Gold Nanoparticle Chemiresistors as a Generic Platform for Sensing

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ABSTRACT

Thiol-functionalized gold nanoparticle chemiresistors can respond to low-molecular weight chemicals through changes in electrical resistance. This low-cost sensor technology is currently being developed for multiple applications including water quality, microbial metabolomics, environmental monitoring, and point-of-care disease diagnostics. Previously, chemiresistors could only be used for gas-phase sensing, restricting their potential applicability. We have now shown that chemiresistors can also be used directly in liquids with the potential to screen contaminants in groundwater and metabolites in body fluids.

Keywords: nanoparticles, biosensors, chemiresistors, diagnostics

1 INTRODUCTION

Thiol-functionalized gold nanoparticle chemiresistors (Fig. 1) represent a class of sensors that are simple to fabricate, have low power requirements and offer tunable selectivity [1-5]. The chemiresistors function by a change in electrical resistance of a gold nanoparticle film in the presence of a chemical species (Fig. 2). The chemical properties of the thiols that coat the gold nanoparticles dictate the extent in which target chemicals change the resistance of the nanoparticle film. The partitioning of a chemical species into the thiol component of the film swells the nanoparticle film, thereby increasing the interparticle separation and the electron tunneling distance. Several factors influence the chemical response of the gold nanoparticle chemiresistors and are described by a theoretical model that relates the response (magnitude and kinetics) to the chemical concentration and partitioning of the chemical between the thiol layer and water phase [6-8].

Through minimization of the size and spacing of the interdigated electrodes in which the gold nanoparticle films are in contact with, we have shown that it is possible to operate such a chemiresistor sensor in a highly ionic solution [5-14]. Previously, such devices were only known to operate in the gas phase. This creates opportunities for a wider range of potential applications, where it may be beneficial to sample directly in liquids by providing access to non-volatile chemical species.

The use of chemiresistor arrays, whereby the chemiresistors are tuned with different thiol-functionalised gold nanoparticles, allows for a semi-selective approach to discriminating solutions of different chemicals [11, 13, 14]. These arrays of gold nanoparticles have been used for a range of liquid-phase applications including discriminating hydrocarbon fuels, bacterial spoilage of milk, and are presently being investigated for human disease diagnosis.

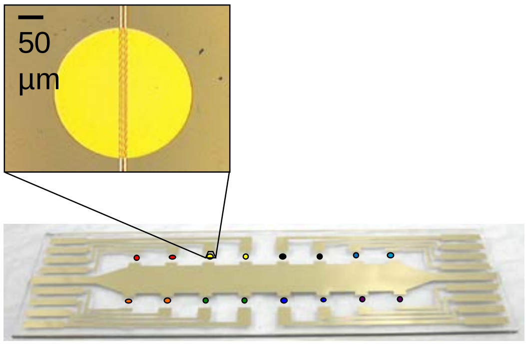

Fig. 1: An array of gold nanoparticle chemiresistors on a glass microslide. Inset shows the gold nanoparticle film deposited between microelectrodes.

2 EXPERIMENTAL

Gold band microelectrodes (nominal length of 3 mm and width of 5 µm) with an electrode spacing of 5 µm were prepared on a glass microscope slide using a standard photolithographic technique as described previously [5]. The electrode-patterned glass slides were pretreated with (3-mercaptopropyl)triethoxysilane prior to deposition of the nanoparticle film.

4-(Dimethylamino)pyridine-coated gold nanoparticles (DMAP-Au_{NP}) with a diameter of 5 nm were prepared by following the procedure described by Brust and co-workers [15] and Gittins and Caruso [16]. 1% w/v DMAP-Au_{NP} ink in 4% v/v *N*-methyl-2-pyrrolidone was then deposited on the microelectrodes using an Autodrop inkjet printing system (Microdrop Technologies, Germany). The thickness of the film can be controlled by varying the volume and the concentration of the nanoparticle ink deposited. After evaporation of the solvent, the exchange of the DMAP ligand with the thiol ligand was performed by immersing the microelectrodes in a 1 mM solution of the thiol in acetonitrile for 2 hours.

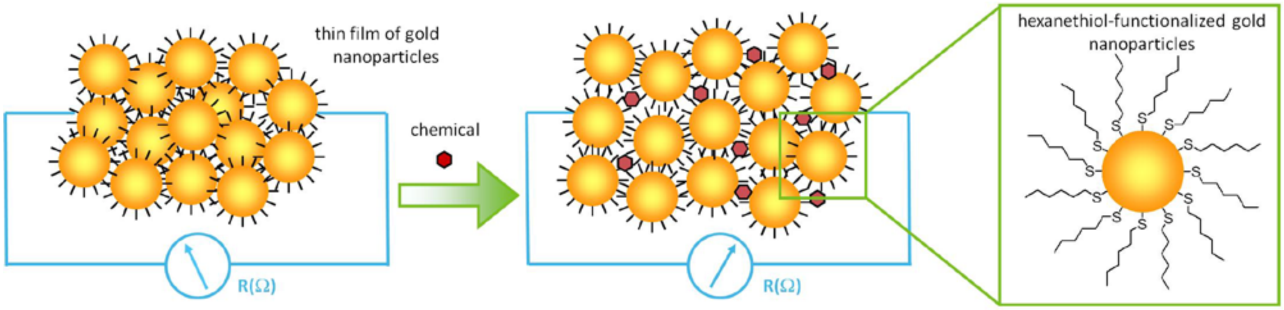

Fig. 2: Principle of gold nanoparticle chemiresistor operation: a chemical species partitions into the thiol-functionalized gold nanoparticle film causing swelling of the film and an increase in measured electrical resistance.

Thiol-functionalised sensors were inserted into a fluidic system [11] whereby the sensor array could be exposed to solutions containing analytes of interest. The responses of the thiol-functionalized gold nanoparticle films to the different test analytes were investigated using DC resistance measurements. An electrical measurement system built in-house was used where the sensors were biased at 100 mV DC. Data were recorded with an eDAQ e-corder at 1000 points/s with eChart 5.5.6 software (eDAQ, Australia).

3 RESULTS AND DISCUSSION

Gold nanoparticle chemiresistors can be characterized by their relative resistance change, $\Delta R/R_0$, in the presence of an analyte. We find that the relative resistance change of the nanoparticle film upon analyte exposure, for instances where film swelling is small, can be approximated as:

$$\frac{\Delta R}{R_0} \propto P_{\mathrm{SAM/water}} c$$

where $P_{\mathrm{SAM/water}}$ is the partition coefficient of the analyte for the thiol self-assembled monolayer (SAM) and water, and c is the analyte concentration [6-8].

When an array of different thiol-functionalized gold nanoparticle chemiresistors is exposed to an analyte, each sensor in the array has a unique response. The responses form a signature that is defined by the chemistry and concentration of that particular analyte. Statistical analyses of these response signatures can determine whether the analytes can be discriminated.

We have investigated several applications for the chemiresistor array technology in liquid environments. For instance, it has been successfully applied to the discrimination of hydrocarbon fuels, such as crude oil, diesel and gasoline, in artificial seawater [11, 13]. It was observed that the 2-naphthalenethiol-functionalized gold nanoparticle chemiresistor gave a strong response to unleaded gasoline whereas the 1-thioglycerol-functionalized gold nanoparticle chemiresistor gave a strong response to diesel and crude oil. Based on the responses of these two sensors alone, the unleaded gasoline could be differentiated from oil and diesel. The use of a 16-sensor array sensor could achieve even higher discrimination (Fig. 3).

We have also demonstrated that gold nanoparticle chemiresistors can operate in biological fluids in combination with ultrafiltration membranes [14]. The use of ultrafiltration membranes protects the gold nanoparticle chemiresistors from fouling by large biomolecules. A 10 kDa molecular-weight cut off membrane on the chemiresistor was found to be optimum for detecting small analytes in a protein-loaded matrix. The sensor could also detect the bacterial spoilage of milk by using a multivariate statistical analysis approach on the collected data. Pasteurised skim milk was exposed to the chemiresistor array at various time points over a three-week period, and the relative resistance changes were recorded. The data revealed observable changes in the chemiresistor sensor array responses as spoilage time increased past 16 days (Fig. 4). Such a quick and easy screening method in the food and drink industry could help prevent the spread of food borne illnesses.

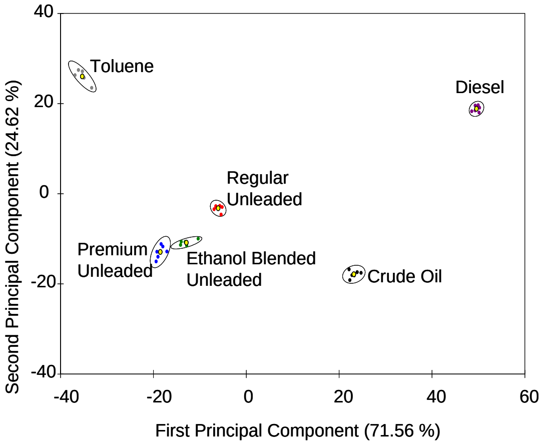

Fig. 3: Principal component plot generated from discriminant analysis of a 16 chemiresistor array response to samples of artificial seawater spiked with hydrocarbon fuels and a toluene control. The ellipses mark the 95% confidence boundaries.

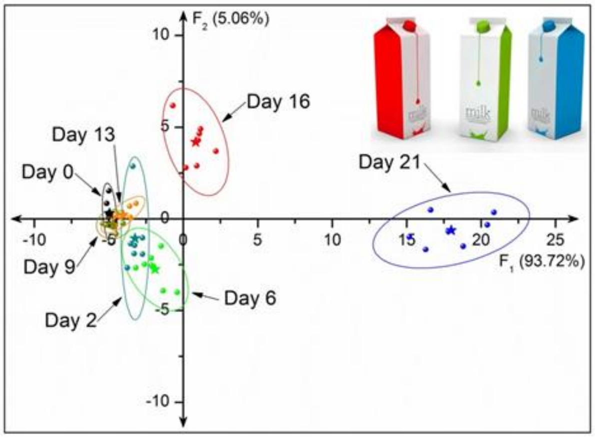

Fig. 4: A two-dimensional discriminant analysis plot of the chemiresistor sensor array response to the spoilage of pasteurised skim milk at various days after opening while being stored at 5°C.

Another research avenue being explored using gold nanoparticle chemiresistors is non-invasive disease diagnostics using human biological samples. Known urinary tuberculosis biomarkers (*o*-xylene, isopropyl acetate, 3-pentanol, dimethylstyrene and cymol) [17] were screened using a 1-hexanethiol-functionalized gold nanoparticle chemiresistor in both water and synthetic urine. The biomarkers were screened over a range of concentrations to generate titration curves from which limits of detection were calculated. Biomarker limits of detection in water and synthetic urine are summarised in Table 1.We have demonstrated that chemiresistor arrays can detect and discriminate tuberculosis biomarkers, with limits of detection for some tuberculosis biomarkers (*o*-xylene) only one order of magnitude away from clinically relevant levels. These preliminary results demonstrate the potential for gold nanoparticle chemiresistors to be developed into low-cost portable diagnostic devices due to their high sensitivity, tunable selectivity, simple fabrication and low-power requirements.

Table 1: Limits of detection for tuberculosis biomarkers in water and synthetic urine for a 1-hexanethiol-coated gold nanoparticle chemiresistor.

Tuberculosis biomarker	Limit of detection	
	Water (ppm)	Synthetic Urine (ppm)
3-Pentanol	16	22
Isopropyl acetate	12	10
o-xylene	0.029	0.048
2,6-Dimethylstyrene	0.022	0.03
Cymol	0.009	0.007

4 CONCLUSIONS

Gold nanoparticle chemiresistors are emerging as potential technologies for applications in environmental monitoring, food quality control and medical device diagnostics and are continuing to advance into new areas. The performance of chemiresistors combined with their simplicity and low cost makes the technology an appealing and exciting alternative to existing methods for small molecule detection in solution.

ACKNOWLEDGEMENTS

This research is supported by the Science and Industry Endowment Fund. The authors would like to acknowledge R. Chai for the electrode fabrication, J. Myers for the synthesis of gold nanoparticles, and M. Roberts for building the electronic testing equipment.

REFERENCES

[1] A. W. Snow, M. G. Ancona, W. Kruppa, G. G. Jernigan, E. E. Foos, and D. Park, "Self-assembly of gold nanoclusters on micro- and nanoelectronic substrates," *J. Mater. Chem.*, vol. 12, pp. 1222-1230, 2002.

[2] S. D. Evans, S. R. Johnson, Y. L. L. Cheng, and T. H. Shen, "Vapour sensing using hybrid organic-inorganic nanostructured materials," *J. Mater. Chem.*, vol. 10, pp. 183-188, 2000.

[3] T. Vossmeyer, B. Guse, I. Besnard, R. E. Bauer, K. Mullen, and A. Yasuda, "Gold nanoparticle/polyphenylene dendrimer composite films: Preparation and vapor-sensing properties," *Adv. Mater.*, vol. 14, pp. 238-242, 2002.

[4] G. Peng, M. Hakim, Y. Y. Broza, S. Billan, R. Abdah-Bortnyak, A. Kuten, U. Tisch, and H. Haick, "Detection of lung, breast, colorectal, and prostate cancers from exhaled breath using a single array of nanosensors," *Brit. J. Cancer*, vol. 103, pp. 542-551, 2010.

[5] B. Raguse, E. Chow, C. S. Barton, and L. Wieczorek, "Gold nanoparticle chemiresistor sensors: Direct sensing of organics in aqueous electrolyte solution," *Anal. Chem.*, vol. 79, pp. 7333-7339, 2007.

[6] B. Raguse, C. S. Barton, K.-H. Müller, E. Chow, and L. Wieczorek, "Gold nanoparticle chemiresistor sensors in aqueous solution: Comparison of hydrophobic and hydrophilic nanoparticle films," *J. Phys. Chem. C.*, vol. 113, pp. 15390-15397, 2009.

[7] E. Chow, K.-H. Müller, E. Davies, B. Raguse, L. Wieczorek, J. S. Cooper, and L. J. Hubble, "Characterization of the sensor response of gold

nanoparticle chemiresistors," *J. Phys. Chem. C*, vol. 114, pp. 17529-17534, 2010.

[8] K.-H. Müller, E. Chow, L. Wieczorek, B. Raguse, J. S. Cooper, and L. J. Hubble, "Dynamic response of gold nanoparticle chemiresistors to organic analytes in aqueous solution," *Phys. Chem. Chem. Phys.*, vol. 13, pp. 18208-18216, 2011.

[9] E. Chow, J. Herrmann, C. S. Barton, B. Raguse, and L. Wieczorek, "Inkjet-printed gold nanoparticle chemiresistors: Influence of film morphology and ionic strength on the detection of organics dissolved in aqueous solution," *Anal. Chim. Acta*, vol. 632, pp. 135-142, 2009.

[10] E. Chow, T. R. Gengenbach, L. Wieczorek, and B. Raguse, "Detection of organics in aqueous solution using gold nanoparticles modified with mixed monolayers of 1-hexanethiol and 4-mercaptophenol," *Sensor. Actuat. B-Chem.*, vol. 143, pp. 704-711, 2010.

[11] J. S. Cooper, B. Raguse, E. Chow, L. Hubble, K.-H. Müller, and L. Wieczorek, "Gold nanoparticle chemiresistor sensor array that differentiates between hydrocarbon fuels dissolved in artificial seawater," *Anal. Chem.*, vol. 82, pp. 3788-3795, 2010.

[12] L. Wieczorek, B. Raguse, E. Chow, K.-H. Müller, J. S. Cooper, and L. J. Hubble, "Gold nanoparticle chemiresistors – Towards a universal (bio) chemical sensor system," *Eur. Cell Mater.*, p. 271, 2010.

[13] J. S. Cooper, E. Chow, L. J. Hubble, L. Wieczorek, K.-H. Müller, and B. Raguse, "Chemical sensor array that can differentiate complex hydrocarbon mixtures dissolved in seawater," *Sensor Lett.*, vol. 9, pp. 609-611, 2011.

[14] L. J. Hubble, E. Chow, J. S. Cooper, M. Webster, K.-H. Müller, L. Wieczorek, and B. Raguse, "Gold nanoparticle chemiresistors operating in biological fluids," *Lab Chip*, vol. 12, pp. 3040-3048, 2012.

[15] M. Brust, D. Bethell, C. J. Kiely, and D. J. Schiffrin, "Self-assembled gold nanoparticle thin films with nonmetallic optical and electronic properties," *Langmuir*, vol. 14, pp. 5425-5429, 1998.

[16] D. I. Gittins and F. Caruso, "Spontaneous phase transfer of nanoparticulate metals from organic to aqueous media," *Angew. Chemie Int. Edit.*, vol. 40, pp. 3001-3004, 2001.

[17] K. M. Banday, K. K. Pasikanti, E. C. Y. Chan, R. Singla, K. V. S. Rao, V. S. Chauhan, and R. K. Nanda, "Use of urine volatile organic compounds to discriminate tuberculosis patients from healthy subjects," *Anal. Chem.*, vol. 83, pp. 5526-5534, 2011.