From *Artificial Chemical Sensing: Olfaction and the Electronic Nose*, Stetter, J.R.; Pensrose, W.R., eds. Electrochem. Soc.: Pennington, NJ, 2001, pp. 8-14.

A COLORIMETRIC NOSE: "SMELL-SEEING"

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Colorimetric array detection of a wide range of odorants has been achieved using a family of metalloporphyrins and other chemo-responsive dyes as immobilized on reverse phase silica gel. Color change patterns obtained from the array with an ordinary flat-bed scanner give striking visual identification of a range of ligating vapors (including alcohols, amines, ethers, phosphines, phosphites, thioethers, and thiols). Even weakly-ligating vapors such as arenes, halocarbons, and ketones can also be differentiated. Diffuse reflectance spectroscopy shows solid-state color changes similar to those known for ligation in solution. The array shows good linear response to single analytes, as well as unique responses for analyte mixtures. In best cases, limits of detection are in the tens of ppb and analytes can be readily identified well below 1 ppm.

INTRODUCTION

Array based vapor sensing has emerged as a powerful approach toward the detection of chemically diverse analytes. Based on cross-responsive sensor elements, rather than receptors for specific species, these systems produce composite responses unique to an odorant, in a fashion similar to the mammalian olfactory system (1). Previous array detectors for electronic noses (2) have employed a variety of strategies that have generally used relatively weak chemical interactions (e.g., physical adsorption), including the use of conductive polymers and polymer composites (3), fluorescent dye/polymer systems (4), tin oxide sensors (5), and polymer coated surface acoustic wave (SAW) devices (6). While previous systems have demonstrated success in chemical vapor detection and differentiation, their primary aim has been the detection of non-coordinating organic vapors. Array detection of metal-binding species, such as amines, phosphines, and thiols, has been relatively unexplored.

Metalloporphyrins are a natural choice for the detection of metal-ligating vapors because of their strong binding of nearly all metal ions, their open coordination sites for axial ligation to the metal ions, their excellent chemical and thermal stability, their large spectral shifts upon ligand binding, and their intense coloration. Metalloporphyrins have been previously employed for optical detection of gases such as oxygen (7) and ammonia (8), and for vapor detection as chemically interactive layers on quartz crystal microbalances (9). We have achieved colorimetric detection of a wide range of odorants using an array of metalloporphyrins as vapor-sensing dyes immobilized on reverse phase silica gel (10). These arrays are based primarily on libraries of metalated tetraphenylporphyrins, as shown in Figure 1.

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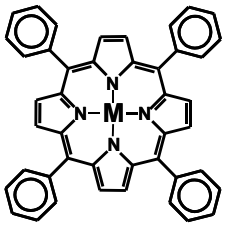

Figure 1. Chemical structure of metalated 5,10,15,20-tetra-phenylporphyrins, MTPP. TPP^{-2} is a dianion capable of strongly binding most M(II) and M(III) metal ions.

THE SMELL-SEEING ARRAY

When an array of metalloporphyrins deposited on an inert support (e.g., reverse phase silica gel) is exposed to various analytes, color changes in the various porphyrin complexes are observed, and the color changes are often dramatic. By simply subtracting the digital images of the array before and after exposure, one may obtain a quantitative color change pattern: we refer to this as "smell-seeing". As shown in Figure 2, these color change patterns give striking visual identification of a range of ligating vapors (including alcohols, amines, ethers, phosphines, phosphites, thioethers, and thiols). Weakly-ligating vapors such as arenes, halocarbons, and ketones can also be differentiated. Diffuse reflectance spectroscopy studies have shown that solid-state spectral shifts are similar to those known for ligation in solution. The array has demonstrated interpretable and reversible responses even to analyte mixtures of strong ligands, such as pyridines and phosphites. Color change patterns for mixtures are distinct from either of the neat vapors.

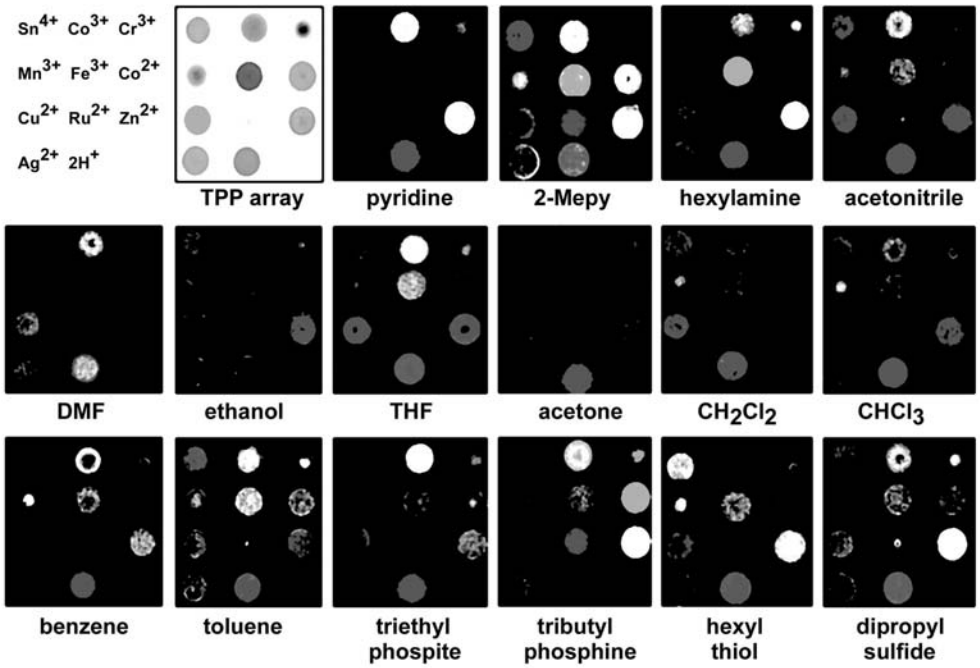

Figure 2. Color change profiles (shown in black and white) for a series of vapors; the degree of analyte softness (roughly the polarizability) increases from left to right, top to bottom. Analytes were delivered in nitrogen streams saturated with the vapor at 20°C. Images obtained upon full equilibration using an HP Scanjet 3C flatbed scanner. Difference maps were obtained by subtracting the RGB images (i.e., { |R(after exporsure to analyte) – R(before)|, |G(after exporsure to analyte) – G(before)|, |B(after exporsure to analyte) – B(before)| }, using Adobe Photoshop®.

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One of the most difficult issues facing current electronic nose technology is their nearly universal sensitivity to changes in water vapor concentration. Since relative humidity is highly variable in practical applications, this substantially increases the complexity of sampling and analysis. Fortunately, smell-seeing is essentially immune to interference from water vapor, as shown in Figure 3. Water is only a weak ligand for metalloporphyrins, the porphyrin face itself is highly hydrophobic, and the substrate used here is reverse phase silica gel, which is also highly hydrophobic. The ability to easily detect species in the presence of a large water background represents a substantial advantage over mass-sensing techniques or methodologies that employ polar polymers as part of the sensor array.

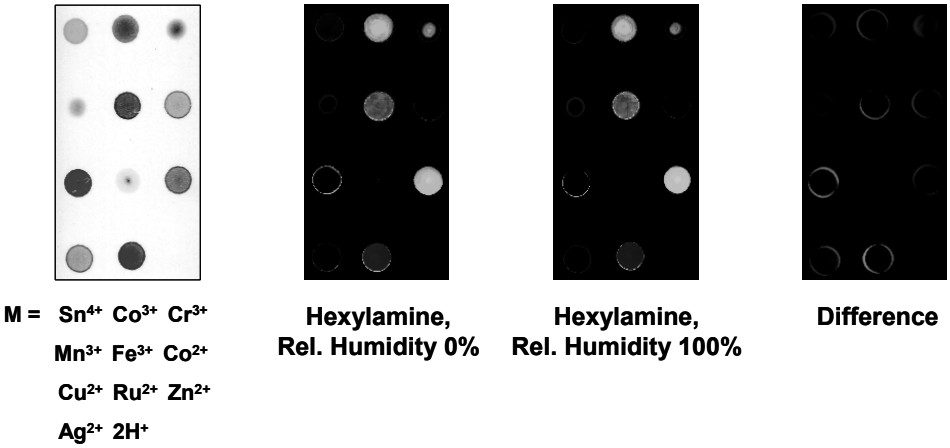

Figure 3. Relative humidity has no effect on the observed color change profiles of M(TPP) arrays.

Chemometric statistical tools have been used to study the porphyrin array responses. Principal component analysis (PCA) studies revealed that the porphyrin array responses are relatively specific, having a low degree of redundancy. Furthermore, almost all of the chosen metalloporphyrins contribute to analyte distinction, meaning the initial array was well-chosen for the vapor sensing task. Hierarchical cluster analysis (HCA) was used to quantitatively compare vapor fingerprints. The HCA analysis revealed distinction of all of the tested vapors, with groupings formed among similar analytes, such as phosphorus-containing ligands, sulfur-based ligands, and nitrogenous bases.

With a 5x5 array, we represent each analyte as a 75-dimensional vector (25 RGB's) each of which can take on one of 256 possible values (for inexpensive 8 bit scanners or digital cameras). The theoretical limit of discrimination, then, would be the number of possible patterns, i.e., $(256)^{75}$. Realistically, however, the RGB vector components do not range over the full 256 possible values; we do observe R, G, and B values vary over a range of 40. To discriminate patterns, let us assume a change of at least 4 is needed in the R, G, or B value (we can actually easily discriminate with changes of 2). From multicomponent analysis, not all of the 75 dimensions are equally important. In fact, roughly 95% of all information is contained in ~12 specific dimensions (i.e., linear combinations of the 75 different R, G, and B values). This implies a 'practical' limit of discrimination

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that is still immensely large: $(40/4)^{12} = 10^{12}$ distinct patterns should be recognizable in a simple 5x5 array. For a translation of this expectation into chemical terms, Figure 4 shows the comparison of color change profiles of n-butylamine to n-hexylamine, of n-butylamine to t-butylamine, and of n-butylamine to cyclohexylamine. The first two pairs of closely related isomers are distinct even in a simple array of sterically unhindered metalloporphyrins. The distinction between n-butylamine and cyclohexylamine, however, is modest at best (but see below).

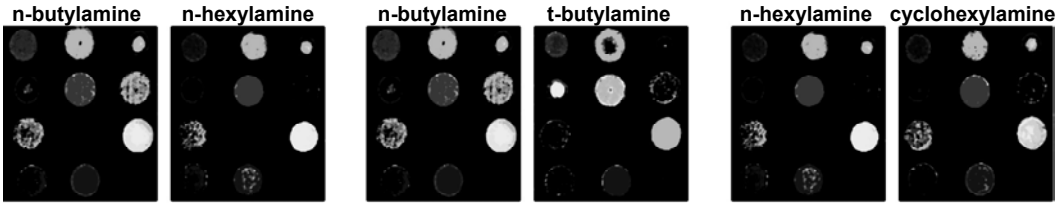

Figure 4. Color change profiles (shown in black and white) for a series of closely related amines on a simple array of sterically unhindered metalloporphyrins. The distinction among n-butylamine, n-hexylamine, and t-butylamine is clear, even in black and white images. The difference in profiles of n-butylamine and cyclohexylamine, however, is modest at best in the absence of sterically-demanding porphyrins. Analytes were delivered in nitrogen streams saturated with the vapor at 20°C.

As shown in Figure 2, libraries based on metal center variation allow for easy differentiation of analyte class (i.e., amine vs. alcohol vs. phosphine, etc.). Arrays of metalloporphyrins with sterically hindered binding sites allow for very subtle intra-functional distinction. Such differentiation has been demonstrated with a family of bis-pocketed dendrimer porphyrins (11, 12) and zinc siloxyl-porphyrins (13). As components of a smell-seeing array, this permits unambiguous differentiation, for example, even of n-hexylamine from cyclohexylamine.

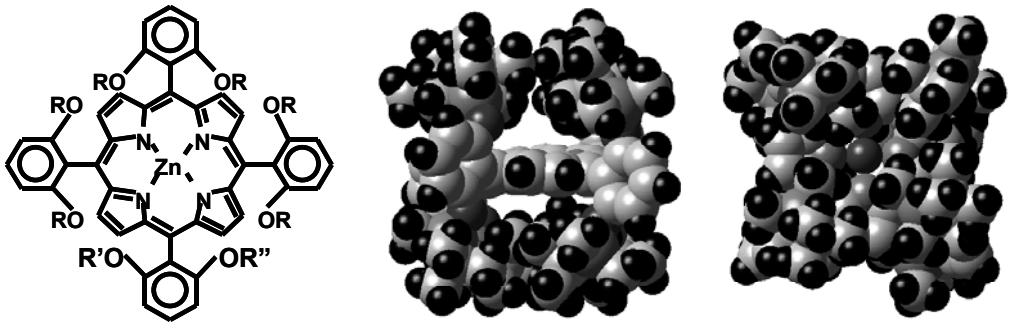

Figure 5. Shape selective sensors are shown based on our recent bis-pocket porphyrins (13), whose chemical structure is shown on the right. Center and left are space filled models (side and top view, respectively) based on the single crystal x-ray structure. Pocket size is as small as 4 Å. R' = R" = H, Zn(Si$_6$PP); R' = H, R" = R, Zn(Si$_7$PP); R' = R" = R, Zn(Si$_8$PP); where R = $Si(CH_3)_2(C(CH_3)_3)$.

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SENSITIVITIES

Most prior electronic nose technology relies on weak interactions between the analytes and the detectors. Smell-seeing relies on *strong* interactions. Metal-ligand (i.e., metal-analyte) bonds range in their bond enthalpies from ~40 to ~200 kJ/mol. In non-coordinating solvents (e.g., alkanes), equilibrium binding constants are often $>10^6$ M^{-1}. For pyridine, the vapor pressure is 0.02 atm at room temperature, so we have a Raoult's constant of ~2 x 10^{-3} atm M^{-1}. For a binding constant of ~10^6 M^{-1}, this is equivalent to *~2 ppb vapor!* In contrast, the enthalpy of physical adsorption (e.g., into polymers) is only ~5 to 20 kJ/mol (i.e., roughly a tenth of a metal bond). Therefore, the equilibrium constant for adsorption will typically be only about 5 x 10^{-5} as large as that for ligation to metal ions. Therefore, ligation is *intrinsically* ~20,000-fold more sensitive than adsorption into polymers. Differences in the sensitivity of detection techniques, of course, can either enhance or diminish this intrinsic advantage of ligation over adsorption.

In order to examine analytes at low concentrations, we have miniaturized the porphyrin array, putting 25 spots in a 0.5 cm^2 array on reverse phase silica gel. This miniaturization is important at low analyte levels to avoid slow response times while the silica gel itself (due to its high surface area) equilibrates with the analyte. The results are shown in Figure 6 for a series of analytes at 1 and 10 ppm.

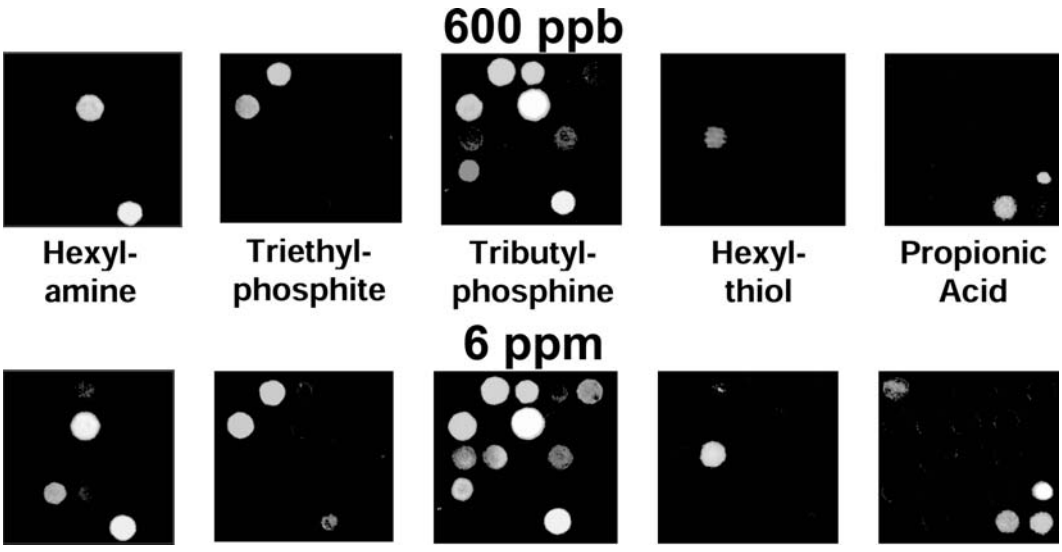

Figure 6. Color change profiles (shown in black and white) for a series of vapors at 600 ppb and 6 ppm; Analytes were delivered by serial dilution of nitrogen saturated with vapor at a thermostated temperature using digital mass flow controllers saturated with the vapor at 20°C. Images are more strikingly differentiable in color.

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FUTURE DIRECTIONS

A very wide range of applications can be imagined for our sensing array. Medical diagnostics, food and beverage quality control, workplace toxin monitoring, and warfare agent detection are all areas that could benefit from the "smell seeing" technique. To this end, we have developed a "smell-camera" prototype that couples a miniaturized metalloporphyrin array with a digital camera for imaging. This format provides a portable version of our invention for the mentioned applications, many of which are now under active investigation.

ACKNOWLEDGMENTS

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