

Author Manuscript

Title: Sensor Technologies Empowered by Materials and Molecular Innovations

Authors: Timothy M. Swager, PhD

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record.

To be cited as: 10.1002/ange.201711611

Link to VoR: <https://doi.org/10.1002/ange.201711611>

Sensor Technologies Empowered by Materials and Molecular Innovations

Timothy M. Swager
Department of Chemistry
Massachusetts Institute of Technology
tswager@mit.edu

Abstract: Functional synthetic designer materials can impact many advanced technologies, and the chemical sensor area is intimately reliant on these new chemical innovations. The transduction of chemical and biological signals is necessary for low cost omnipresent chemical sensing and will be realized by chemical designs of new transduction materials. We are poised for many new innovations to empower new generations of sensor technologies. Materials innovations promise to expand the capabilities of present hardware, drive down the cost, and ensure broad implementation of these methods.

Chemists need not be reminded of how innovation in our discipline provides the foundation for technological change. Polymers have economic impact in everything from packaging for mass distribution and improved shelf life of food, to the weight savings that allow commercial airplanes to travel half way around the globe without refueling. Structural plastics are by necessity inexpensive materials, and big companies have built businesses around their ability to scale production and processing of these materials. Chemistry will continue to deliver innovations that bring new, higher performance structural materials to market with attractive costs and less environmental impact. However, we are now in a new era wherein low volume organic materials and polymers need not be inexpensive. In fact, these new materials can potentially command the top position of the value chain. There are a number of great examples. Merck commercialized high performance ultra-pure nematic liquid crystal mixtures, which have brought portable displays and flat screen television to the masses. Another noteworthy example is in the manufacturing of silicon electronics. High performance photoresists command extraordinary value and enabled the electronic age. This is just the beginning, and small amounts of highly functional materials will be of increasing importance in ushering in new technologies. Nowhere will the impact be greater than in the field of chemical sensors, which is predicted to grow rapidly but relies on innovation in molecular and material interfaces.

The power of chemical sensors is their ability to provide distributed, portable, and inexpensive alternatives to conventional analytical instrumentation. Analytical instrumentation continues to evolve incrementally with miniaturization as one of the central goals. The success of analytical chemists is unquestioned, and we not only benefit from their innovations that power our ability to characterize our molecules and materials, but also build on to their technology to develop more specialized sensing systems.

Ubiquitous sensing will soon be considered as an imperative need for society to comprehensively understand and protect our health and environment. Herein lies many beautiful opportunities for the molecular or materials designer to recognize and develop a convergence of knowledge, spanning from molecular or biological recognition, to mass or charge transport phenomena, and

nanofabrication. The central theme is to put the technology into the responsive/transducing materials in order to achieve high performance with simplified and/or low-cost hardware. This can be realized through the development of novel sensing modalities or technologies that synergize with existing characterization techniques.

In designing a sensory material, it is important to note that the goal is to detect microscopic species ranging in size from a few microns (cells) to angstroms (molecules). As a result, the recognition interface often needs to span only a monolayer (10^{-9} m) in one direction and can be microscopic (10^{-6} m) in the other directions. Mass manufacturing the micrograms or less of critical materials needed to create commercial sensors therefore only requires a fume hood and associated bench top equipment. The cost of the active transducing molecule or material in chemical sensors is almost never the cost driver. The manufacturing expenses are generally associated with the electronics or even the sensor substrate and a transduction material costing \$100,000/g might only add 10 cents or less to the total cost of a sensor. Because only such small quantities are needed, even practically minded scientists need not restrict themselves to simple structures. In reality, sensing materials can be more costly and complex than pharmaceuticals.

The challenges associated with the design of useful chemical sensors are intrinsically chemical in nature, and although novel devices and interfaces will play a role, they tend to be a secondary consideration. The cliché “it takes one to know one,” which is usually applied to people with similar characteristics, applies here to molecules. If you want to recognize a molecule or class of molecules selectively, it is generally best to develop molecular responsive units with matching chemical structure or reactivity. We have much to build on, and our chemical colleagues around the world have provided us with arsenals of beautiful chemical reactions and receptors.

So where are the opportunities for chemists to make impact in chemical sensing? Clearly this is an open-ended question that cannot be answered comprehensively by me or anyone else. However, I offer some thoughts and examples on how to interface with the opportunities presented by current and emerging electronic and instrumental resources. I will highlight innovations in the emerging field of smartphone-based sensing and opportunities for chemists to tailor traditional characterization methods (IR, Raman, NMR) to increase sensitivity, selectivity, or portability.

Smartphone Sensing Systems

Ideally, materials can be created that enable inexpensive sensors to be built from existing electronic devices that can interface with laptop computers or smartphones. In some cases, we can consider the access to these resources as effectively free, because they will exist independent of the sensor modality being deployed. The smartphone is an omnipresent computation, communication, and sensor node that detects our position and velocity and connects us to the world around us. However, a smartphone can be much more when paired with chemical and biological sensors.

All smartphones and even the most rudimentary cellular phones have built-in optical sensors (cameras) that can read a colorimetric sensor array. There are countless ways to interface chemistry and color changes. Excellent examples of colorimetric sensor arrays come from

Suslick and coworkers. They have developed highly discriminating arrays of chromophores that are matched the chemical characteristics (acidity, basicity, H-bonding, etc.) of target analytes to create sensor arrays for a variety of species, including explosives.¹ As can be seen from the color bars shown in Figure 1, unique patterns are generated as a result of the careful selection of the indicators. The differentiation of these sensors is impressive, however much is still needed to create a universal sensor that can detect any trace target analyte in a highly complex or confounding background. Presently, all cross-reactive array sensors have limited capability in terms of recognizing two or more chemicals simultaneously. This is particularly challenging when one of the targeted analytes is present only in trace concentrations, as is often the case. Ideally, we would like to have a sensor that could determine concentrations of multiple chemical constituents in a single measurement. One might think that we need only add more sensor elements and if 40 is not enough, perhaps we make 1000 sensors. Such an expansion is laced with complexity and the assembled sensors must be able to be produced reproducibly with precision and not change with time. The latter aspect is an intrinsic challenge for most chemical sensors because using the sensor generally involves repeated exposure to reactive chemicals. In practice, sensor arrays need to be optimized for specific applications and variable backgrounds. The ideal approach is the integration highly specific sensor elements for the key analytes that have minimal cross-reactivity with the other constituents to create the most robust and sensitive signal. There will be an ongoing need for integrated designs that pair molecular recognition and transduction.

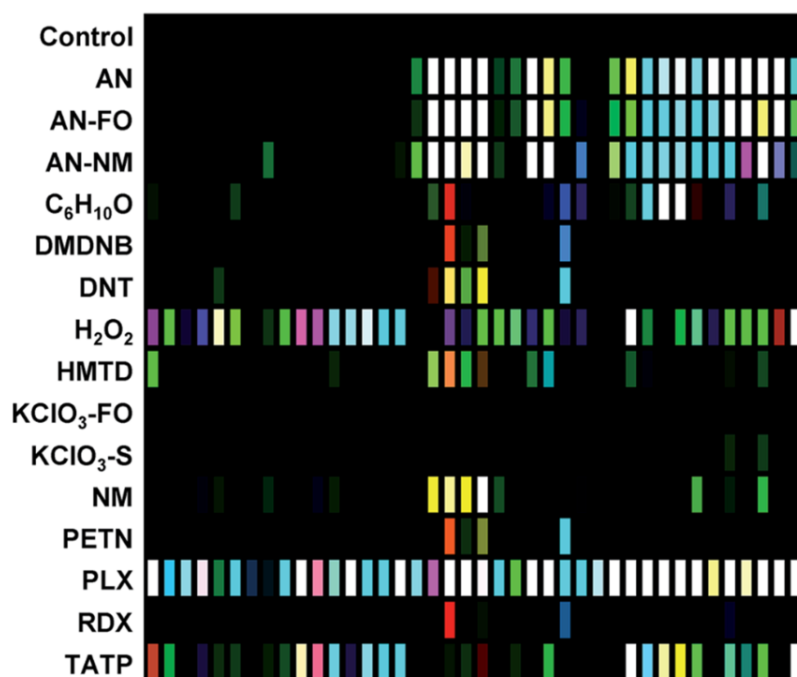


Figure 1. Difference maps taken from a number of explosives using a 40-element colorimetric sensor array. Reprinted from Ref. [1] with permission. Copyright Royal Society of Chemistry.

Optical scattering can also be used as a detection method and turbidity measurements represent a trivial example of this method. However, optical systems that have chemically responsive dynamic refractor optical behavior can produce more powerful systems. These biomimetic soft optical focusing devices are inspired by our eyes. The human eye focuses by deforming a lens rather than changing the distance to the backplane as is done in classical photography and optical microscopes. Gel materials have dominated soft optics, however for liquid droplets \ small changes in interfacial tensions can cause large and rapid optical effects. Liquid droplet optics require lens alignment, which is accomplished through gravity and droplets assembled from fluids of different densities and refractive indices. Alternatively, magnetic particles in droplets provides for alignment with applied magnetic fields.² An illustrative example are complex droplets comprising an organic phase with an index higher than water and a fluoruous phase with an index lower than water. In this case droplets have the qualitative ray diagrams as shown in Figure 2.³ A matrix of symmetric Janus droplets based on these fluids will maintain parallel alignment of the light rays and an image can be transmitted through this medium. A reduced hydrocarbon-water or fluoruous-water interfacial tension will change the droplet morphology to give divergent (scattering) optical properties (F/H/W and H/F/W in Figure 2). These morphology changes may be enzymatically triggered and enzyme kinetics can be monitored with a smartphone using the camera's light meter to measure the transmitted light intensity.⁴

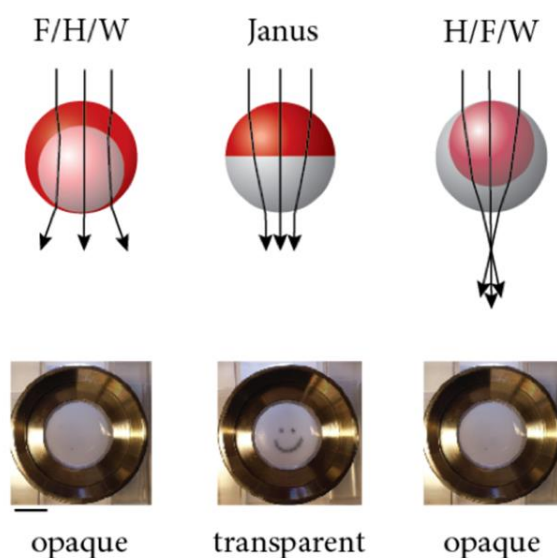


Figure 2. Ray diagrams for different droplet structures wherein the red phase is heptane ($\eta_{\text{heptane}} = 1.3876$), the gray phase is FC770 (fluoruous) solvent ($\eta_{\text{FC770}} = 1.27$) and the bulk phase is water ($\eta_{\text{H}_2\text{O}} = 1.33$). These indices are close to a matching condition, $\eta_{\text{H}_2\text{O}} / \eta_{\text{heptane}} = \eta_{\text{FC770}} / \eta_{\text{H}_2\text{O}}$, which generates an infinite focal length for the perfect symmetric spherical Janus droplet. The structures align with the higher density FC770 phase on the bottom as a result of gravity.

The aligned Janus droplets in Figure 2 and 3a are transparent when viewed along their C_{∞} symmetry axis. However, if these droplet lenses are linked together by a molecular event, they become powerful optical scattering elements. As shown in Figure 3, droplets functionalized with mannose-based surfactants agglutinate around concanavalin A (Con A) or *E. coli* to provide signals that can be read out with a conventional smartphone.⁵ Higher fidelity detection is accomplished using imaging processing software and magnifying optics that allow for counting of the agglutinated versus non-agglutinated droplets.

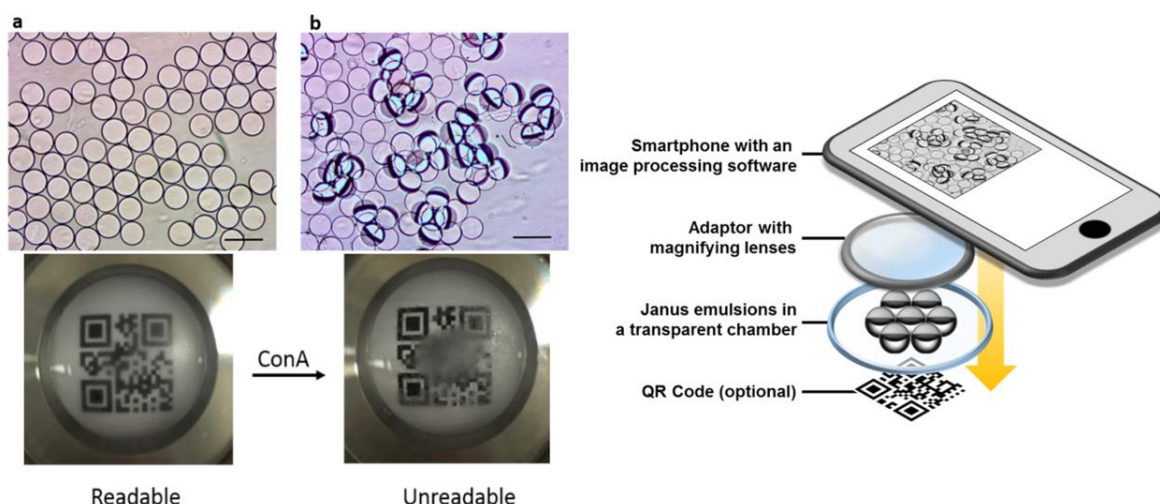


Figure 3. (a) Density aligned Janus droplets under a microscope and in a solution held over a QR code. (b) Droplets agglutinate immediately after addition of a small amount of Con A with gentle mixing and the QR code under the droplet solution is no longer readable by a smartphone. (right) Schematic for quantitative analysis of droplet agglutination by Con A or *E. coli* using a commercial magnifying device, a smartphone, and image processing software.

Smartphones are also able to detect optical changes that occur outside of the spectral range of human vision. The optical detectors of smartphones, either charge coupled devices (CCD) or complementary metal-oxide semiconductor (CMOS), can detect light past 1000 nm whereas human vision is limited to < 700 nm. Hence, smartphones have the potential to detect both absorption and emission from near IR dyes. Although the solar spectrum has some intensity over this region, > 700 nm is generally a “quite” spectral region in interior environments and naturally occurring materials do not have absorptions/emissions at this wavelength. Another advantage of longer wavelengths is reduced light scattering and potential for detection through turbid media or tissue.

Emissive Sensors

Over the last decade, there have been many advances in the design of low band-gap molecules and polymers and abundant opportunities await the clever chemists who integrate these chromophores with receptors. In particular, single walled carbon nanotubes (SWCNTs) display

prominent emission features at around 1000 nm and have been identified for use within the leaves of plants or as implantable sensors in living tissue.⁶ Obtaining efficient emission from SWCNTs requires a minimum of defects and hence non-covalent functionalization methods based upon physisorption of recognition elements are preferred. However, SWCNTs also have endgroups that are generally presumed to contain carboxylate groups and selective functionalization of these sites would not be expected to perturb the π -system sufficiently to cause unwanted losses in emission intensity.

Fluorescence methods are often said to be more sensitive than absorbance schemes. For individual fluorescent groups is true only when no background light is present and a new emission can be easily detected, just as a small dim light can be readily detected visually in a dark room. When detecting differences in the magnitude of signals it is not always obvious that fluorescence has an unequivocal edge in sensitivity. However, multichromophore systems can provide signal gain as the excited states encounters a number of potential analyte interaction sites during its lifetime.⁷ This effect is highest in the solid state wherein there are a continuum of chromophores. Hence an emissive film of a semiconductive polymer (Figure 4) creates a gain

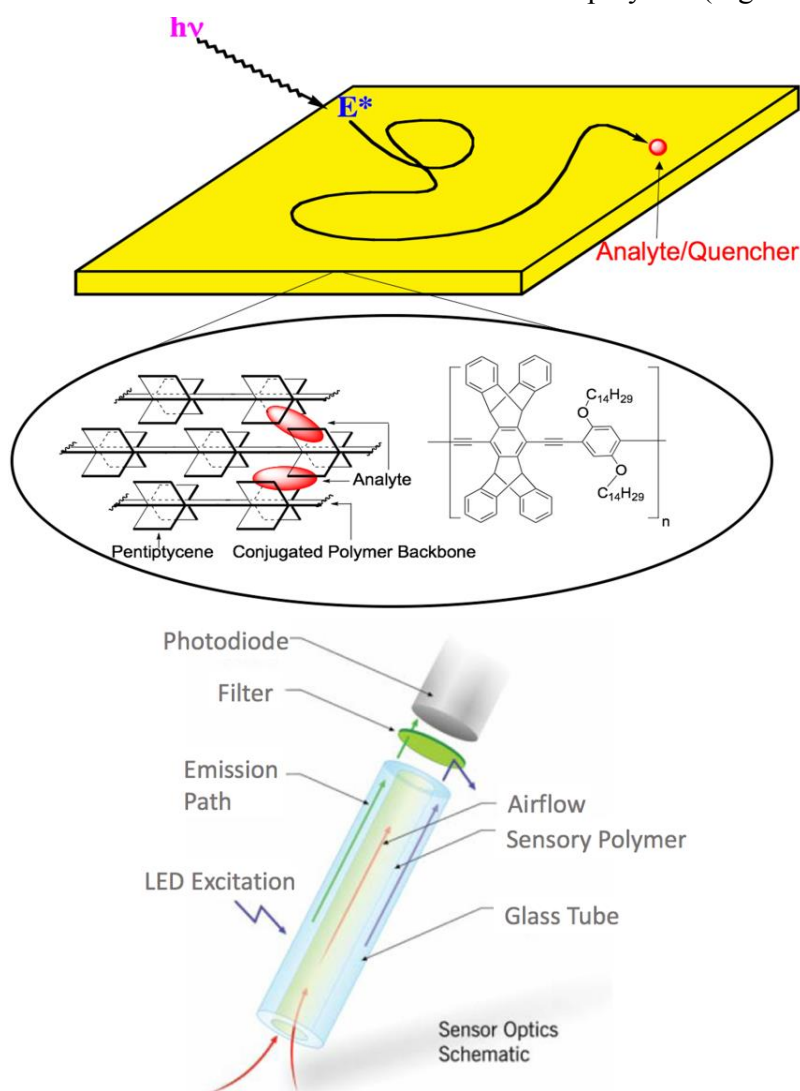


Figure 4. (top) Schematic showing the random diffusion of an optically generated excitation in a thin film of a conjugated polymer. This material can be coated on the interior of a capillary tube (bottom) and the emission from this film is transmitted via a waveguide effect to a photodiode detector. The presence of a quenching analyte in the sampled air causes a reduction in the emission intensity.

medium for the detection of quenching analytes. Apart from the relative energies of the analyte's lowest unoccupied molecular orbital (LUMO) and the highest occupied molecular orbital (HOMO), the selectivity towards a given analyte of this polymer based sensor also depends on size. The size exclusion properties are a result of the structure of porous network, which excludes molecules larger than those containing a single phenylene group from diffusing into the polymer film (Figure 4).⁸ The exceptional sensitivity to quenching analytes is the basis of commercial portable explosives detectors⁹ with femtogram detection limits.¹⁰ A key feature is that each sensor requires less than a microgram of polymer and hence the cost of the enabling polymer coating is inconsequential.

Raman Based Sensing Systems

Metal nanoparticles and their functionalization also offers many opportunities for the development of novel sensor modalities. Microphotonic devices for optical data processing and transfer have become increasingly sophisticated and present the possibility to produce miniaturized (chip based) spectrometers. These include fluorescent methods and information rich vibrational methods. Hand-held Raman spectrometers are now widely used by law enforcement or first responders to identify unknown bulk substances. As a result of its limited sensitivity, Raman is generally a bulk detection method. However, it can become an ultratrace detection method when optimally paired with gold or silver nanoparticles deposited on the surface of the substrate. In these surface-enhanced Raman scattering (SERS)¹¹ methods, plasmonic enhancements up to 10^{14} compensate for lower performance specifications that often accompany spectrometer miniaturization. The unique molecular fingerprint of the Raman spectrum provides precision that is not possible in lower information content chemical sensors.

New generations of Raman-based chemical sensors can be developed through the incorporation of surface bound receptors into SERS methods. There are unique opportunities for synthetic

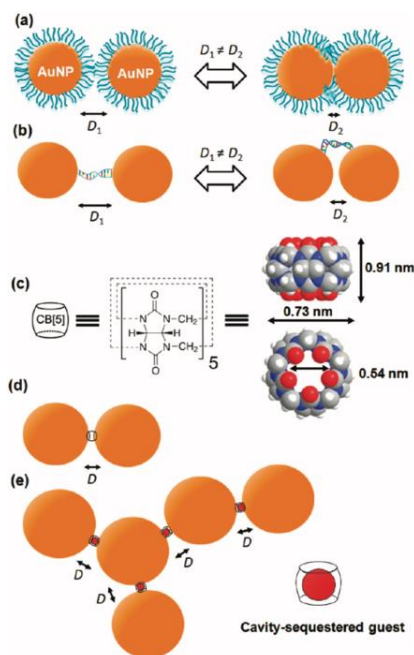


Figure 5. Schemes for assembly of plasmonic gold nanoparticles by surface coatings (a) or DNA (b), which have poorly defined spacing. Cucurbit[5]uril (CB[5]) (c) has a precise rigid geometry and when used to assemble the nanoparticles (d, e) creates a well-defined 0.9 nm spacing and assembling guest molecules in the CB[5] allows for SERS detection. Reprinted from Ref. [12] with permission. Copyright American Chemical Society.

chemists to progress this field forward by integrating recognition elements into low band gap dyes or molecules that can be bound to metal interfaces. Beyond simply functionalizing particles as nanotransducers, the prospects for integrating molecular recognition elements between nanoparticles has promise. A particular innovation involves the binding of cucurbit[n]uril container molecules between gold particles that are capable of binding analytes (Figure 5).¹² An advantage of this chemically enhanced SERS scheme is that the receptor:guest interaction need not be designed to have a purposeful transduction element, such as a change in absorption, conductance, etc. The detection is spectroscopic and will be enhanced by coupling to the metal nanoparticles.

NMR and Magnetic Sensing

It is indisputable that NMR is the most widely used method for chemical structure identification in laboratory settings. In recent years, bench top spectrometers with rapidly improving performance have appeared. A limitation in NMR has been that the spectral resolution is dependent on the applied magnetic field and the field homogeneity. There has been progress in this area and handheld magnets have been produced (Figure 6) that allow for line widths (0.15 ppm), which can enable resolution at modest fields.¹³ However, hand held NMR devices that can record spectra with the resolution necessary to precisely transduce the presence of complex molecules in a mixture are still elusive. Molecular transducers will likely be the key to enabling

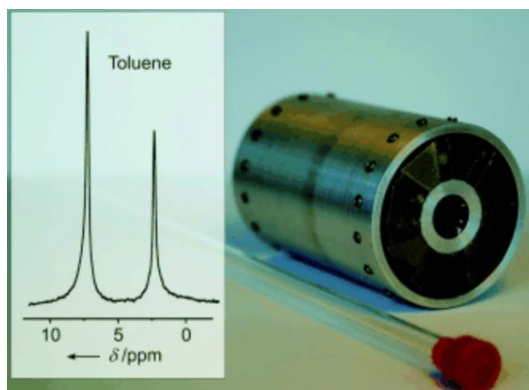


Figure 6. A small magnet designed to have high field homogeneity for NMR and the spectrum of toluene taken in this magnet displaying a line-width at half height of 0.15 ppm.

portable NMR based chemical sensors. In a recently realized sensor system, host molecules are designed with fluorine substitution about an analyte binding pocket. ¹⁹F NMR displays approximately 300 ppm chemical shift dispersion, which is nearly 30 times that of ¹H NMR and ¹⁹F is a 100% abundant spin 1/2 nuclei. In this case binding of the analytes by the host is not highly specific and the host molecule will ideally bind a whole class of analytes. It is however necessary that the host-analyte association/dissociation rates are slow on the NMR timescale and thereby produce sharp resonances associated with bound and unbound species. Thus, the ¹⁹F NMR peaks of the host will not broaden or average upon interacting with the analyte as would be the case with a rapid equilibrium on the NMR timescale. The strategic positioning of fluorine in a host molecule is used to create unique spectral fingerprint for each bound analyte (Figure 7).

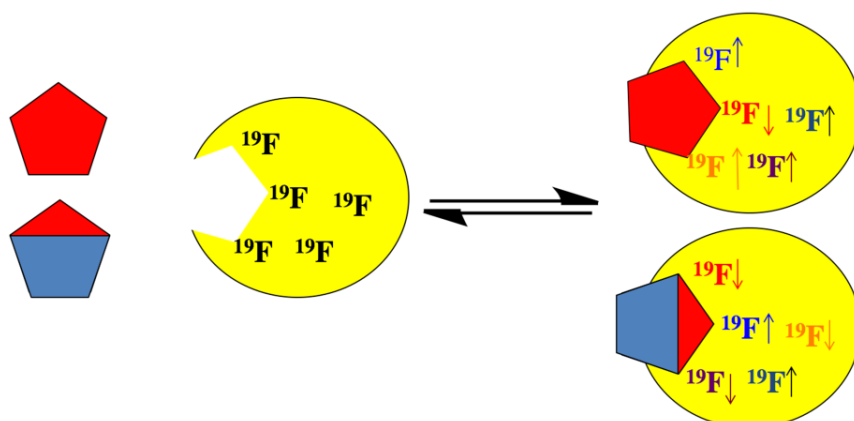


Figure 7. Schematic illustration of how a container molecule can bind two similar molecules and create unique signatures in the ^{19}F NMR signals.

Strong associations, such as Lewis acid-base interactions, produce static complexes for ^{19}F NMR sensing. An example is shown in Figure 8, wherein a metallo-calix[4]arene behaves as an endohedral Lewis acid for the binding sterically unencumbered nitriles.¹⁴ The four-dimensional plot illustrates how the different ^{19}F signals uniquely vary with the binding each of the analytes. Detection need not be performed in NMR solvents and for example insecticide cyanophos can be detected at 20nM in river water by adding the chemosensory metallo-calix[4]arene to the sample. A wide variety of other sensor modalities are possible including Lewis acidic palladium pincer compounds that can be used to detect caffeine levels in coffee and a wide range of ionic and Lewis basic constituents in commercial energy drinks by simply adding it to the sample and taking ^{19}F NMR spectra.¹⁵

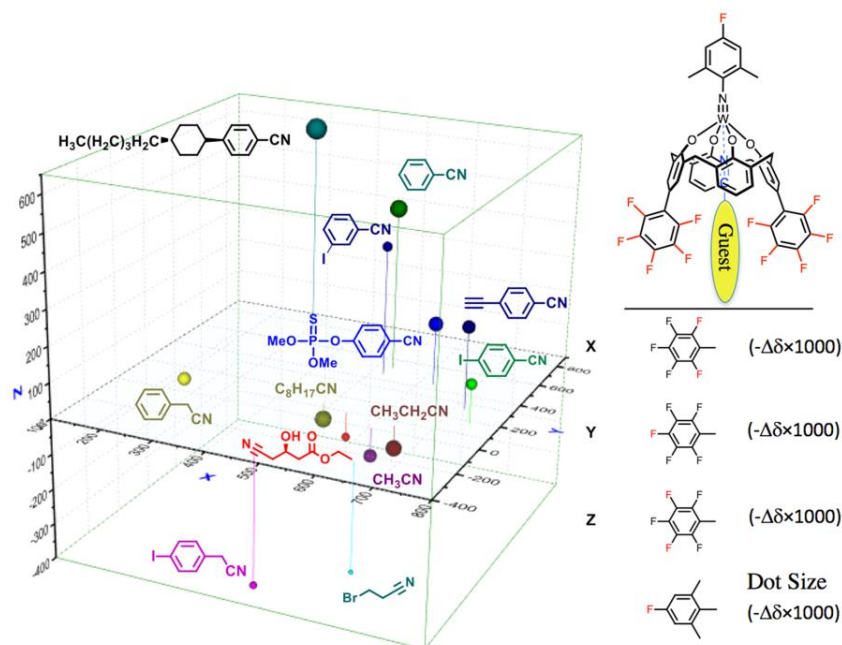


Figure 8. 3D plot of ^{19}F resonances upon bonding nitrile analytes. Axis X: *ortho*- ^{19}F ($-\Delta\delta \times 1000$); axis Y: *para*- ^{19}F ($-\Delta\delta \times 1000$); axis Z: *meta*- ^{19}F ($-\Delta\delta \times 1000$). The sphere radius is correlated to *imido*- ^{19}F ($-\Delta\delta \times 1000$).

Apart from these bulk NMR techniques, there have been material-driven advances in spatially resolved NMR technologies. Nanoscale NMR with the detection limit of 10^4 nuclear spins has been achieved by using emission changes from nitrogen doped diamond as a spin detector.¹⁶ On a larger length scale giant magnetoresistive (GMR) sensors originally developed for reading magnetic recording disks, have been used to detect DNA¹⁷ and create biosensors (Figure 9).¹⁸ GMR sensors make use of tunneling processes between metals having different spin populations wherein the spin of the tunneling electrons is conserved. Magnetic perturbations cause changes in spin populations and the resistance across a stack of tunnel junctions. GMR devices can be used to create sensors to detect particles flowing through microfluidic devices to create parallel methods similar to existing fluorescence based flow cytometry.¹⁹

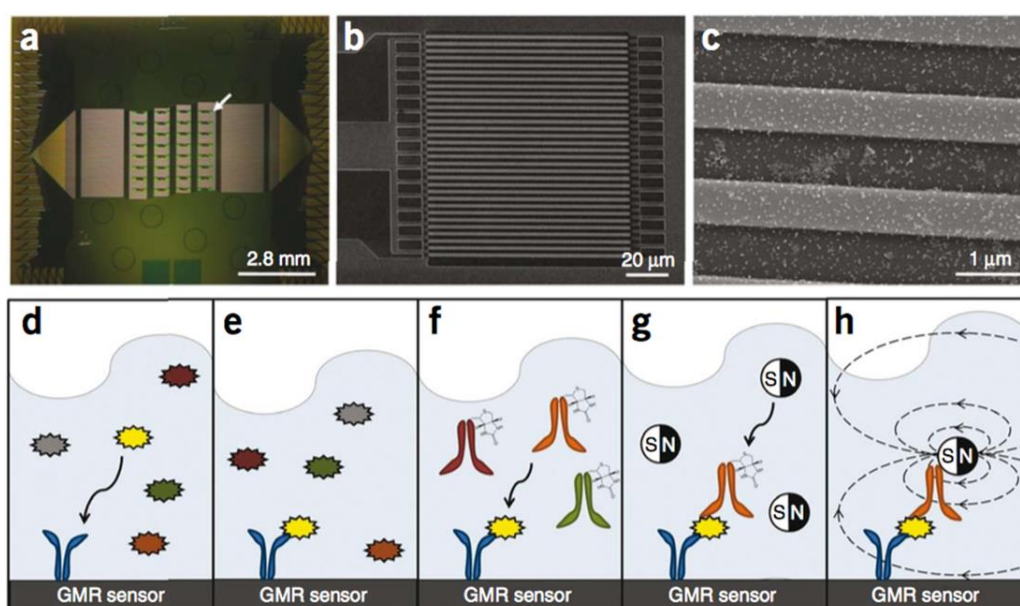


Figure 9. (a) A GMR biosensory device wherein the green squares (see arrow) are independently addressable sensors. (b,c) SEM of a single spin valve sensor. (d-h) Progression showing immobilization of analyte, an antibody, and magnetic nanoparticle in a sensing event. Reprinted from Ref. [18] with permission. Copyright Nature Publishing.

Superconducting quantum interference devices (SQUIDs) offer superior sensitivity, however even with high temperature superconductors, these devices require cryogenic cooling. Optical detection of differences in the spectra of atomic vapors as function of applied magnetic fields, have been offered as miniaturizable non-cryogenic alternatives with similar sensitivity to SQUIDs.²⁰ In principle, another method to measure magnetic fields is the use of the Faraday rotation, which historically has been the domain of paramagnetic containing optical materials. In this method, polarized light passing through the transduction material undergoes a rotation that is directly dependent upon the applied magnetic field. The magnitude of the Faraday rotation is expressed as a Veret constant (V) and inorganic optical materials such as terbium gallium garnet display $V \approx -1 \cdot 10^4 \text{ degT}^{-1}\text{m}^{-1}$. However, there have been recent discoveries in multiple laboratories around the world that reveal extraordinary V 's in regioregular poly(3-

alkylthiophene)s,²¹ poly(arylene-ethynylene)s,²² chiral poly(dialkyfluorene):radical composites,²³ and small molecule liquid crystals²⁴ (Figure 10). The physics governing these large effects are far from understood, however the fact that materials have been discovered that are more than 20 times larger than conventional materials suggests that there may be some big advances on the horizon and wherein these cost-effective magneto-optical materials could be used as transducers for biosensing or even in magnetometry.

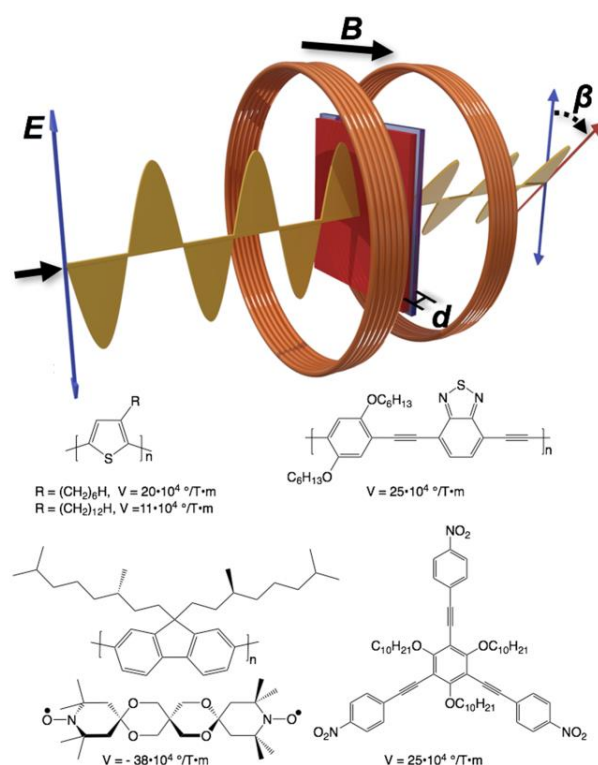


Figure 10. Schematic of apparatus for measuring Verdet constant and structures of polymers and molecules displaying large magneto-optical effects.

Chemiresistive Sensors

Outputs from optical and magnetic transduction materials eventually need to be converted into electrical signals. As a result, it is logical to suppose that direct electrical detection provides for greater simplicity and efficiency in chemical/biological sensors. Chemiresistors, materials that change their conductivity in response to a chemical stimulus, are perhaps the simplest possible element upon which to build an instrumented sensor. Current voltage characteristics are the basis of all electronics and a simple resistance measurement can be performed with exceedingly small power. These aspects when combined with the fact that chemiresistive sensors, like conventional integrated circuits, are readily miniaturized and connected into large arrays, make for a compelling case for impact with this type of sensor.

The challenge for chemiresistors is selectivity and stability. Metal oxides based chemiresistors are a commercial success, however these systems generally require high temperatures ($> 300^{\circ}\text{C}$) to operate and experience considerable drift when transitioning from a dormant unheated to heated state. The need for constant high temperature results in higher power requirements, which have been mitigated to some degree by miniature heating elements. However, by virtue of the high temperature, selectivity through molecular recognition is not possible. The integration of selectors or receptors into chemiresistive materials in ways that affect electrical transport was first explored with conducting polymers. An advantage of this approach is that with chemical synthesis the recognition elements could be directly integrated into the polymer structure.²⁵ There are clearly new chapters to be written for conducting polymer based chemiresistors, however the bottom-up multistep synthesis needed to create materials with high selectivity is not conducive to rapid experimentation. Additionally, the soft nature of the molecular lattice and the fact that most structures incorporate heteroatoms, produces localized soliton, polaron, or bipolaron charge carriers in conducting polymers that are very sensitive to ions and humidity.

Carbon nanotubes (CNTs) have a number of desirable attributes needed to make chemiresistors. The π -surface of the sidewalls of SWCNTs provide for direct interaction with analytes. Alternatively, in the case of multiwall or double wall CNTs, the inner walls are insulated from the surroundings and hence the interactions with analytes. Although this factor tends to limit sensitivity, it can give rise to very robust sensors with dense functionalization of the other walls.²⁶ The sensing mechanism in many sensors is swelling of the CNT network by partitioning of the analytes into the insulating, covalently attached or physisorbed molecular coatings. Given that electrons need to migrate through the completed circuit they must encounter many tunnel junctions between neighboring CNTs. The tunneling probability decreases exponentially with increasing distance to provide for increases in the network's resistance with analyte induced swelling.

In addition to swelling of the random nanowire network, SWCNTs also display conductance changes induced by charge transfer or dipolar pinning/scattering caused by the analyte. Pinning and charge transfer result in a reduction of the mobile charge carriers and this feature can be detected by changes in the threshold gate voltages in field effect transistor (FET) devices.²⁷ Functionalization of SWCNTs to impart selectivity is key, however the chemistry is complicated by the fact that core characterization methods like solution NMR and crystal structure determination are not possible with these nanomaterials. However, the field continues to evolve with refinement of methods for the attachment of functional groups with greater precision²⁸ and that can undergo subsequent functionalization²⁹ to add recognition elements.³⁰

The use of nanowires for chemical sensing has recently been reviewed.³¹ Of these materials systems, CNTs offer some significant advantages for the construction of chemical sensors. They can be functionalized by organic chemistry and hence integrated systems containing the latest molecular and biomolecular recognition elements can be constructed. One limitation is that CNTs are a mixture of materials with different diameters, lengths, and electronic structures. Depending upon the orientation of the graphene π -system with respect to the SWCNT axis the materials may be intrinsic metals or semiconductive. Chemiresistors with modes of action dominated by carrier injection/depletion/pinning will be most sensitive with semiconductive SWCNTs.³² Metallic SWCNTs need not be charged to conduct, and as a result are less

susceptible to charge transfer processes, but are also experience less interference from humidity. Sensors that operate solely on modulating the junctions between SWCNTs will be less sensitive to the nature of the carbon nanotubes.

The simplicity of a chemiresistor offers clear advantages and allows for the easy fabrication of sensor arrays or integration into radio-frequency identification technologies.³³ As shown in Figure 11, arrays can be easily printed on flexible substrates and these materials can be used to detect alkenes for the monitoring of produce ripening,³⁴ or biogenic amines for monitoring the quality of meat.³⁵ When the signals are sufficiently large SWCNT sensor compositions can be used to create smartphone compatible RFID sensors.³⁶

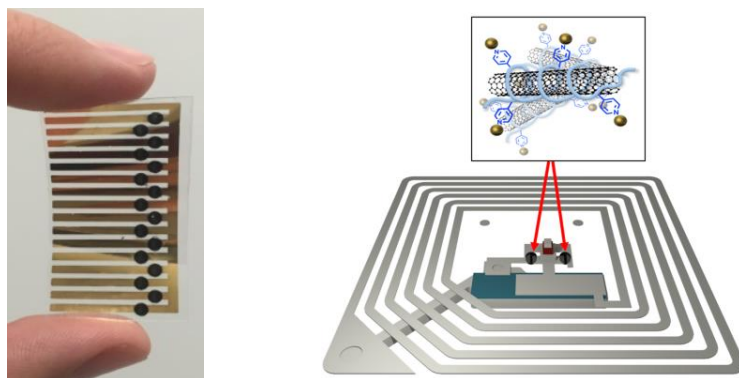


Figure 11. A simple chemiresistive array of functionalized carbon nanotubes and a rendering of a passive RIFD sensor having SWCNTs functionalized by a polymer and metal ions which is powered and read by a smartphone.

Concluding Remarks and Outlook

An important trend in evaluating sensory materials is to move beyond the laboratory and test in real-world conditions with confounding chemical signals. Laboratory testing is still critical, and the controlled exposure of sensors to variances in temperature and humidity, for example, are needed to evaluate any technology. Exposing sensors to a battery of chemical vapors also characterizes the scope of the molecular recognition. Sometimes the real-world is simpler than the laboratory stress tests to which we subject our sensors. If you are seeking to detect biogenic amines coming from meat spoilage or ethylene associated with fruit ripening, you should not have to worry about competition with typical organic solvents. It is important to note that chemical sensors will always suffer from limited selectivity as all sensing materials, with the exception of DNA, display cross-reactivity. This realization gave birth to the ideas of artificial olfaction and the use of multiple sensors to create unique composite signatures for particular odors.³⁷ In the earliest implementation of this concept, a large number of non-specific sensors were used to create signatures for different analytes. However, this approach seldom produces robust, selective responses, and this is a particular limitation for trace detection in highly complex environments. The reason is that there tend to be synergistic effects between analytes, and parsing small differences in signal strength is complicated by sensor drift (shifting baselines). Progress in this area is critically dependent upon creating arrays with clear

recognition elements that parse out the chemical space of interest for the specific application. Optical and electrical devices are ideally suited for the creation of cross reactive arrays, and the benefits of applying molecular recognition and chemical principles have been demonstrated.^{38,39}

The grand challenges for the future of chemical sensors are deceptively simple to articulate and include: selectivity, sensitivity, and stability. Out of this S³ triad, stability is often the weak link in the translation from the laboratory to the marketplace. Just as is the case with electronics systems, we can try to reduce noise by filtering or detecting coincident signals. A signal of individual sensors in array devices or in networks of distributed sensors monitored simultaneously can be fit to a spatial-temporal map of a vapor over an extended area to differentiate between the real signal and the noise. Another alternative method is to use a molecular recognition material to preconcentrate the analyte. Triggered release can present a larger concentration to a sensor. This controlled delivery in an expected time window can allow discrimination between real signals and background noise or drift. However, in all cases materials that have precise and strong signals, or that selectivity sequester and release molecules of interest are core to the technology.

The continued evolution of chemical sensors will benefit from clever chemists translating advanced molecular and biological recognition into sensory systems. I use the term system purposely to emphasize that the limits of detection and the specificity of a sensor are never completely determined by the transduction material. We need to consider sampling and how we move the chemical signal from the source to the sensor. There is also the realization that the fusion of different sensor modalities together will provide for the most robust systems. This is natural to consider, as in our daily life, we make use of a fusion of our vision, smell, taste, and touch. To mirror this multisensory integration and to advance sensor methods, we rely on multifunctional responsive materials. For example, SWCNTs not only provide for electrical or optical transduction, but also have rigid physical structures with high surface areas for interactions with the molecules of interest. The pallet of materials is broad, including inorganic/metallic/organic nanoparticles, polymers, microelectromechanical (MEM) devices, and colloids. We can expect new advances in the understanding of materials and emerging chemical structures to provide abundant additional opportunities.

In framing the sensor field in chemical terms, I am hoping to inspire others to join in this field. We are at a critical nexus in the sensor field wherein innovations will benefit from the confluence of the internet of things, omnipresent wireless data transmission, cloud computing, and chemistry. There is societal interest in knowing about our health and environment, and abundant value propositions to industry and retailers to create new markets, perfect processes, or differentiate their products from their competitors.

Acknowledgement: I am grateful for the enduring support of my sensor research by the funding programs associated with the US Department of Defense, National Institutes of Health, and NSF. I also thank Ms. Vera Schröder for her critical reading and suggestions for this essay.

Bio-Sketch

Timothy M. Swager is the John D. MacArthur Professor of Chemistry and the Director, Deshpande Center for Technological Innovation at the Massachusetts Institute of Technology. His group focuses broadly on synthetic, materials and polymer chemistry. A major theme of Swager's

materials research is directed at the demonstration of new conceptual approaches to the construction of sensory materials. In addition to advancing fundamental science, he is engaged in translating technology to the market place both from his group and more broadly from MIT in his role as the director of the Deshpande Center.



¹ Askim, J. R.; Li, Z.; LaGasse, M. K.; Rankin, J. M.; Suslick, K. S. "An Optoelectronic Nose for Identification of Explosives" *Chem. Sci.* **2016**, 7, 199-206.

² Zarzar, L. D.; Sresht, V.; Sletten, E. M.; Kalow, J. A.; Blankschtein, D.; Swager, T. M. "Dynamically Reconfigurable Complex Emulsions via Tunable Interfacial Tensions" *Nature*, **2015**, 518, 520-524.

³ Nagelberg, S.; Zarzar, L. D.; Nicholas, D.; Subramanian, K.; Kalow, K. A.; Sresht, V.; Blankschtein, D.; Barbastathis, G. Kreysing, M.; Swager, T. M.; Kolle, M. "Reconfigurable and Responsive Droplet-based Compound Micro-Lenses" *Nature Comm.* **2017**, 8, 14673.

⁴ Zarzar, L. D.; Kalow, J. A.; He, X.; Walish, J. J.; Swager, T. M. "Optical Visualization and Quantification of Enzyme Activity using Dynamic Droplet Lenses" *Proc. Nat. Acad. Sci.* **2017**, 115, 3821-3825.

⁵ Zhang, Q.; Savagatrup, S.; Kaplonek, P.; Seeberger, P. H.; Swager, T. M. "Janus Emulsions for the Detection of Bacteria" *ACS Central Science* **2017**, 3, 309-313.

⁶ Giraldo, J. P.; Landry, M. P.; Kwak, S.-Y.; Jain, R. M.; Wong, M. H.; Iverson, N. M.; Ben-Naim, M.; Strano, M. S. "A Ratiometric Sensor Using Single Chirality Near-Infrared Fluorescent Carbon Nanotubes: Application to In Vivo Monitoring" *Small* **2015**, 11, 3973-3984.

⁷ Zhou, Q.; Swager, T. M. "Methodology for Enhancing the Sensitivity of Fluorescent Chemosensors: Energy Migration in Conjugated Polymers" *J. Am. Chem. Soc.* **1995**, 117, 7017-7018.

⁸ Yang, Y.-S.; Swager, T. M. "Fluorescent Porous Polymer Films as TNT Chemosensors: Electronic and Structural Effects" *J. Am. Chem. Soc.* **1998**, 120, 11864-11873.

⁹ These sensors are now produced by FLIR Systems:
<http://www.flir.com/threatdetection/display/?id=63323>

¹⁰ Cumming, J. C.; Aker, C.; Fisher, M.; Fox, M.; la Grone, M. J.; Reust, D.; Rockley, M. G.; Swager, T. M.; Towers, E.; Williams, V. "Using Novel Fluorescent Polymers as Sensory Materials for Above-Ground Sensing of Chemical Signature Compounds Emanating from Buried Landmines" *IEEE Transactions on Geoscience and Remote Sensing* **2001**, 39 (6), 1119-1128.

¹¹ Wang, Y.; Yan, B.; Chen, L. "SERS Tags: Novel Optical Nanoprobes for Bioanalysis" *Chem. Rev.* **2013**, 113, 1891-1428.

¹² Taylor, R. W.; Lee, T.-C.; Scherman, O. A.; Esteban, R.; Aizpurua, J.; Huang, F. M.; Baumberg, J. J.; Mahajan, S. "Precise Subnanometer Plasmonic Junctions for SERS within Gold Nanoparticle Assemblies Using Cucurbit[n]uril "Glue"" *ACS Nano* **2011**, 5, 3878-3887.

¹³ Ernesto, D.; Perlo, J.; Blümich, B.; Casanova, F. "Small Magnets for Portable NMR Spectrometers" *Angew. Chem. Int. Ed.* **2010**, 49, 4133 –4135

¹⁴ Zhao, Y.; Markopoulos, G.; Swager, T. M. "¹⁹F NMR Fingerprints: Identification of Neutral Organic Compounds in a Molecular Container" *J. Am. Chem. Soc.* **2014**, 136, 10683-10690.

¹⁵ Zhao, Y.; Chen, L.; Swager, T. M. "Simultaneous Identification of Neutral and Anionic Species in Complex Mixtures without Separation" *Angew. Chem. Int. Ed.* **2016**, 55, 917-921.

¹⁶ Mamin, H. J.; Kim, M.; Sherwood, M. H.; Rettner, C. T.; Ohno, K.; Awschalom, D. D.; Rugar, D. "Nanoscale Nuclear Magnetic Resonance with a Nitrogen-Vacancy Spin Sensor" *Science* **2013**, 339, 557- 560.

¹⁷ W. Shen, B. D. Schrag, M. J. Carter, J. Xie, C. Xu, S. Sun, and G. Xiao, "Detection of DNA Labeled with Magnetic Nanoparticles using MgO-Based Magnetic Tunnel Junction Sensors," *J. Appl. Phys.* 2008, 103, 07A306.

¹⁸ Gaster, R. S.; Hall, D. A.; Nielsen, C. H.; Osterfeld, S. J.; Yu, H.; Mach, K. E.; Wilson, R. J.; Murmann, B.; Liao, J. C.; Gambhir, S. S.; Wang, S. X. "Matrix-Insensitive Protein Assays Push the Limits of Biosensors in Medicine" *Nature Med.* **2009**, 15, 1327-1332

¹⁹ Lin, G.; Makarov, D.; Schmidt, O. G. "Magnetic Sensing Platform Technologies for Biomedical Applications" *Lab on a Chip* **2017**, 17, 1884-1912.

²⁰ Budker, D.; Romalis, M. "Optical Magnetometry" *Nat. Phys.* **2007**, 3, 227-234.

- ²¹ Gangopadhyay, P.; Koeckelberghs, G.; Persoons, A. "Magneto-optic Properties of Regioregular Polyalkylthiophenes" *Chem. Mater.* **2011**, 23, 516–521.
- ²² Araoka, F.; Abe, M.; Yamamoto, T.; Takezoe, H. "Large Faraday Rotation in a π -Conjugated Poly(arylene ethynylene) Thin Film" *Appl. Phys. Exp.* **2009**, 2, 011501.
- ²³ Lim, C.-K.; Cho, M. J.; Sing, A.; Li, Q.; Kim, W. J.; Jee, H. S.; Fillman, K. L.; Carpenter, S. H.; Neidig, M. L.; Baev, A.; Swihart, M. T.; Prasad, P. N. Manipulating Magneto-Optic Properties of a Chiral Polymer by Doping with Stable Organic Biradicals *Nano Lett.* **2016**, 16, 5451–5455.
- ²⁴ Vandendriessche, S.; Cleuvenbergen, S. V.; Willot, P.; Hennrich, G.; Srebro, M.; Valev, V. K.; Koeckelberghs, G.; Clays, K.; Autschbach, J.; Verbiest, T. "Giant Faraday Rotation in Mesogenic Organic Molecules" *Chem. Mater.* **2013**, 25, 1139–1143.
- ²⁵ McQuade, D. T.; Pullen, A. E.; Swager, T. M. "Conjugated Polymer-Based Sensory Materials" *Chem. Rev.* **2000**, 100, 2537–2574.
- ²⁶ Wang, F.; Swager, T. M. "Diverse Chemiresistors Based Upon Covalently Modified Multi-Walled Carbon Nanotubes" *J. Am. Chem. Soc.* **2011**, 133, 11181–11193.
- ²⁷ Wang, F.; Gu, H.; Swager, T. M. "Carbon Nanotube/Polythiophene Chemiresistive Sensors for Chemical Warfare Agents" *J. Am. Chem. Soc.* **2008**, 130, 5392–5393.
- ²⁸ He, M.; Swager, T. M. "Covalent Functionalization of Carbon Nanomaterials with Iodonium Salts" *Chem. Mater.* **2016**, 28, 8542–8549.
- ²⁹ Setaro, A.; Adeli, M.; Glaeske, M.; Przyrembel, D.; Bisswanger, T.; Gordeev, G.; Maschietto, F.; Faghani, A.; Paulus, B.; Weinelt, M.; Arenal, R.; Haag, R.; Reich, S. "Preserving π -Conjugation in Covalently Functionalized Carbon Nanotubes for Optoelectronic Applications" *Nat. Commun.* **2017**, 8, 14281.
- ³⁰ Schnorr, J. M.; van der Zwaag, D.; Walish, J. J.; Weizmann, Y.; Swager, T. M. "Sensory Arrays of Covalently Functionalized Single-Walled Carbon Nanotubes for Explosive Detection" *Adv. Funct. Mater.* **2013**, 23, 5285–5291.
- ³¹ Fennell, J. F.; Liu, S. F.; Azzarelli, J. M.; Weis, J. G.; Rochat, S.; Mirica, K. A.; Ravnsbæk, J. B.; Swager, T. M. "Nanowire Chemical/Biological Sensors: Status and a Roadmap for the Future" *Angew. Chem. Int. Ed.* **2016**, 55, 1266–1281.
- ³² Ishihara, S.; O'Kelly, C. J.; Tanaka, T.; Kataura, H.; Labuta, J.; Shingaya, Y.; Nakayama, T.; Ohsawa, T.; Nakanishi, T.; Swager, T. M. "Metallic vs. Semiconducting SWCNT Chemiresistors: A Case for Separated SWCNTs Wrapped by Metallo-Supramolecular Polymer" *ACS Appl. Mat. & Interfaces* **2017**, 9, 38062–38067.

-
- ³³ Zhu, R.; Azzarelli, J. M.; Swager, T. M. “Wireless Hazard Badges for Nerve Agent Simulants” *Angew. Chem. Int. Ed.* **2016**, *55*, 9662–9666.
- ³⁴ Esser, B.; Schnorr, J. M.; Swager, T. M. “Selective Detection of Ethylene Gas Using Carbon Nanotube based Devices: Utility in Determination of Fruit Ripeness” *Angew. Chem. Int. Ed.* **2012**, *51*, 5752-5756.
- ³⁵ Liu, S. F.; Petty, A. R.; Sazama, G. T.; Swager, T. M. “Single-walled Carbon Nanotube-Metalloporphyrin Composites for the Chemiresistive Detection of Amines and Meat Spoilage” *Angew. Chem. Int. Ed.* **2015**, *54*, 6554-6557.
- ³⁶ Zhu, R.; Desroches, M.; Yoon, B.; Swager, T. M. “Wireless Oxygen Sensors Enabled by Fe(II)- Polymer Wrapped Carbon Nanotubes” *ACS Sensors*, **2017**, *2*, 1044-1050.
- ³⁷ 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” *Chemical Reviews*, **2000**, *100*, 2595-2626.
- ³⁸ Wang, F.; Swager, T. M. “Diverse Chemiresistors Based Upon Covalently Modified Multi-Walled Carbon Nanotubes” *J. Am. Chem. Soc.* **2011**, *133*, 11181–11193.
- ³⁹ Askim, J. R.; Mahmoudi, M.; Suslick, K. S. “Optical Sensor Arrays for Chemical Sensing: The Optoelectronic Nose” *Chem. Soc. Rev.*, **2013**, *42*, 8649-8682