A nanoparticle based chromogenic chemosensor for the simultaneous detection of multiple analytes†

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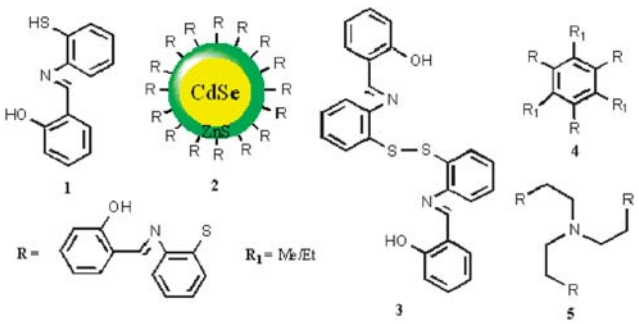
Quantum Dot–Schiff base conjugate 2 displays selectivity for Cu^{2+} and Fe^{3+} enabling the simultaneous detection of these ions in semi-aqueous solution; in contrast, the Schiff base itself displayed no selectivity.

Designing functional chemosensors for the identification and quantification of important physiological and environmental analytes is of considerable importance.[1] High sensitivity and selectivity of these chemosensors are pre-requisites for their effective operational usage.[2] Within this context, the development of sensors for multianalyte detection in real time is a challenge. Some examples of such sensors have been reported and tend to use either: the insertion of multichromogenic units combined in a single receptor,[3] a variety of detection methods (*i.e.* fluorescence and electrochemical)[4] or require detailed mathematical tools to help process the data.[5] But these methods can be tedious either from a receptor synthesis or operational viewpoint. More recently, a move from selective to differential receptors has enabled the detection of two analytes simultaneously by a single chromophore.[6]



In this study, we adopt an alternative strategy to enable differential receptor behaviour. The incorporation of an organic receptor onto the surface of a preformed CdSe/ZnS Quantum Dot (QD) results in a nanocrystal hybrid (**2**) with selectivity for both Cu(II) and Fe(III) ions. Thus, the nanoparticle surface appears to provide a framework for the self-organization of the receptors. The rationale behind the present design is based upon the fact that both **1** and its disulfide analogue **3** have effective binding affinity toward many transition metal ions (Fig. S1 and S2†). But when the same receptor pod is inserted into a framework of tripodal receptors, the final sensors (**4**, **5**) display selectivity for a particular metal ion, meaning receptor binding ability is reduced.[7] Thus, the platform (either aliphatic or aromatic) of these tripodal receptors provides a framework with divergent pods. The cation binding sites present on different pods are not easily accessible simultaneously to make an effective complex with various types of metal ions and hence selectivity is improved. For differential sensing the receptor should be semi-selective. The present design may provide some steric organization to pods and thus will not allow interaction with every metal ion. Nevertheless, the system should have enough binding sites from adjacent pods to complete the coordination sphere of some metal ions. As **1** has a thiol group present in its structure, it is an ideal candidate for attachment to a QD. To the best of our knowledge, this is the first reported example of a nanocrystal chemosensor for the simultaneous estimation of two metal ions.

Receptor **1**, 2-[(2-mercaptophenylimino)methyl]phenol, was synthesized in one step from 2-mercaptoaniline and salicylaldehyde following a literature procedure.[8] CdSe/ZnS QDs were then surface functionalized with **1** after refluxing in chloroform for 18 h. Following removal of the solvent by rotary evaporation the product was precipitated from acetonitrile and centrifuged to yield **2** as a yellow solid.

^{1}H NMR spectroscopy (Fig. 1) confirmed an almost complete ligand exchange with signals at 0.85–1.80 ppm, present in the parent QD and reflecting the methyl and methylene protons of the native trioctylphosphine oxide (TOPO) groups, being absent in the spectrum of **2**. In addition, there were significant changes in the spectra of the free receptor before

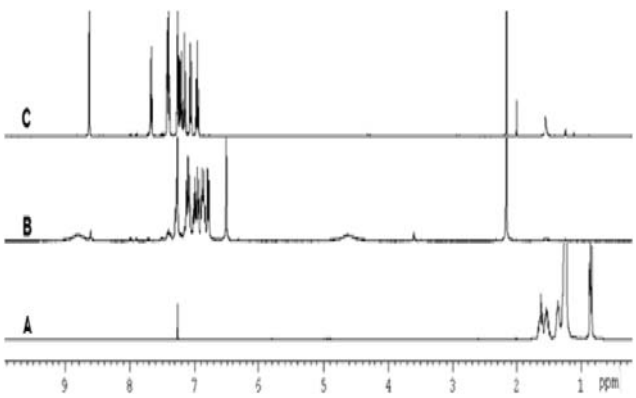


Fig. 1 Stacked ^{1}H NMR spectra of CdSe/ZnS QDs (A), **1** (B) and **2** (C). All spectra recorded in $CDCl_3$ at ambient temperature.

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and after conjugation to the QD surface. Most notable was the large downfield shift for the imine proton from 7.25 ppm in the free receptor to 8.70 ppm in **2**. The UV spectrum of **2** showed peaks in both the UV and visible regions, the former originating from the bound receptor and the latter due to the first exciton peak of the QD (Fig. S4†). The mean particle size of **2**, measured by dynamic light scattering (Fig. S5†), was found to be 15 ± 2 nm, slightly larger than the parent QD (12 ± 2 nm), most likely due to the presence of the more rigid **1** on the surface of the QD compared to flexible TOPO groups. However, when **2** was excited at 370 nm there was no evidence of QD emission. This suggests that the electron rich receptor quenches QD fluorescence, most likely by electron transfer, as has been observed when other electron rich entities have been added to solutions of QDs.[9]

Nonetheless, **2** shows remarkable chromogenic selectivity for Cu(II) and Fe(III) ions when tested against a range of other physiologically and environmentally important cations in a buffered THF–H_2O (80 : 20) solvent system. As shown in Fig. 2a, **2** is characterized by two UV bands, one centered at 275 nm and the other at 355 nm. Addition of Fe(III) resulted in a substantial increase in absorbance of these bands while the addition of Cu(II) caused a substantial bathochromic shift of both bands to 295 and 410 nm respectively. In fact these changes were so significant they could be detected by the naked eye (Fig. 3) with Fe(III) causing a change from colourless to orange and Cu(II) from colourless to green. In contrast, the addition of the other ions had a negligible effect on the UV profile of **2**. Fig. 2b shows the selectivity of **2** for various metal ions when measured at 325 and 410 nm. These particular wavelengths were chosen as 325 nm represents an isosbestic point for all ions except Fe(III) while 410 nm was the λ_{max} for Cu(II) induced changes. As is evident from Fig. 2b, only Fe(III) causes significant inference with Cu(II) at 410 nm while no

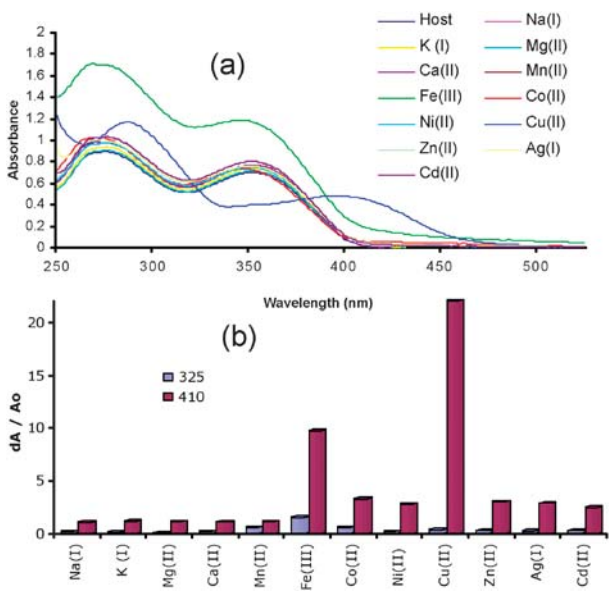

Fig. 2 (a) UV spectra for **2** in the presence of various metal ions and (b) bar chart revealing the selectivity of **2** for metal ions when determined at 325 nm (purple) and 410 nm (blue). [**2**] = 4.0×10^{-8} M; [ion] = 50 μM.

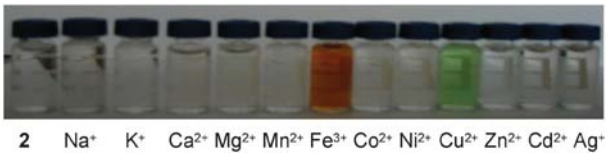

Fig. 3 Photograph illustrating the naked eye identification by **2** of Cu(II) and Fe(III). [**2**] = 4.0×10^{-8} M; [ion] = 100 μM; in an 80% THF–20% 0.01 M HEPES buffer solution at pH = 7.0.

metals produced any significant interference for Fe(III) at 325 nm.

The UV profile of **2** was also observed to be strongly dependent on solution pH (Fig. S7†). At low pH (~3.5) **2** displayed a prominent UV band with λ_{max} 325 nm. Upon increasing the pH, this absorbance gradually decreased while a new red shifted band appeared with λ_{max} 382 nm. This band most likely reflects the deprotonation of the phenolic group of the receptor and from a plot of absorbance against pH the pK_a was calculated as 8.92.[10] Thus, operating at pH 7.0 enables the clear observation of Cu(II) induced changes at 410 nm.

The titration of **2** with Cu(II) and Fe(III) is shown in Fig. 4. Both ions displayed good linearity up to a concentration of 40 μM with their binding constants (log β) being determined as 4.86 and 4.69 respectively.[11] Importantly, Fig. 4c shows that **2** is also capable of measuring Cu(II) in the presence of Fe(III) and of measuring Fe(III) in the presence of Cu(II) up to a concentration of 20 μM. Although it was possible to monitor Fe(III) concentrations in the presence of equimolar Cu(II) it was only possible to monitor Cu(II) in 0.25 molar equivalents of Fe(III). To the best of our knowledge this is the first reported

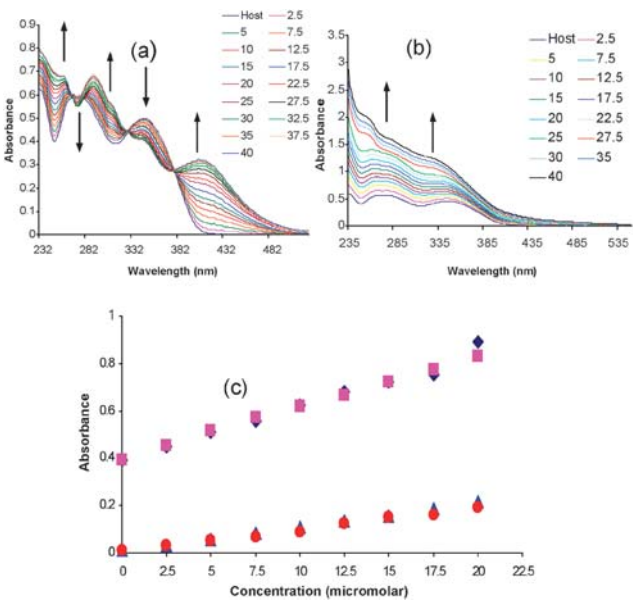

Fig. 4 UV spectra of **2** in the presence of (a) increasing Cu(II) concentration and (b) increasing Fe(III) concentration. (c) Plot of absorbance intensity of **2** against metal ion concentration for Fe(III) (blue diamonds), for Fe(III) in the presence of equimolar Cu(II) (purple squares), for Cu(II) (blue triangles) and Cu(II) in the presence of 0.25 molar equivalents of Fe(III) (red circles). Fe(III) and Cu(II) measurements were recorded at 325 and 410 nm respectively. [**2**] = 4.0×10^{-8} M.

example of a single sensor capable of measuring both Cu(II) and Fe(III) simultaneously.

We have demonstrated for the first time that the selectivity of a receptor can be altered by its incorporation onto the surface of a QD. The organization offered to the receptors by the three-dimensional surface of the nanoparticle was sufficient to enable the determination of Cu(II) and Fe(III) simultaneously, in buffered solution at physiological pH. This offers the ability to screen for these ions in competitive media by UV or the naked eye. The principle may also be extended to other receptors to help improve their selectivity and could potentially lead to a new generation of optical sensors.

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