Delinquent Sensors & Schizophrenic Materials: Using Molecular Switches to Make Materials with multiple personalities

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Introduction

Chemical sensors and biosensors are devices that provide information about binding events happening at the interface between a sensitive film/membrane and a sample phase. The function of the sensitive film/membrane is to ensure that the binding at this interface is as selective as possible and hence the film/membrane usually contains entrapped or covalently bound sites (*e.g*. ligands, enzymes, antibodies) to impart the selectivity. The binding event is further coupled with a transduction mechanism of some kind; and in optical sensing, this usually involves a change in the colour or fluorescence of the film/membrane.

Clearly, these materials are 'active' in that they must interact with the sample, and binding processes must occur that lead to signal transduction for them to be of any analytical use. However, it is self-evident that these sensitive interfaces will change over time, for example due non-specific binding in real samples that can lead to surface poisoning, or leaching of active components into the sample phase. Consequently, the response characteristics of chemical sensors and biosensors tend to change over time, and there tends to be a gradual decrease in sensitivity, loss of selectivity and drifting of the baseline signal. These effects are well-known to those experienced in using these devices, and in practice, they may be overcome by regular calibration, until the device deterioration reaches some limiting level.

Currently, there is very significant interest in the deployment of sensor networks, and many important applications require the involvement of chemical sensors and biosensors. However, for this to happen in large scale, there needs to be a revolution in the way chemical sensors/biosensors are employed, as conventional calibration is inappropriate for large-scale deployments due to the cost of ownership (particularly maintenance) of these rather complex devices.[1-3]

In this article, we consider the use of 'adaptive' materials (*i.e*. materials that can be switched reversibly between two or more different forms with radically different characteristics). This may open the way to the development of materials that can exist in a passive form (non-binding) until a measurement is required, at which point the material is switched to an 'active' form. Binding then occurs and a signal is generated, and the material subsequently switched back to the 'passive' form. We have demonstrated that binding of metal ions and amino acids at spiropyran modified surfaces can be controlled photonically using LEDs.[3-5] It is possible that this may provide a route to more sophisticated materials whose host-guest binding behaviour and signal generation can be activated or deactivated on demand. This effect has important potential applications in sensors, purification resins, separation science and drug delivery. In this article we report progress on the modification of several materials with spiropyran and their incorporation within microfluidic devices.

Spiropyran- Photoswitchable ligands

Upon irradiation with UV light, spiropyran (SP) undergoes a heterolytic cleavage of the C-O bond switching from an aco-planar uncharged, colourless isomer to a planar zwitterionic, highly coloured merocyanine (MC) isomer.[6-8] The MC isomer possesses an electron-rich phenolate oxygen atom capable of serving as a binding site for certain metal ions (Figure 1).[7, 9] Conversely, irradiation with visible (green) light causes the ejection of bound metal ions from the MC-complex and regeneration of the passive SP form. This very interesting behaviour stimulated us to investigate whether SP could be used to make intelligent surfaces that exhibit photo-reversible ion-binding behaviour.

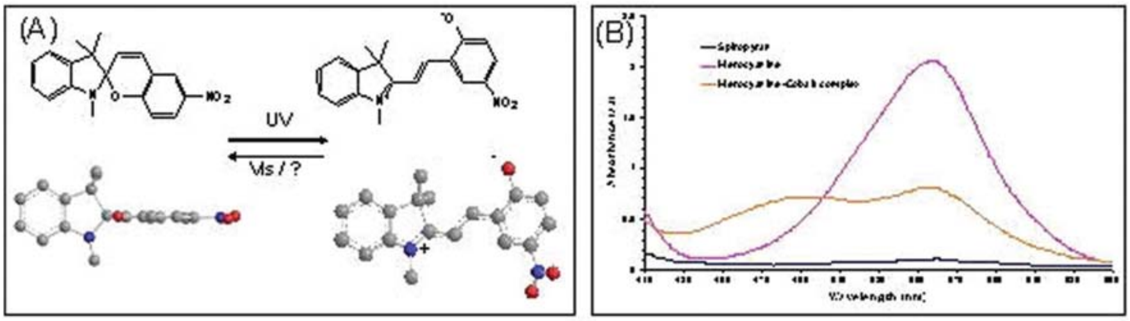

Figure 1. A: Molecular structures of nitro-benzospiropyran (left) and its photo-isomer merocyanine (right). Chem 3D structures included to emphasize the dramatic change in the molecular geometry when irradiated with UV or visible light. B: UV-vis spectra of 10-3 M spiropyran in acetonitrile, irradiated with 60 seconds UV light, and treated with $CoCl_2$.

Attachment of SP to a polymer matrix or surface is a useful way to overcome the limited aqueous solubility of SP.[10, 11] Coupled with the increasing spectral coverage and power output of LEDs, surface immobilised photoswitchable ligands offer exciting opportunities for new ways to control and mediate binding processes occurring at solution-surface interfaces. Recently, we have been using clusters of LEDs for triggering events and monitoring the resultant colour changes for colorimetric analysis.[5] Previously, we produced a polymethyl methacrylate-based polymer which was SP-modified via a carboxylic handle and an 8-carbon linker. By solvent casting this onto a polymethyl methacrylate (PMMA) sheet we were able to form SP-modified films on the substrate that were approximately 130 μm thick.[12] We also demonstrated that the binding of metal ions such as Co^{2+} could be photonically controlled on these modified surfaces. It was found that an 8-carbon spacer from the polymer backbone was the minimum length needed to provide the necessary flexibility for effective formation of the 2:1 SP:metal ion sandwich complexes.[13]

Spiropyran functionalised microbeads

Microbeads are small spherical units that can be suspended in different solvents according to the nature of the beads matrix and whose diameter, on the microscale range (10^{-6} m), allows the development of relatively high surface areas when compared to flat film surfaces. The use of micro and nanobeads for different applications in life sciences, medicine and drug delivery has been widely reported in the literature,[14-16] as they provide extensive surface areas upon which a molucule can be immobilised (solid-like behaviour), yet they are easily transported (liquid-like behaviour), and easily separated from the solution medium.

Photoswitchable silica and polystyrene microbeads with different diameters have been prepared by covalently functionalising with a spiropyran derivative. The spiropyran on the microbead surface can be switched using LEDs (Figure 2) between a passive SP state which exhibits no ion-binding behaviour, and an active MC state which forms complexes with certain metal ions, especially transition metals, such as Cu^{2+}, Co^{2+} and Zn^{2+}. Upon formation of the merocyanine-metal ion complex, the microbeads undergo a further ion-dependent spectral and colour change (see Figure 1). Exposure of these beads to a white LED causes the guest metal ion to be expelled and reformation of the passive MC form. The process to photocontrolled ion loading and release from the SP modified beads is fully reversible and can be recycled.

Microfluidic systems have emerged as novel analytical tools in many areas of science and industry. Their inherent qualities include low power requirements, small sample and reagent consumption, rapid analysis times, and these, coupled with autonomous operation provide unique opportunities to create novel and more powerful devices with a myriad of applications.[17] Although highly desirable, examples of on-chip liquid chromatography microfluidic platforms (unlike electrophoresis) are relatively rare, partly because the integration of LC columns without external packing remains a difficult challenge.[18]

However, the spiropyran functionalised microbeads mentioned previously can be incorporated into microfluidic flow systems, such as capillary separation columns, whose binding behaviour can be externally modulated using LEDs. By utilizing the photoswitchable ion-binding properties of the microbeads, it is possible to spatially control certain areas of the column, switching on ion-binding, and inducing release of bound species using light. Figure 3 presents a simple chip device fabricated using soft lithography techniques. It consists of two independent 360 μm internal diameter quasi-circular channels fabricated in polydimethylsiloxane (PDMS)/glass, Figure 3A, with the chip channels connected to the macro-world by 50 μm internal diameter (I.D.) silica fibres.

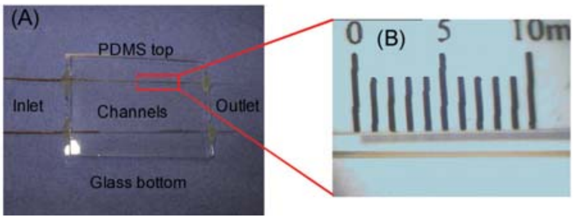

Figure 3. A: hybrid PDMS-glass chip with two 360 μm I.D. channels. B: PDMS channels packed with 5 μm diameter SP-modified beads

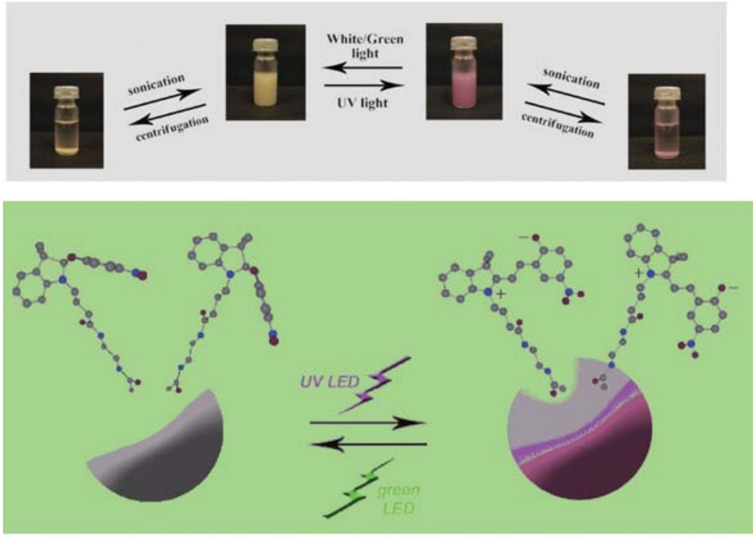

Figure 2. Molecular and macroscopic colour change on the microbead surface; irradiation with a UV LED causes SP modified microbeads to convert to the ion-binding active, purple MC form, while exposure to white LED regenerates the inactive, clourless SP form. In contrast to the inactive SP form, the MC form will bind certain metal ions, and this process is fully reversible using a white or green LED

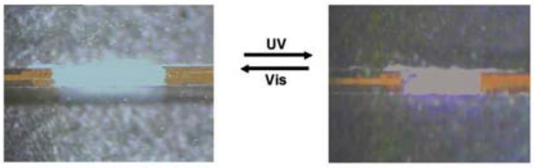

Figure 4. Polystyrene beads packed in a 360 μm PDMS channel chip. Photochromic switching of microbead column between the SP isomer (left) and the MC isomer (right) using LEDs.

5 μm diameter polystyrene microbeads functionalized with spiropyran were packed into the PDMS channels to form microbead columns. These were obtained by placing a filter at the channel outlet and introducing a suspension of functionalized microbeads into the channel (flow rate 5 μL min^{-1}). The microbead columns generated in the PDMS channels were approximately 2 cm in length, and could be successfully switched between the SP and MC isomers, using a 375 nm UV LED (for the SP →MC conversion), and a white 430-760nm LED (for the MC→SP conversion), see Figure 4. In principle, this system could be used to preconcentrate certain metal ions from samples, and subsequently release them entirely under photonic control. In addition, the system is inherently self-indicating, in terms of which isomer is present (SP-inactive, MC-active) and whether the guest ion is bound or not.

Furthermore, as beads can be mobile, they can be used to pick up a chemical payload in one location, and transport it to another location where it can be released, again under photonic control. In addition, as MC interacts also with more complex guests like amino acids, it may be possible to use this concept to pick up and release a much wider range of molecular payloads.

Conclusion

In conclusion, we are beginning to witness the emergence of new, sophisticated functionalized materials with binding properties that can be turned on and off using light. They are inherently self-indicating in terms of whether the active or passive form is present, and whether a guest is bound. This can happen in solution, or on planar functionalized polymer surfaces, on beads, or within channels. The user can decide when and where binding will occur, and for how long the guest remains bound, using light, and the entire process is fully reversible. We regard these preliminary results presented in this paper point the way towards even more sophisticated materials capable of switching reversibly between active and passive forms, and simultaneously providing a number of transduction modes for gathering information about the molecular environment in the immediate vicinity of the binding site when in the active mode. We are witnessing the emergence of new, switchable materials, capable of binding molecular guests, transporting them to remote locations and releasing them, and telling us what is happening at the same time. Clearly, fundamental materials science, and particularly the chemistry of these materials, is going to be an exciting area to work in for the foreseeable future.

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Prof. Dermot Diamond was a speaker at the 2008 ICI congress.

References

1. D. Diamond, *Anal. Chem.* **2004**, *76*, 278A-286A.
2. D. Diamond, *NATO Security through Science, Series A: Chemistry and Biology* **2006**, *2*, 121-146.
3. R. Byrne, D. Diamond, *Nature Materials* **2006**, *5*, 421-424.
4. S. Stitzel, R. Byrne, D. Diamond, *J. Mater. Sci.* **2006**, *41*, 5841-5844.
5. A. Radu, S. Scarmagnani, R. Byrne, C. Slater, K. T. Lau, D. Diamond, D. *J. Phys. D* **2007**, *40*, 7238-7244.
6. R. C. Bertelson, *Organic Photochromic and Thermochromic Compounds* **1999**, 11-83.
7. H. Gorner, A. K. Chibisov, *J. Chem. Soc. Faraday Trans.* **1998**, *94*, 2557-2564.
8. H. Gorner, Phys. *Chem. Chem. Phys.* **2001**, *3*, 416-423.
9. A. K. Chibisov, H. Gorner, *Chem. Phys.* **1998**, *237*, 425-442.
10. L. Evans, G. E. Collins, R. E. Shaffer, V. Michelet, J. D. Winkler, *Anal. Chem.* **1999**, *71*, 5322-5327.
11. J. D. Winkler, C. M. Bowen, V. Michelet, *J. Am. Chem. Soc.* **1998**, *120*, 3237-3242.
12. R. J. Byrne, S. E. Stitzel, D. Diamond, *J. Mat. Chem.* **2006**, *16*, 1332-1337.
13. D. Diamond, R. Byrne, S. Stitzel, (Invent DCU Ltd., Ire.) WO, 2007, pp 23pp.
14. F. L. Yap, Y. Zhang, *Biosensors and Bioelectronics* **2007**, *22*, 775-788.
15. D. Maysinger, *Org. Biomol. Chem.* **2007**, *5*, 2335-2342.
16. U. Bilati, E. Allemann, E. Doelker, *Drug Delivery Technology* **2005**, *5*, 40-47.
17. M. Brivio, W. Verboom, D. N. Reinhoudt, *Lab on a Chip* **2007**, *6*, 329-344.
18. J. Park, D. Lee, W. S. Kim, S. Lee, C. H. Ahn, *Anal. Chem.* **2007**, *79*, 3214 -3219.

Corrections

In the last issue we published an appreciation of the late Prof. Wesley Cocker. In this article Prof. Brian McMurry's name was spelt incorrectly and the time of Prof. Cocker's passing (January 30th 2007) was inaccurately reported.