Micropatterned diffraction gratings: new chemical and biological sensors

by Dr. Ryan Bailey and Professor Joseph Hupp

Chemical and biological sensing are problems of tremendous contemporary technological importance. Recently a new methodology based upon the modulation of diffracted light by micropatterned gratings has been demonstrated for the detection of volatile and aqueous phase chemical and biological targets. This article highlights recent developments and future applications of this promising new approach.

The design of chemical and biological sensors for use in multiple regulatory and human health contexts is of great interest. Possible applications for such sersors include environmental monitoring, water quality assurance, workplace air quality assessment, many aspects of biodiagnostics, and, of course, many facets of homeland security. When developing new sensing methodologies, two distinct considerations must be addressed. First, target molecules must be localised into or onto the sensing media by either chemical or physical means. Upon target localisation, the binding events are converted into externally observable signals via an array of transduction mechanisms. Differences in transduction mechanism are the major distinction between sensor technologies and often establish the advantages or set the limitations of a particular system.

While the aforementioned sub-problems are, in principle, independent, requirements of a particular transduction scheme often impose limitations on allowable receptor media, thus limiting the scope of detectable analytes. Particularly interesting are versatile transduction methodologies capable of detecting any chemical or biological target, so called "universal" sensors. By definition a universal platform must have sensitivity to an entity or property possessed by every molecular species. As discussed below, diffraction-based sensors, which belong to the family of refractive index-based sensors including SPR [1], LSPR [2] and interferrometric sensors [3, 4], fulfill this requirement by virtue of their universal sensitivity and lack of significant design constraints.

Principles of diffraction-based sensing

Micropatterning of a "receptor" material, regardless of atomic or molecular structure, into a periodic array on the length scale of the wavelength of visible light results in the creation of a visible-region diffraction grating [5]. This occurs because of a periodic contrast in the complex index of refraction ($\tilde{n} = n+ik$) between the patterned lattice and the surrounding media, typically air or water. If the incident radiation is coherent and monochromatic, interaction with the pattern or grating will generate a characteristic diffraction pattern that is related to the physical pattern via a Fourier transform. The amount of light that is diffracted, measured as the diffraction efficiency (DE), is dependent upon the refractive index, $\Delta\tilde{n}$, between the patterned regions. If, upon exposure to an analyte, the grating material has some specific or non-specific interaction, localising the target within or on the surface of the grating, the refractive index contrast is changed, leading to a modulation in grating diffraction efficiency. Monitoring this change, using inexpensive photodiodes or CMOS device, provides the sensor transduction mechanism.

Non-resonant detection of volatile organic compounds

Because all molecular species have, by definition, a refractive index greater than that of vacuum ($n=1$), diffraction-based chemosensors are responsive to volatile organic compounds as they displace void volume air within a porous sensing framework [6]. Inspired by surface acoustic wave arrays [7], polymeric materials were configured into chemoresponsive diffraction gratings [Figure 1], and evaluated against a representative set of volatile analytes over environmentally relevant concentration ranges [8]. These sensor elements were found to respond in a rapid and reproducible fashion to each analyte in a four-

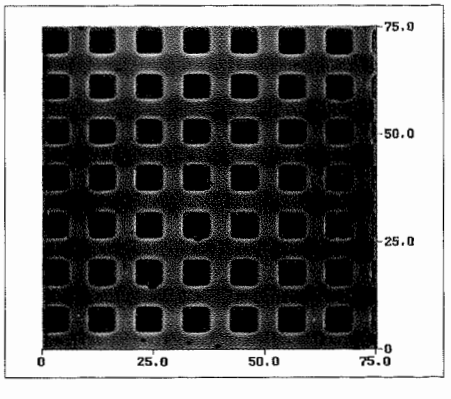

Figure 1. Atomic force microscope image of a representative micropatterned polymeric grating used for diffraction-based VOC detection. The grating shown features 5 x 5 mm features and is ~165 nm thick.

member set. The relative magnitudes of responses differed for different polymeric materials, but showed good qualitative agreement with responses reported for surface acoustic wave measurements. It seems clear that together with additional elements, these polymeric gratings could be assembled into an array-based sensor system affording simultaneous identification and quantification of unknown analytes and simple analyte mixtures. In this configuration, detection limits for polymeric gratings are limited solely by analyte partitioning, a property inherent to the sensing media. However, as discussed below, strategies are in place by which enhanced sensitivity can be achieved.

Resonant amplification of grating responses: signal enhancement and analyte differentiation

Based upon a vapochromic charge transfer salt [9], gratings were fabricated that undergo an analyte-specific colour change upon target intercalation. As the colour of the material changed, becoming more or less in registry with the diffraction probe laser, dramatic resonance amplification and deamplification of sensor responses has been demonstrated, taking advantage of changes in the imaginary component of the index of refraction, k [10]. The enhanced sensitivity, described theoretically, is in part due to the intimate coupling between changes in absorptivity, α, and real refractive index component, n, as described by the Kramers-Kronig transformation. An example of wavelength-dependent resonant signal enhancement is illustrated in Figure 2 for the detection of chloroform, where the response of a grating constructed by soft lithography from a charge-transfer salt increases 3,500-fold when the probe wavelength is changed from non-resonant to resonant.

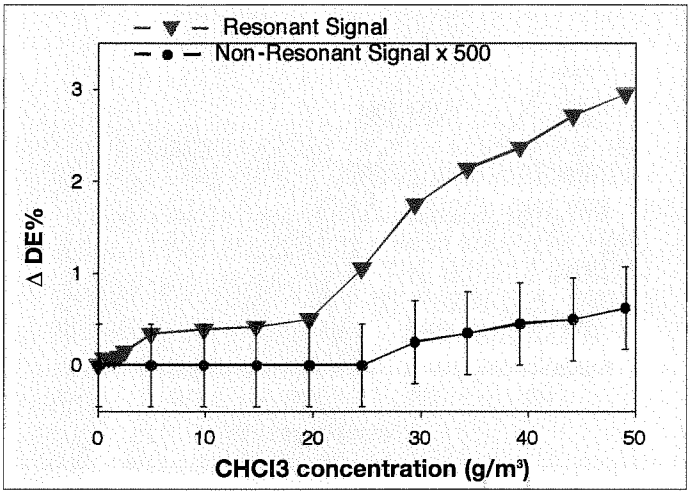

Figure 2. For a given exposure to an analyte, chloroform in this case, measurements made with resonant probe diffraction beams (-▼-) are significantly amplified compared to non-resonant laser wavelengths (-●-).

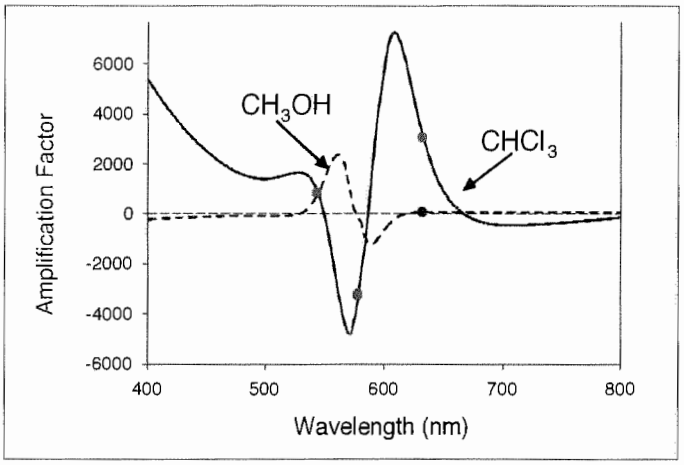

Figure 3. Besides enhancing signal magnitudes, resonance amplification also imparts chemical specificity. In this plot, the circles are experimental points and the solid line is a theoretical calculation demonstrating how, at appropriate wavelengths such as 633 nm, certain analytes can be selectively detected even in the presence of a potentially interfering chemical.

Equally important is that the resonance enhancement can be engendered selectively. As shown in Figure 3, two analytes, in this case chloroform and methanol, interact to similar degrees with the grating material. However, because their sorption results in different optical responses, they are easily distinguished via a multicolor diffraction-based assay. In fact at a given wavelength, here 633 nm, the signal for chloroform is selectively enhanced by over 3.5 orders of magnitude compared to methanol. In other words, selectivity here is achieved entirely at the readout stage, rather than the recognition and binding stage, not only enhancing signal differentiation, but potentially engineered to eliminate responses from interfering species.

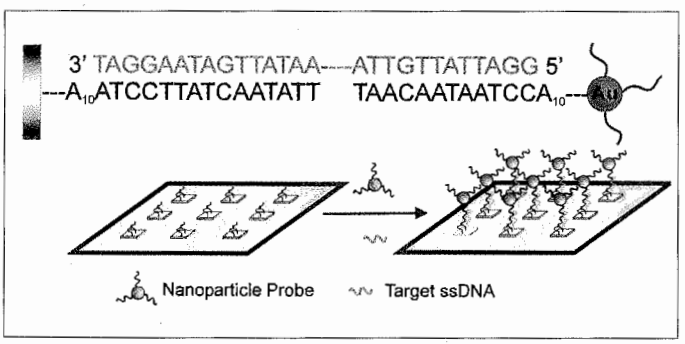

Figure 4. Schematic diagram illustrating the general approach to resonantly-enhanced biomolecule detection.

Diffraction-based biosensing

The diffraction-based detection methodology has also been extended to the sensing of biological targets. For example, binding of unlabelled target ssDNA strands to a complementary-ssDNA derivatised gold micropattern [Figure 4] alters the refractive index contrast of the grating and yields easily measured changes in diffraction efficiency. Alternatively, using a nanoparticle probe heavily functionalised with ssDNA complementary to the target DNA as a hybridisation beacon results in significant signal amplification [11]. The components on which the amplification is based are the same as those in the case of the detection of VOCs. These are namely both the optical absorption properties of the nanoparticles that are anchored proximal to the grating and their resonant refractive index contributions. The degree of spectral overlap between the diffraction probe beams and the nanoparticles plasmon absorption largely defines the wavelength dependence of the amplification, which can be either positive or negative. This first-generation device displays detection limits comparable with conventional fluorescent approaches, while providing real-time observation of hybridisation events with increased sequence specificity. Finally, the theoretical understanding of the observed nanoparticle absorption dependence points to the intriguing possibility of target multiplexing. This might be realised by simultaneously utilising multiple shapes, sizes, and/or compositions of nanoparticle tags, each possessing unique optical properties and encoding for different target molecules. While this multiplexing strategy is not entirely new, the diffraction-based assay provides an excellent detection platform for its implementation.

Several variations of this approach, where receptor molecules are directly patterned onto the underlying substrate, have been described for the detection of bacteria [12, 13] and proteins [14-16]. In contrast to the aforementioned experiments, there is minimal initial refractive index contrast in these reports meaning that no diffraction pattern is present at the onset of the experiment. Detection is therefore achieved by the emergence of a visible diffraction pattern. While the function of a "turn-on" sensor is often desirable, at times it can also lead to systematic constraints upon a device's limit of detection. This arises because a critical number of binding events must occur before a signal is observed. In the case of the aforementioned protein reports, without secondary labeling, these limits of detection appear to be in the microgram/milliliter range. This relative lack of sensitivity, as compared to monitoring changes in diffraction efficiency, is balanced by the extreme ease-of-use of such devices, possibly eliminating the need for detection equipment.

Future directions

Since the field of diffraction-based chemo- and biosensors is in its infancy, the future is wide open. Initial demonstrations have proven the sensitivity, selectivity and versatility of the technique, with applications in volatile and aqueous phase detection of chemical and biological species. Specific directions that are currently being pursued include the detection of chemical

warfare agents, interfacing the detection scheme with lab-on-a-chip technologies, pursuing high levels of biological multiplexing and implementing new grating materials and motifs for enhancing device sensitivity and versatility. Some of these directions, as well as others, are currently being pursued by a newly founded company, Alexa Biosensors. Whether in applications of air/water quality analysis, homeland security or biodiagnostics, the future of diffraction-based sensor technologies appears to be bright.

References

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CORRECTION:

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