Biomimetic Nanosensor Arrays for Selective Small Molecule Detection

Michael C. McAlpine*, H. D. Agnew‡, R. D. Rohde‡, M. Blanco‡, H. Ahmad‡, A. D. Stuparu‡, W. A. Goddard‡, J. R. Heath‡
* Princeton University, Department of Mechanical and Aerospace Engineering
‡ California Institute of Technology, Department of Chemistry and Chemical Engineering

Statement of Purpose: The promise of designing a universal platform consisting of miniaturized sensors which can be programmably "tuned" to respond only to analytes of interest and reject all others could stimulate revolutionary scientific and technological opportunities. Biomimicking smart materials which integrate chemical recognition moieties with sensitive transducers could provide a general platform for highly specific smell sensors. Oligopeptides are robust substrates for the selective recognition of a variety of chemical and biological species. Likewise, semiconducting nanowires are extremely sensitive gas sensors. Here we propose a bio-inspired approach to mimicking olfaction by linking peptides to silicon nanowire sensors for the selective detection of small molecules. The silica surface of the nanowires is passivated with peptides using amide coupling chemistry. The peptide/nanowire sensors are designed, via the peptide sequence, to exhibit highly selective responses to a range of target analytes, and to detect traces of these gases from "chemically camouflaged" mixtures. We anticipate that this work will reveal fundamental understandings of the relative contributions of inter-molecular reactivity and structural identification in the function of olfactory protein receptors. Furthermore, the unique capability to tailor odorant sensing should open up revolutionary opportunities in medical and sensing applications.

Methods: Silicon nanowires (SiNWs) were fabricated via the previously described superlattice nanowire pattern transfer (SNAP) technique, which can produce NW arrays from virtually any thin-film material with a width and pitch translated from the precisely controlled film thickness and spacing of a superlattice template. SiNW surfaces terminate in intrinsic silica, which has a well established chemistry, permitting NW surface modification without strongly affecting the semiconducting core. Peptides can thus be immobilized onto the NWs using amide coupling. The SiNW sensor chip was treated to an O_2 plasma oxidation step, then immersed in a 1% toluene solution of the surface modifying reagent 3-aminopropyltrimethoxysilane for 50 min to generate amine-terminated SiNW surfaces. Next, oligopeptides synthesized with the desired recognition sequences, plus an aspartic acid "linking residue" tail at the carboxy-terminus, were dissolved in DMF (20 mM), mixed with coupling reagents, and immediately injected into PDMS (polydimethylsiloxane) microfluidic chambers aligned to the device islands such that the channels intersected with the sensors. Once this coupling reaction was complete (2 hrs), the microfluidic channels were removed and the chip thoroughly rinsed to remove uncoupled peptide. Finally, the chip was treated to a piperidine solution to cleave the Fmoc protecting group.

Results: For these preliminary studies, we chose acetic acid and ammonia target molecules, because peptide sequences against both have been identified, and they can serve as exhaled breath disease biomarkers for asthma (acetic acid), and kidney diseases (ammonia). NW sensor libraries were fabricated to evaluate the selectivity of NW-peptide sensors. The components comprised one sensor modified with an acetic acid recognition peptide sequence (RVNEWVID), and one with an ammonia recognition sequence (DLESFLD). The figure shows normalized responses of these NW sensors to 100 ppm levels of acetic acid and ammonia vapors diluted in N_2. We assign these responses as arising from physisorption of the analyte onto the NW surface. Furthermore, these responses were reproducible and reversible, although sensor recovery required vacuum pumping and gentle heating. Most strikingly, the NH_3 recognition peptide displays ca. 75:1 selectivity towards ammonia over acetic acid. This specificity is clearly reversed in the AcOH recognition peptide, demonstrating an orthogonal sensing response of the acetic acid peptide to AcOH relative to NH_3.

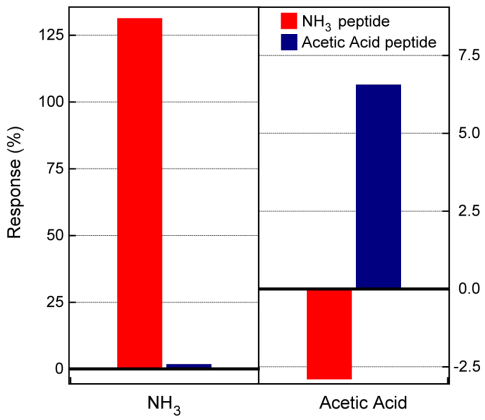

Figure 1. Conductance responses of the peptide-nanowire hybrid sensors. The abscissa is labeled with the analytes.

Conclusions: The "holy grail" of sensing is a rationally designed platform in which any given target analyte is inputted into a combinatorial process to generate a highly sensitive (sub-ppb) and specific device or device array towards the target compound. Promisingly, our preliminary data has indicated that oligopeptides can be covalently coupled to surfaces of NW sensor arrays using straightforward on-chip modifying reaction chemistry. Upon exposure to target small molecules, the hybrid materials demonstrate the ability to orthogonally sense at low concentrations. These results serve as a model platform in the use of sensors for targeted applications such as noninvasive breath monitoring for molecular disease indicators.