-carbon black chemiresistor (solid line) in response to a nearly square-wave pulse of methanol vapor (thin gray line).

to probing time-dependent changes in the environment, such as in the cabin air of the U. S. Space Shuttle,<sup>15</sup> or for use in quality control applications in the food, beverage, chemical, and medical industries.<sup>3</sup>

**3. Response Time and Reversibility.** The diffusion coefficients of small molecule permeants into polymers with low glass transition temperatures,  $T_g$ , are well-known to be in the range of  $10^{-7}$ – $10^{-8}$   $\text{cm}^2 \text{s}^{-1}$ .<sup>16</sup> Hence, for 200 nm film thicknesses, less than 1 s response times are expected for diffusion-driven analyte sorption and desorption processes into the polymer composite sensing films. Detailed time-response measurements on a poly-(ethylene-co-vinyl acetate), PEVA, carbon black composite detector are in accord with this expectation (Figure 4). The response of this particular system has been analyzed in detail using Fickian diffusion in conjunction with a model for the film involving a parallel arrangement of lamella of

swellable resistors.<sup>17</sup> The responses in Figure 4 are averages of 64 responses collected in <5 s, thereby illustrating the rapid, reversible response properties that can be obtained from these sensors.

**4. Sensing Mechanism.** Figure 5 presents data showing that the sensors indeed operate through a “smelling-by-swelling” mechanism. In this set of experiments, the relative thickness changes as monitored by ellipsometric measurements on unfilled polymer films have been related to the relative differential resistance changes of composites that contained the same swellable polymer material but which additionally contained the carbon black filler.<sup>18</sup> At the carbon black loading levels used in our work, the mass uptakes of analyte vapor were very similar for both filled and unfilled films. The data of Figure 5 thus show that the thickness change is linearly related to the resistance change of such films, and additionally

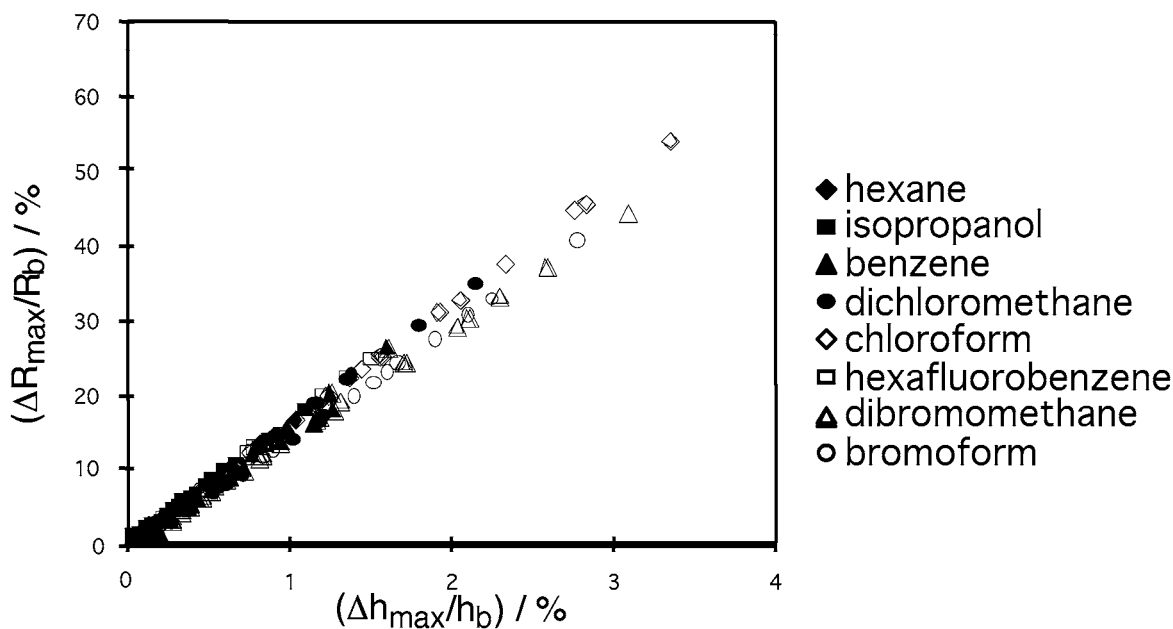


FIGURE 5. Relative differential resistance response vs relative thickness change for a poly(caprolactone)-carbon black composite exposed to a series of analytes at a variety of concentrations.

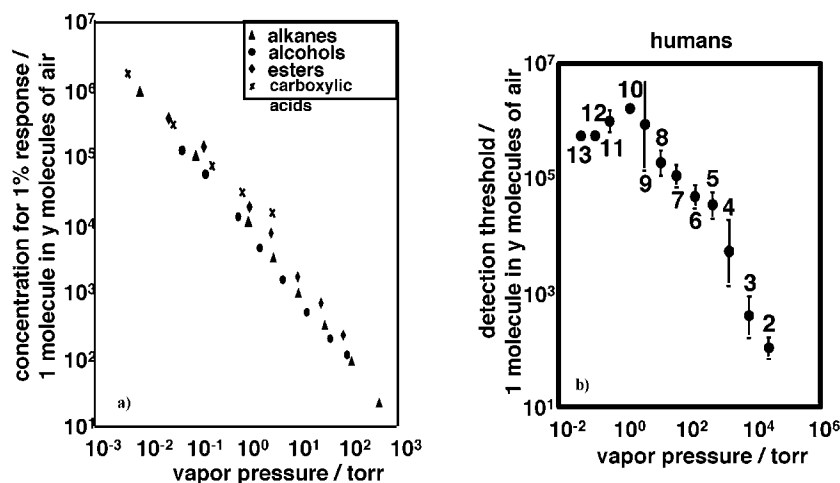


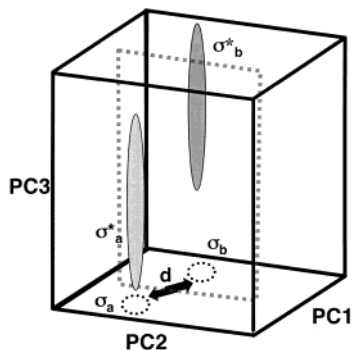
FIGURE 6. Comparison of sensitivity trends for (a) a carbon black-polymer composite sensor array and (b) mean human olfactory detection thresholds to *n*-alkanes as a function of the vapor pressure of the analyte at room temperature.

that a given thickness change produces a given resistance change regardless of the analyte. Hence the carbon black particles act as an inert filler that transduces the swelling-induced film thickness change into a dc electrical resistance change.<sup>18,19</sup>

**5. Sensitivity Characteristics.** The sensitivity of these sorption-based sensors can be readily understood by considering the  $\Delta R/R_b$  response as a function of the thermodynamic activity of analyte in the vapor phase, which is the pressure of the analyte,  $P$ , divided by its vapor pressure,  $P^\circ$ , at the temperature of interest (generally room temperature). Figure 6a presents the array sensitivity toward a homologous series of compounds, including a series of alkanes, alcohols, and esters.<sup>20,21</sup> The ordinate of Figure 6a is the concentration of analyte required to produce an average 1%  $\Delta R/R_b$  response over an array of chemically diverse carbon black-polymer composite sensors, and the abscissa indicates the vapor pressure of the

analyte of interest. For comparison, Figure 6b depicts the mean human olfactory detection thresholds for a homologous series of hydrocarbons.<sup>22</sup> The data clearly show that on a concentration basis, both the human olfactory system and the sorption-based carbon black-polymer composite sensors exhibit increasing sensitivity in a homologous series to compounds that have lower vapor pressures.

This behavior can be understood through consideration of the thermodynamics of sorption of analytes into polymers. At equilibrium, the chemical potential of the analyte must be equal in all phases of interest. Hence, the sorbed analyte concentration is given by  $P/P^\circ = \alpha\chi$ , where  $\alpha$  is the activity coefficient and  $\chi$  is the mole fraction of analyte in the polymer film. Because  $\alpha$  is not very different for sorption of a homologous series of analytes into an individual polymer film, the value of  $\chi$  for the different analytes in a homologous series is determined primarily by the variation in  $P^\circ$ . In the electronic nose, the equi-



**FIGURE 7.** Classification of analytes based on the Fisher linear discriminant. The ellipses enclose data from repeated exposures to the two different analytes, and the hyperplane is normal to the vector that maximizes the discrimination between the different analyte clusters.

bration of the polymer composite sensors with analyte vapor is ensured by limiting the analysis of  $\Delta R/R_b$  to the signals obtained at steady state. It is not clear that humans detect odors under equilibrium conditions; nevertheless, the similarity between the response trends for the human and artificial olfactory systems suggests that sorption of the odorant into the mucous is a primary factor in determining the sensitivity to the odorant in the human olfactory system. At constant  $P/P^0$ , the differences between  $\alpha$  values for a given analyte sorbing into different polymers determines the differences in response patterns that are produced for those analytes at a fixed value of  $P/P^0$ . The data of Figure 6 furthermore indicate that for most simple volatile organic compounds, the carbon black–polymer composites have a vapor phase detection limit that is similar to, or slightly better than, that of the average human.

### III. Properties of Sensor Arrays

Having established the response properties and response mechanisms of the individual carbon black–polymer composite vapor sensors, we now consider the analysis of the patterns of signals produced by the sensor array. A quantitative analysis of the differences between two array response patterns requires the use of a signal processing algorithm. We prefer to utilize statistical methods that facilitate understanding of the classification performance inherent in the data, as opposed to neural network methods in which the overall performance of a system is intimately linked to the performance of a particular algorithm as it couples to the data set of interest.

#### 1. Classification Using the Fisher Linear Discriminant.

A useful approach is to utilize the Fisher linear discriminant, which is a supervised classification algorithm.<sup>23</sup> In this approach, exposures to two analytes, A and B, are collected in a training set period. The exposures are then sorted by analyte, and the vector,  $\bar{w}$ , is determined along which the two different data sets are maximally separated. A hyperplane is then constructed normal to this vector with the position of the hyperplane determined by the relative weightings of the standard deviations of the data for the two analyte classes (Figure 7). Hence, a data point

that falls on the hyperplane has an equal probability of being a member of either of the two analyte classes. Subsequent (unknown) analyte exposures that fall on one side of this decision boundary are designated to be one analyte, and exposures that fall on the other side of the boundary are designated to be the other analyte. Use of the Fisher linear discriminant ensures that sensors are weighted by the signal/noise that they contribute to the discrimination task of interest and noisy sensors are only weighted for tasks in which they are useful (i.e., noisy chiral sensors would only be weighted significantly for use in chiral discrimination tasks, etc.). The entire response space of a collection of analytes can be parsed up into a collection of such pairwise decision boundaries. To the extent that the array response patterns are independent of analyte concentration, only one discriminant boundary is necessary for each analyte pair, provided that the data are first sum-normalized (i.e., mapped onto the unit sphere) to remove any concentration-dependent terms from the analysis.

Table 1 shows some representative rf values for a set of different vapor discrimination tasks obtained from concentration-normalized response data on an array of 14 carbon black–polymer composite sensors<sup>11</sup> with rf defined as follows:

$$\text{rf} = \frac{d_{\bar{w}}}{\sqrt{\sigma_{a,\bar{w}}^2 + \sigma_{b,\bar{w}}^2}} (>)$$

where  $d_{\bar{w}}$  is the distance between cluster centroids and  $\sigma_{a,\bar{w}}$  and  $\sigma_{b,\bar{w}}$  are the standard deviations arising from repeated exposures to A and B projected along  $\bar{w}$ . The minimum rf value for the 153 pairwise analyte separation tasks was 28, and the mean value was 140. Hence, even though the array was not designed in advance to be specific toward any individual odorant, robust discrimination is present for a wide range of analytes. Robust discrimination has been shown between, for example, *o*-xylene and *p*-xylene, *R*-2-butanol and *S*-2-butanol, 1-propanol and 2-propanol, compositionally close mixtures of hexane and heptane, and H<sub>2</sub>O and D<sub>2</sub>O.<sup>11,24</sup> This level of discrimination strikingly emphasizes that an array of even relatively unselective sensors, taken together in analyzing their collective response properties, can provide a powerful discrimination tool for classifying and quantifying organic vapor analytes.

It is also possible to evaluate analyte classification performance using other discriminants, including those that are nonlinear and can therefore produce a decision boundary that is more precisely tailored to the form of the array response data. For Gaussian sensor responses arising from multiple exposures to analytes that produce two well-separated analyte clusters in odor space, nonlinear algorithms will generally not outperform the Fisher linear discriminant. In fact, such algorithms generally will produce marginally worse performance due to the need estimate more parameters in construction of the nonlinear decision surface.<sup>24</sup> Hence, when the sensors are sufficiently chemically diverse that analytes are robustly sepa-



Table 1. Resolution Factors between Various Solvent Pairs

	acetone	acetonitrile	anisole	benzene	butylamine	chloroform	cyclohexane	dichloromethane	ethanol	ethyl acetate	isopropanol	methanol	n-heptane	n-pentane	tetrahydrofuran	toluene	triethylamine	trifluorotoluene
1,2-dimethoxyethane	121	194	71	49	58	95	287	130	135	164	184	230	156	354	130	179	73	119
acetone		51	102	98	44	106	88	42	58	93	107	41	95	172	42	227	138	198
acetonitrile			154	173	54	153	152	73	58	171	207	75	119	135	88	317	174	200
anisole				106	23	178	146	130	107	126	131	129	140	182	145	59	78	60
benzene					52	65	177	132	117	58	140	202	112	195	102	229	47	82
butylamine						55	63	53	48	36	82	86	76	54	48	41	57	65
chloroform							123	102	122	133	126	204	92	231	159	303	146	180
cyclohexane								109	103	180	108	151	202	152	153	528	132	312
dichloromethane									57	121	60	72	132	54	63	489	246	384
ethanol										119	102	57	77	77	51	279	125	137
ethyl acetate											88	201	123	181	59	253	122	151
isopropanol												135	161	119	73	313	218	206
methanol													107	58	87	401	308	260
n-heptane														177	161	380	156	90
n-pentane															217	556	171	343
tetrahydrofuran																359	93	178
toluene																	246	180
triethylamine																		168

rated based on their different sorption characteristics on the array, a relatively simple, linear algorithm is sufficient to provide excellent classification performance. In cases where the analyte response clusters are extremely close together, a nonlinear decision boundary can improve classification performance in certain cases.<sup>25</sup>

**2. Classification Performance as a Function of Array Diversity.** A fundamental question arises with respect to how many sensors are sufficient to span the rank of smell space, that is, to produce robust discrimination between any two possible odorants. Clearly, no two analytes can elute with precisely identical retention times down an extremely long column having a chiral supporting phase. Hence, measurement of only a single parameter, with sufficient precision, is in principle sufficient to discriminate between any two analytes of interest. Of course, the practically realizable discrimination ability of a real sensor array system is determined by the interplay between the precision of the measurement on each sensor and the signal/noise and variability of the sensors in the array. For a given task, typically 5–10 sensors possess most of the variance that is needed to separate two analytes of interest.<sup>26</sup>

However, both experimental data and fundamental considerations reveal that a different collection of 5–10 broadly cross-reactive sensors will provide the best performance for different analyte separation tasks.<sup>26</sup> Figure 8 shows the subsets of a 20-sensor carbon black–polymer composite sensor array that provided optimal discrimination for four different discrimination tasks. The hydrophobic sensors responded most strongly and contained the best signal/noise and discrimination ability for separating hexane from heptane, while the polar sensors provided the best performance for separating 1-propanol from 2-propanol. Other five-sensor subsets of the 20-sensor array were optimal for other analyte separation

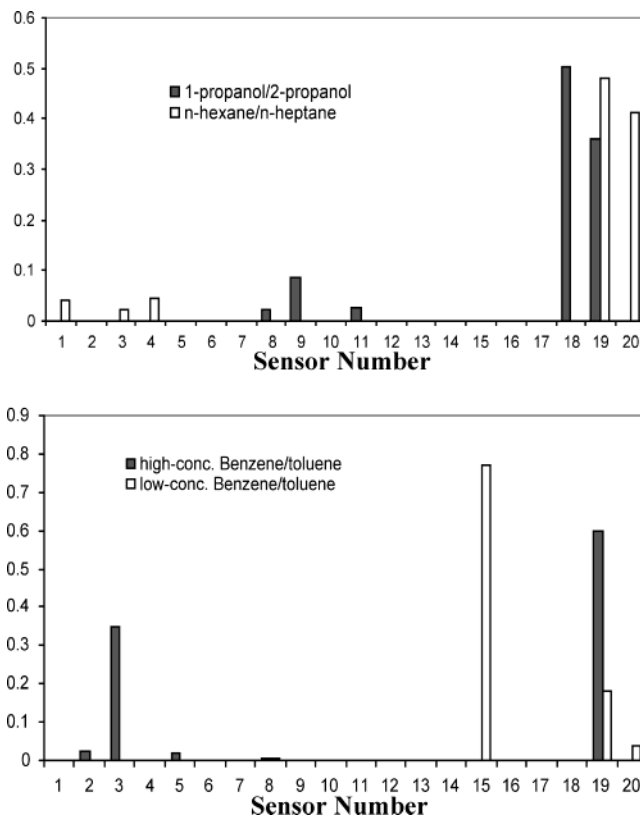
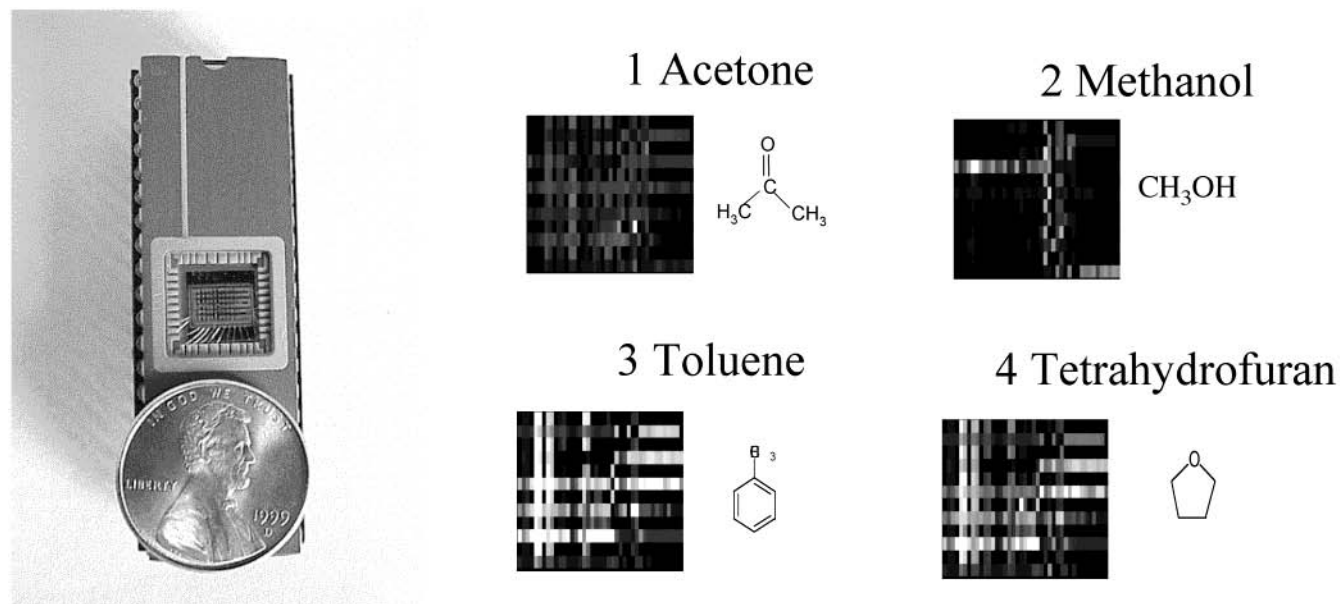


FIGURE 8. Weightings of five-sensor subsets of a 20-sensor chemiresistor array that produced maximal classification performance in different pairwise analyte separation tasks, showing that different five-sensor subsets provided optimal classification performance for different tasks.

tasks, and still other five-sensor subsets were optimal for separations performed at high vs low analyte concentrations. Any individual sensor subset was outperformed in at least some separation task by either another equally sized sensor subset or the entire set of 20 sensors or both.<sup>26</sup>



**FIGURE 9.** Photograph (a) of a  $6 \times 12$  sensor array fabricated on a Si chip that contained a row–column multiplexer and readout circuitry to send the signals to a single pinout and (b) response patterns produced upon exposure of a denser sensor chip to four different analytes.

Thus, provided that the cost of adding sensors and associated data analysis is not prohibitive, better overall performance can be obtained by collecting all of the data on the entire array of sensors and then selecting the optimal sensor sets for the task of interest, as opposed to selection of sensors for a particular task in advance and therefore discarding sensors that are optimal for some other, subsequent task for which the array might be used.

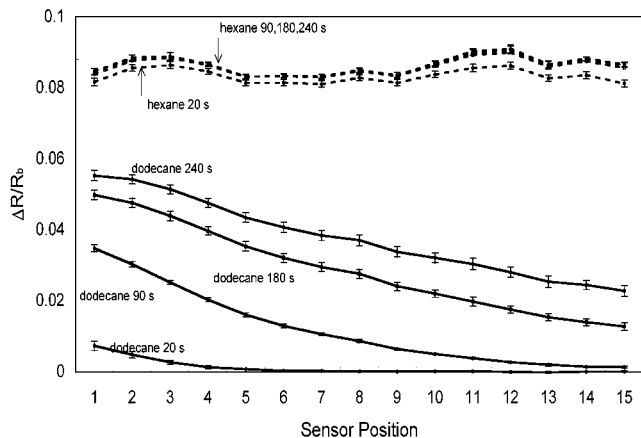
To exploit these principles, we have constructed “nose chips” that contain many sensors in a relatively small spatial footprint (Figure 9).<sup>27</sup> The sensors are prepared combinatorially by first spraying selected polymer composites onto the rows of the chip and then spraying other composites onto the columns of the chip. Still greater chemical diversity could be achieved by spraying a plasticizer, another compositionally different material, or both diagonally across the array. Each electrical cell contains a transistor-based switch that only is closed, and allows a current to pass, when +5 V is applied to both its row lead and its column lead. The resulting voltage signal produced by the chemically sensitive resistor in the addressed electrical cell is then routed to a common output pin, and the time sequence of the signals at that output pin allows a mapping of the observed response to the spatial position of the sensor on the chip. Such “nose chips” allow robust discrimination between odorants, are relatively insensitive to the degradation of an individual sensing cell, and provide a simple approach to preparing large numbers of chemically distinct sensors for use in a wide range of vapor classification and discrimination tasks.

Another aspect of using large numbers of sensors is facile calibration of the array response. If the array has been trained on a large number of odorants, it is highly desirable to reestablish classification performance and thereby correct for any residual sensor response drift through use of a relatively small subset of analytes as a

calibration set. Measurements have shown that carbon black–polymer composite sensor arrays exhibit relatively little response drift and use of a Fisher linear discriminant classification model developed from an initial training set produces error-free classification performance even after 1 month of continuous use in discrimination between analytes such as *n*-hexane vs cyclohexane and *n*-octane vs isooctane. Even for low concentrations of *n*-hexane vs *n*-heptane, calibration of the entire array response after a 1 month period could be reestablished robustly with the use of a few carefully chosen analytes as calibrants of the array response.<sup>24,28</sup>

**3. Spatiotemporal Aspects of Odor Detection and Discrimination.** Another interesting feature of the mammalian olfactory system is the relatively recent finding that perception of odor mixtures is distinctly different in the different nostrils of the same human. Specifically, the flow rate at which sniffing occurs affects the human perception of an odor mixture.<sup>29</sup> To explore this in an artificial system, we constructed an array in which each sensor was placed in a different location relative to a defined analyte flow path.<sup>30</sup> The hypothesis being evaluated was that, under laminar flow conditions, the same odorant should yield different patterns of response if the receptor signals are monitored as a function both of the time relative to the initial sniff and the spatial position of the receptor in the odor sampling chamber.

Figure 10 illustrates representative sensor responses for two different analytes as a function of time on an array of poly(ethylene-*co*-vinyl acetate)–carbon black sensors. Analytes with a small polymer/vapor sorption coefficient produced an equal response on all of the sensors at even short times with the time delay between sensor responses determined solely by the flow rate of analyte along the path of the array. In contrast, analytes with large polymer/vapor sorption coefficients were sorbed strongly into the first sensors that were encountered by the analyte flow.



**FIGURE 10.** Time dependence of the response of hexane and dodecane on an array of nominally identical PEVA-carbon black sensors showing the different responses as a function of position and time relative to the injection of analyte vapor. The responses for dodecane are also a function of the analyte flow velocity in the sensor chamber.

This sorption of analyte by the first sensor locally depleted analyte vapor from the flow stream and thereby produced a smaller response from the sensors located at positions downstream of the first position in the array. The effect persisted until additional analyte was provided to the other sensor locations, at which point all of the sensors produced equivalent responses. The effect was dependent on both the type and flow rate of the analyte and therefore allowed discrimination between analytes by variation in the sampling flow rate. Clearly, this behavior offers a natural explanation of how the mammalian olfactory system can perceive the same odorant differently at different flow rates and also offers a mechanism for obtaining additional discrimination power between components of complex odor mixtures in an artificial olfactory sensing system.<sup>30</sup>

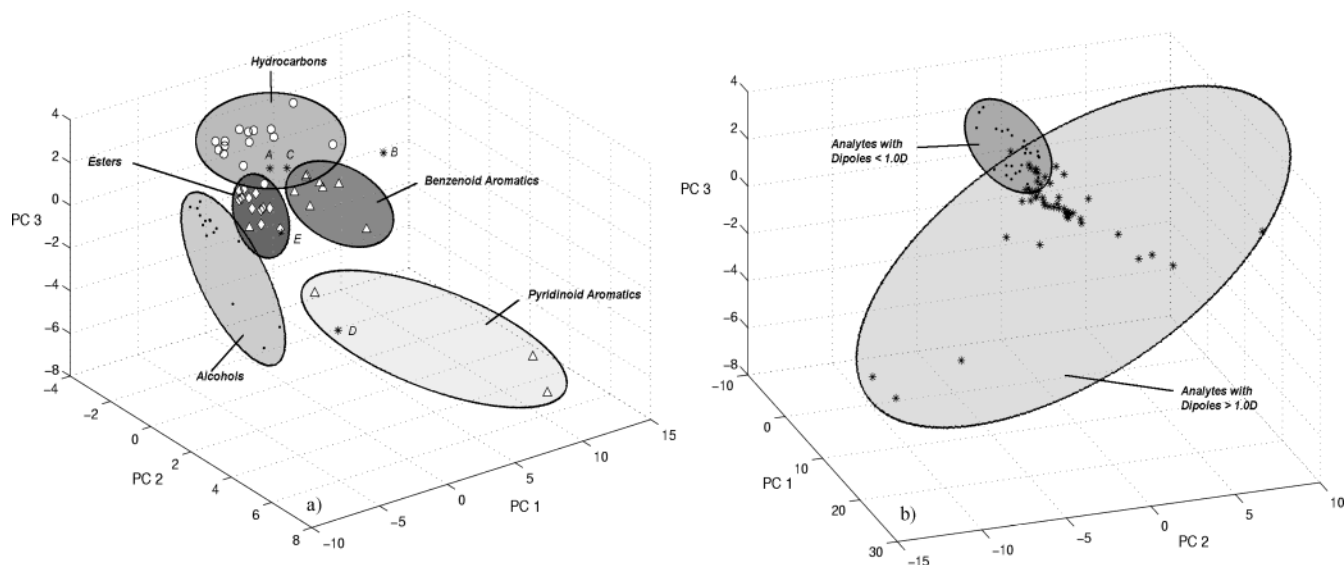
**4. Geometric Optimization of Signal/Noise For Detection of Analytes.** The different responses to a particular analyte of compositionally identical sensors that were located at different positions in space indicated that analyte detection should be a function of the geometric form factor of the sensors in an array. At sufficiently long times, the compositionally identical sensors responded equally no matter where they were located in space, so under such conditions averaging their responses together would yield an improved signal/noise ratio for analyte detection. However, at shorter times, only the first few detectors in the array responded to the analyte, indicating that the remaining sensors contributed noise, but not signal, to the analysis. Hence different geometric areas of the same sensor composition should be optimal for analysis of different analytes. To investigate this issue experimentally, an array was constructed with sensors having two extremes of geometric area, one being very small in area and positioned such that it was immediately impacted by the analyte flow, and the other being much larger in area and positioned to interact at a later time with the analyte flow.<sup>30,31</sup>

The noise in carbon black-polymer chemiresistors has been shown to decrease proportionally to the square root of the area of the sensor film (at constant film thickness), as expected for  $1/f$  noise on length scales longer than the coherence length of the percolative network of conductor in the carbon black-polymer composite.<sup>30</sup> Hence for analytes with small polymer/gas partition coefficients, large sensor areas are optimal because they provide a decreased noise and a constant signal strength at a given vapor phase concentration of analyte. In contrast, analytes with large polymer/vapor partition coefficients will be strongly sorbed into the first, small sensor area that they encounter, and no additional analyte will be available to sorb into subsequent sensor films. In this situation, increasing the sensor area will dilute the sorbed analyte, providing less signal and offering only a modest compensating reduction in the sensor noise level. An optimal sensor area can be derived analytically at which the signal-to-noise ratio is maximized with the optimal area depending only on the partition coefficient and the flow rate of analyte over the sensor array.<sup>30</sup> Optimally, an exponentially increasing grid of sensor areas would be positioned parallel to the flow with an array of sensor compositions placed perpendicular to the analyte flow. It is not yet clear whether this principle is implemented in a biological olfactory system, but it is clear that an optimized odor detection device would take advantage of this basic physical phenomenon.

**5. Superstructure of Odor Space.** If no two analytes produce identical response patterns on a sufficiently chemically diverse array of sensors, then the important chemical properties in all of the analytes are likely being probed by the array of sensors. Hence, another set of questions involves whether analytes that produce responses in a common region of odor space are related chemically, physically, or both to each other. Specifically, is there a superstructural organization to the response space produced by the sensor array such that by cataloging the properties of neighboring, known analytes, associated chemical or physical properties can be robustly assigned to an analyte that has not been previously presented to the array?

As displayed in Figure 11, analysis of the responses of a carbon black-polymer composite chemiresistor array indicates that with some robustness chemical class, chain length, unsaturation, molecular size, and dipole moment information can be assigned to unknown analytes.<sup>32</sup> An analyte's response can also be projected onto a biological activity, such as the binding constant for competitive inhibition of alcohols in the para-hydroxylation of aniline by cytochrome P-450.<sup>33</sup> The correlation between the properties and sensor array response of an analyte should be robust for properties that are driven by thermodynamic partitioning (blood-brain barrier crossing, binding to albumin, etc.) and possibly even, in certain scenarios, for kinetically driven properties. However, it is not possible at present to correlate robustly the electronic nose array response of an analyte to its perceived human odor quality.<sup>34</sup> Such a correlation fails in part because human





**FIGURE 11.** Clustering of 75 different analytes in principal components space with ellipses drawn according to (a) functional group class or (b) dipole moment of the analyte.

olfaction is a nonlinear system and the carbon black–polymer composites are linearly responding sensors and in part because little quantitative information exists on precisely how differently two odorants are perceived by humans. The latter shortcoming prevents establishment of a self-consistent analytical mapping from artificial olfactory space to human perceptual olfactory space.

**6. Sensitivity Enhancements for Targeted Classes of Odorants.** Finally, we discuss the responses to two classes of analytes to which humans are extraordinarily sensitive, thiols and amines. These odors are metabolic byproducts of certain bacteria,<sup>35,36</sup> so humans might have developed enhanced sensitivity to these odorants to assist in the olfactory-based identification of unhealthy food samples. Sorption of the light gases  $\text{H}_2\text{S}$  or methylamine into polymers is not expected to be significantly stronger than sorption of, for example, water or methanol into the same polymers.

We have identified two separate sensing mechanisms that can provide enhanced detection sensitivity for volatile amines and thiols. Clearly, amines are unique in being volatile organic compounds that are also reasonable Brønsted bases. Carbon black–polymer composites formed from dendrimers having deprotonatable charged groups on their periphery undergo acid–base interactions with volatile amines, and the resulting change in charge on the dendrimer periphery greatly affects the swelling of the polymer composite. This swelling change produces a large enhancement in the resistance response of such chemiresistors in the presence of organic amines. Use of an array of compositionally different dendrimers then allows identification of the type of amine.<sup>37</sup> A similar approach has been used to obtain enhanced sensitivity toward volatile carboxylic acids that are important in certain disease diagnostics.<sup>38</sup>

For thiols, the interactions with organic functionality are expected to be much weaker than those of alcohols. Yet humans are more sensitive to  $\text{CH}_3\text{SH}$  than to  $\text{CH}_3\text{OH}$

by a factor of approximately  $10^6$ . To sensitively detect thiols using chemiresistors, we have made sensors using Au colloids that are capped by long-chain alkylamines. Sorption of a small quantity of thiol vapor into such films only produces a small amount of swelling, but the thiol displaces the long-chain alkylamine caps and introduces short-chain thiol caps, producing a large decrease in the resistance of the sensing film.<sup>39</sup> This reaction is of course irreversible, but nevertheless provides a mechanism for obtaining sensitivity enhancements to thiols so that the array is comparable in detection sensitivity to humans. Approaches such as these appear to be useful to provide targeted screens for particular classes of compounds while obtaining high sensitivity to specific classes of odors detected with high sensitivity by the human olfactory system.

## IV. Summary

In summary, bioinspired olfactory systems can provide useful test beds for investigating the collective behavior of arrays of broadly cross-reactive sensors and for elucidating the basis for some of the phenomena displayed by mammalian olfactory systems. Collections of such sensors can provide excellent discrimination performance, along with good sensitivity, short response times, and reversible behavior, for a variety of organic vapors. Similarities and differences between the behavior both at the sensor level and at the systems level of the artificial and biological olfactory systems can provide useful insight into the organizing principles of olfaction. Polymer–conductor composite chemically sensitive resistors provide an especially simple implementation of the array-based sensing approach and allow investigation of a wide variety of phenomena from odor tracking and localization to odor classification and odor quality assignment in an artificial olfactory system. The ultimate goal of producing an artificial olfactory system that is indistinguishable in

system-level performance from that of a human or a canine has not yet been achieved, but good progress is being made toward this goal through use of new array-based sensing systems in conjunction with continued advances in algorithmic analysis of the output signals of such sensor arrays.

*The investigations described herein were performed by an extremely talented group of graduate students and postdoctoral fellows. These people, cited as coauthors in the reference list, along with generous support from the ARO, DARPA, DOE, NASA, NIH, and NSF, have made this work possible.*

## References

- Buck, L.; Axel, R. A novel multigene family may encode odorant receptors – a molecular-basis for odor recognition. *Cell* **1991**, *65*, 175–187.
- Axel, R. The molecular logic of smell. *Sci. Am.* **1995**, *273*, 154–159.
- Gardner, J. W.; Bartlett, P. N. *Electronic noses: Principles and applications*; Oxford University Press: Oxford, U.K., 1999.
- Moore, S. W.; Gardner, J. W.; Hines, E. L.; Gopel, W.; Weimar, U. A modified multilayer perceptron model for gas-mixture analysis. *Sens. Actuators, B* **1993**, *16*, 344–348.
- Gardner, J. W.; Hines, E. L.; Tang, H. C. Detection of vapors and odors from a multisensor array using pattern-recognition techniques. 2. Artificial neural networks. *Sens. Actuators, B* **1992**, *9*, 9–15.
- Albert, K. J.; Lewis, N. S.; Schauer, C. L.; Sotzing, G. A.; Stitzel, S. E.; Vaid, T. P.; Walt, D. R. Cross-reactive chemical sensor arrays. *Chem. Rev.* **2000**, *100*, 2595–2626.
- Harsanyi, G. *Polymer films in sensor applications*; Technomic: Lancaster, PA, 1995.
- Freund, M. S.; Lewis, N. S. A chemically diverse conducting polymer-based electronic nose. *Proc. Natl. Acad. Sci. U.S.A.* **1995**, *92*, 2652–2656.
- Lonergan, M. C.; Severin, E. J.; Doleman, B. J.; Beaber, S. A.; Grubbs, R. H.; Lewis, N. S. Array-based vapor sensing using chemically sensitive, carbon black–polymer resistors. *Chem. Mater.* **1996**, *8*, 2298–2312.
- Koscho, M. E.; Grubbs, R. H.; Lewis, N. S. Properties of vapor detector arrays formed through plasticization of carbon black–organic polymer composites. *Anal. Chem.* **2002**, *74*, 1307–1315.
- Doleman, B. J.; Lonergan, M. C.; Severin, E. J.; Vaid, T. P.; Lewis, N. S. Quantitative study of the resolving power of arrays of carbon black–polymer composites in various vapor-sensing tasks. *Anal. Chem.* **1998**, *70*, 4177–4190.
- Severin, E. J.; Sanner, R. D.; Doleman, B. J.; Lewis, N. S. Differential detection of enantiomeric gaseous analytes using carbon black–chiral polymer composite, chemically sensitive resistors. *Anal. Chem.* **1998**, *70*, 1440–1443.
- Severin, E. J.; Doleman, B. J.; Lewis, N. S. An investigation of the concentration dependence and response to analyte mixtures of carbon black/insulating organic polymer composite vapor detectors. *Anal. Chem.* **2000**, *72*, 658–668.
- Hopkins, A. R.; Lewis, N. S. Detection and classification characteristics of arrays of carbon black/organic polymer composite chemiresistive vapor detectors for the nerve agent simulants dimethylmethylphosphonate and diisopropylmethylphosphonate. *Anal. Chem.* **2001**, *73*, 884–892.
- Ryan, M. A.; Lewis, N. S. Low power, lightweight vapor sensing using arrays of conducting polymer composite chemically sensitive resistors. *Enantiomer* **2001**, *6*, 159–170.
- Fujita, H. *Diffusion in polymers*; Academic Press: New York, 1968.
- Briglin, S. M.; Lewis, N. S. Characterization of the temporal response profile of carbon black–polymer composite detectors to volatile organic vapors. *J. Phys. Chem. B* **2003**, *107*, 11031–11042.
- Severin, E. J.; Lewis, N. S. Relationships among resonant frequency changes on a coated quartz crystal microbalance, thickness changes, and resistance responses of polymer–carbon black composite chemiresistors. *Anal. Chem.* **2000**, *72*, 2008–2015.
- Tillman, E. S.; Lewis, N. S. Mechanism of enhanced sensitivity of linear poly(ethylenimine)–carbon black composite detectors to carboxylic acid vapors. *Sens. Actuators, B* **2003**, *96*, 329–342.
- Doleman, B. J.; Severin, E. J.; Lewis, N. S. Trends in odor intensity for human and electronic noses: Relative roles of odorant vapor pressure vs molecularly specific odorant binding. *Proc. Natl. Acad. Sci. U.S.A.* **1998**, *95*, 5442–5447.
- Doleman, B. J.; Lewis, N. S. Comparison of odor detection thresholds and odor discriminabilities of a conducting polymer composite electronic nose versus mammalian olfaction. *Sens. Actuators, B* **2001**, *72*, 41–50.
- Devos, M.; Patte, F.; Rouault, J.; Laffort, P.; Van Gemert, L. J. *Standardized human olfactory thresholds*; Oxford University Press: New York, 1990.
- Duda, R. O.; Hart, P. E. *Pattern classification and scene analysis*; John Wiley & Sons: New York, 1973.
- Vaid, T. P.; Burl, M. C.; Lewis, N. S. Comparison of the performance of different discriminant algorithms in analyte discrimination tasks using an array of carbon black–polymer composite vapor detectors. *Anal. Chem.* **2001**, *73*, 321–331.
- Pardo, M.; Sisk, B. M.; Lewis, N. S., submitted for publication.
- Burl, M. C.; Sisk, B. C.; Vaid, T. P.; Lewis, N. S. Classification performance of carbon black–polymer composite vapor detector arrays as a function of array size and detector composition. *Sens. Actuators, B* **2002**, *87*, 130–149.
- Dickson, J. A.; Freund, M. S.; Lewis, N. S.; Goodman, R. A. *Proceedings of the Hilton Head Conference*; Hilton Head, SC, 2000.
- Sisk, B. M.; Lewis, N. S. *Sens. Actuators, B*, in press.
- Sobel, N.; Khan, R. M.; Saltman, A.; Sullivan, E. V.; Gabrieli, J. D. E. Olfaction – the world smells different to each nostril. *Nature* **1999**, *402*, 35.
- Briglin, S. M.; Freund, M. S.; Tokumaru, P.; Lewis, N. S. Exploitation of spatiotemporal information and geometric optimization of signal/noise performance using arrays of carbon black–polymer composite vapor detectors. *Sens. Actuators, B* **2002**, *82*, 54–74.
- Briglin, S. M.; Burl, C. M.; Freund, M. S.; Lewis, N. S.; Matzger, A.; Ortiz, D. N.; Tokumaru, P. Progress in use of carbon black–polymer composite vapor detector arrays for land mine detection. *Proc. SPIE–Int. Soc. Opt. Eng.* **2000**, *4038*.
- Sisk, B. M.; Lewis, N. S. Estimation of chemical and physical characteristics of analyte vapors through analysis of the response data of arrays of polymer–carbon black composite vapor detectors. *Sens. Actuators, B* **2003**, *96*, 268–282.
- Vaid, T. P.; Lewis, N. S. The use of ‘electronic nose’ sensor responses to predict the inhibition activity of alcohols on the cytochrome p-450 catalyzed p-hydroxylation of aniline. *Bioorg. Med. Chem.* **2000**, *8*, 795–805.
- Burl, M. C.; Doleman, B. J.; Schaffer, A.; Lewis, N. S. Assessing the ability to predict human percepts of odor quality from the detector responses of a conducting polymer composite-based electronic nose. *Sens. Actuators, B* **2001**, *72*, 149–159.
- Simenhoff, M. L.; Burke, J. F.; Saukkonen, J. J.; Ordinario, A. T.; Doty, R. Biochemical profile of uremic breath. *N. Engl. J. Med.* **1977**, *297*, 132–135.
- Preli, G.; Clark, L.; Cowart, B. J.; Feldman, R. S.; Lowry, L. D.; Weber, E.; Young, I. M. Nonoral etiologies of oral malodor and altered chemosensation. *J. Periodontol.* **1992**, *63*, 790–796.
- Gao, T.; Tillman, E. S.; Lewis, N. S. Detection and classification of volatile organic amines and carboxylic acids using arrays of carbon black–dendrimer composite vapor detectors. Submitted for publication.
- Tillman, E. S.; Koscho, M. E.; Grubbs, R. H.; Lewis, N. S. Enhanced sensitivity to and classification of volatile carboxylic acids using arrays of linear poly(ethylenimine)–carbon black composite vapor detectors. *Anal. Chem.* **2003**, *75*, 1748–1753.
- Briglin, S. M.; Gao, T.; Lewis, N. S. Detection of organic mercaptan vapors using thin films of alkylamine-passivated gold nanocrystals. *Langmuir* **2004**, *20*, 299–305.

AR030120M