Nanosized luminescent superparamagnetic hybrids†

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The combination of fluorescent and magnetic properties in single nanosystems is of current interest for applications in the biomedical and biological sciences, including drug delivery, and cell separation and labelling procedures. These nanocomposite particles are generally synthesised using high-temperature procedures, and many involve encapsulation in a silica or polymer coating. The resulting large particle size may limit the use of these nanocomposites in biological work. We demonstrate an aqueous self-assembly route to fabricate nanohybrids combining cadmium telluride quantum dots and magnetite nanoparticles. The entire procedure is conducted under aqueous conditions to improve sustainability and physiological compatibility. The resulting nanocomposite displays strong fluorescent emission, and superparamagnetic behaviour.

Introduction

Research at the intersection of physics, chemistry, and biology has led to the development of many applications of nanotechnology in the biological and biomedical sciences. Numerous reports describing nanocomposite materials have been published, which combine the features of two or more nanoparticles into a new, single, discrete entity. In particular, nanocomposites incorporating magnetic and luminescent functionalities are of interest for biological application as magnetic resonance imaging (MRI) contrast and drug delivery agents, and in cell separation and labelling procedures.[1-5] The majority of these functional materials are currently prepared using high temperature routes in organic solvents,[6] which means they cannot be directly dispersed in physiological media.[7] An aqueous approach, on the other hand, would help overcome physiological dispersibility issues for biological applications. Some work in the area of multifunctional nanocomposites has been undertaken, and there have been reports of silica- or polymer-coated magnetic composites, where luminescent particles have been embedded in the coating material.[8] Also, magnetic and fluorescent particles have been encapsulated simultaneously in giant vesicles.[9] In these approaches, however, small particle size is sacrificed and many of the reported ‘beads’ are several hundred nanometres in diameter.[8] Furthermore, high temperature syntheses still prevail in these reports.

The selection of magnetic and luminescent components is driven by the need for high saturation magnetisation and intense luminescence; nanoparticles of iron oxides and cadmium chalcogenides are often chosen for their respective strengths in these properties, which we will now discuss in more detail. First, of the many magnetic materials that may be prepared in nanoparticulate form, the iron oxides—including magnetite (Fe_3O_4) and maghemite (γ-Fe_2O_3)—are of particular interest because they are biocompatible, but for biomedical applications, magnetite is preferred over maghemite because of its higher saturation magnetisation and susceptibility.[10] Furthermore, the size dependent superparamagnetic behaviour of magnetite nanoparticles has resulted in its application as an MRI contrast agent.[11] Magnetite nanoparticles may be prepared by the co-precipitation route, which is a popular method because it is both simple and scalable; the pH and ionic strength may be controlled to give control of the particle size from 2 to 15 nm.[11] Second, semiconductor nanoparticles, or quantum dots (QDs), hold several benefits over traditional organic fluorophores used in biology. They show good stability, sharp and symmetrical emission spectra, nearly continuous excitation spectra above the threshold of absorption, and tunable emission allowing simultaneous excitation of different colour probes using a single excitation source.[12-14] Nanoparticles of CdTe, a cadmium chalcogenide, are an example of QDs whose fluorescence emission wavelength may be tuned across the red to green part of the optical spectrum by controlling particle size. In addition, CdTe QDs may be conveniently prepared in a microwave-assisted aqueous ‘green’ route with fluorescence quantum yields in excess of 60%, using a biomolecule, L-glutathione (GSH), as a stabiliser.[13] The green synthesis methodology requires less time and uses less toxic and cheaper raw materials with a lower reaction temperature, permitting practical large-scale preparation of QDs.[15]

The production of sub-100 nm particles is of particular importance for cellular labelling, where there is likely to be a marked difference in the uptake of colloidal quantum dots and comparatively large silica microspheres.[16] For cellular applications, the particle size must be less than 30 nm if particles are to cross the nuclear membrane,[17] and less than 15–20 nm if particles are to be used for labelling minute subcellular features.[18] The preparation of nano-sized (<100 nm) multifunctional composites is a desirable outcome, for then these particles may be of use in more advanced cell separation and labelling

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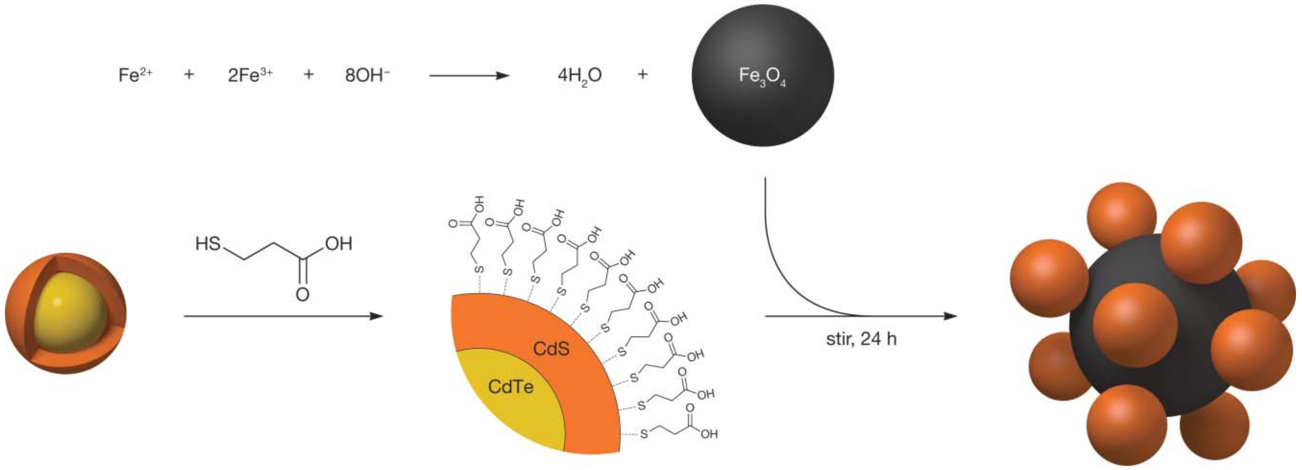
† Electronic Supplementary Information (ESI) available: Full indexed powder X-ray diffraction pattern for the nanocomposite material, with reference patterns and *d*-spacings; TEM of CdTe and magnetite nanoparticles and nanocomposite particles; magnetisation curve for as-prepared magnetite. See DOI: 10.1039/b925531a



Scheme 1 Schematic reaction summarising the preparation of the CdTe–Fe_3O_4 nanocomposite.

applications. The aim of the work herein was to prepare a luminescent and magnetic nanocomposite in an entirely aqueous procedure, by directly attaching the functional components, rather than embedding them within a comparatively large matrix. We have identified a simple aqueous self-assembly route for the attachment of cadmium telluride (CdTe) quantum dots to magnetite (Fe_3O_4) nanoparticles, both also prepared *via* aqueous routes. These materials were chosen based on the ability to prepare highly luminescent CdTe QDs in a rapid aqueous procedure and the high saturation magnetisation of magnetite. We believe that a general procedure for direct attachment of the magnetic and luminescent functional moieties will allow the design of smaller materials, where a thick polymer or silica coating to achieve a sufficient incorporation of QDs or to ensure dispersibility in water will be unnecessary.

Results and discussion

In this work, the constituent QDs and magnetic particles were formed first, and were subsequently attached to one another to form the nanocomposite (Scheme 1). First, CdTe QDs were prepared using GSH as both a stabiliser and source of sulfide ions, forming a cadmium sulfide passivating shell on the CdTe nanoparticles *in situ*, Fig. 1(a, b).[13,19] The ability of the microwave reactor to heat under pressure allowed reactions above the boiling point of the solvent, with a corresponding increase in reaction rate, permitting a fast, convenient preparation. The safer aqueous synthesis route was preferred over the ‘hot injection’ approach, which uses high temperatures, high-boiling solvents, toxic and/or unstable precursors, and dry atmospheres.[20] Superparamagnetic magnetite nanoparticles were prepared by the co-precipitation of ferrous and ferric ions in basic solution.[11] The CdTe and Fe_3O_4 nanoparticles prepared herein formed well-defined nanocrystals as seen in previously published reports.[13,21] (See supporting information for characterisation of representative QDs and Fe_3O_4 nanoparticles†).

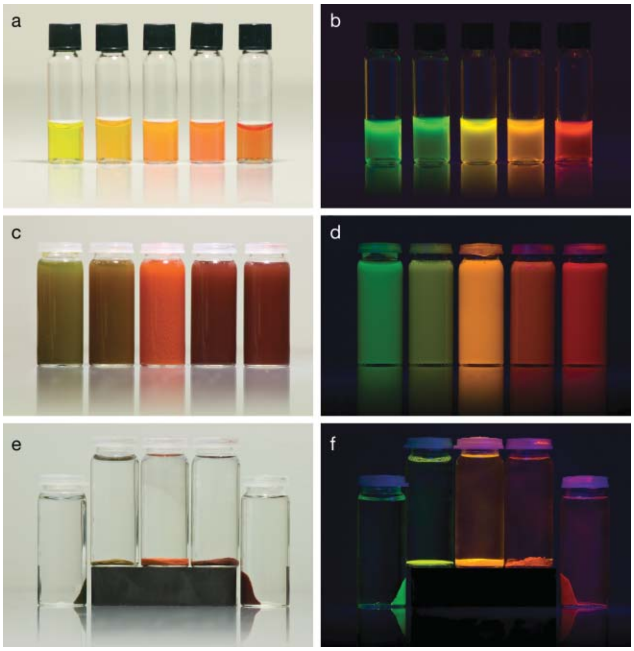


Fig. 1 Samples under white light and UV illumination at 380 nm. (a, b) Colloidal QD samples prior to treatment, (c, d) nanocomposite material suspended in water, and (e, f) the same nanocomposite samples collected by the application of a magnetic field.

Given that thiol groups readily bind to cadmium[22] and magnetite has an affinity for carboxylic acids,[23] we reasoned that the spontaneous attachment of the as-prepared QDs to magnetite particles to form the nanocomposite might have been possible due to the presence of both functionalities in GSH. We found, however, that mixing the GSH-stabilised QDs and uncoated Fe_3O_4 resulted in very little attachment; isolated magnetic particles did not fluoresce. It was likely that there was an insufficient density of carboxylic acid groups on the surface of the QDs as GSH undergoes thermal degradation to provide sulfide ions for the formation of the passivating CdS layer. Furthermore, it has been reported that both the carboxylate and thiolate groups can interact with the QD surface, resulting in a further drop in the number of free groups available.[24] Therefore, we hypothesised that a monolayer of short chain molecules incorporating thiol and carboxylic acid functional groups was necessary to provide enough grafting density for efficient attachment. For this purpose we chose 3-mercaptopropanoic acid (MPA), which has been used to replace hydrophobic ligands to solubilise nanoparticles in aqueous systems.[23] To a QD dispersion we added MPA and then uncoated Fe_3O_4 under constant stirring; after 24 h the particles were attracted to a permanent magnet indicating attachment of the two materials.

The addition of MPA to the GSH-functionalised QD particle dispersion resulted in a drop in pH of the solution. We queried whether MPA was really necessary, and if the addition of H^+ was enough to effect attachment to Fe_3O_4 by the two carboxylic acid groups on GSH. No attachment was observed by fluorescence spectroscopy for a QD dispersion acidified by dilute HCl to the same pH (pH = 4), however, which suggested that MPA served an important role in facilitating the interaction between the QDs and Fe_3O_4. We found that the analogous compound thioglycolic acid (TGA) was a successful substitute for MPA in this regard. The nanocomposite material ranged in colour from dark yellow to red as depicted in Fig. 1(c–f). The characterisation of this material is presented below.

Fluorescence properties

In order to form the composite, the addition of MPA or TGA was a crucial step. MPA and TGA have been extensively used as effective surface modification agents not only to improve the photoluminescence quantum yield of CdTe nanocrystals but also to impart stability and functionality.[25] It has been reported that the photoluminescence properties of CdTe-MPA and CdTe-TGA QDs depend upon pH, and in both cases the fluorescence intensity has a maximum (CdTe-TGA: pH 4.5, CdTe-MPA: pH 6).[25] This pH-dependent photoluminescence behaviour originates from the interaction of the carboxylate groups of MPA/TGA at the particle surface. The quantum yields of the nanocomposite samples described herein were up to 7%. The broad absorption profile of magnetite (which did not contribute to emission) and surface modification with the acidic thiol was responsible for the observed drop in quantum yield following attachment of the QDs to magnetite particles.

A red shift in PL is expected following surface modification using TGA and MPA, and is attributed to the sulfuration reaction taking place on the CdTe surface; the S : Te ratio has a strong influence on the absorption and fluorescence spectra of CdTe QDs.[25] One possible explanation is the increase of the particle size due to the increase of cadmium sulfide on the QD surface, resulting in a more uniform passivating layer and stronger PL intensity. Upon addition of the acid, a red shift in the particle emission wavelength was visibly discernable. We confirmed the shift in peak emission wavelength (about 17 nm on average) by fluorescence spectrophotometry (Fig. 2). This observation was consistent with previously reported values.[26]

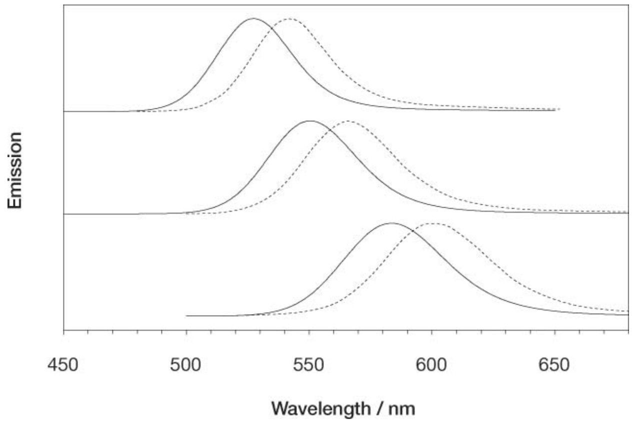


Fig. 2 Normalised fluorescence spectra of three representative nanocomposite samples, before (solid lines) and after (dashed lines) addition of MPA.

Powder X-ray diffraction

The powder X-ray diffraction pattern of the nanocomposite material revealed the presence of cubic Fe_3O_4, while the peaks for the cubic semiconductor nanoparticles (which contained CdTe and a shell of CdS) were positioned between those for each of the corresponding bulk materials, as previously reported.[7,13] Reference patterns and pattern indexing are presented in further detail in the supporting information†. Essentially, the pattern for the composite was formed by the superposition of the individual patterns for QD and Fe_3O_4 nanoparticles (Fig. 3). We concluded that there was no reaction between the luminescent and magnetic moieties that altered the crystal structures, and the attachment of the two was achieved only through surface interactions.

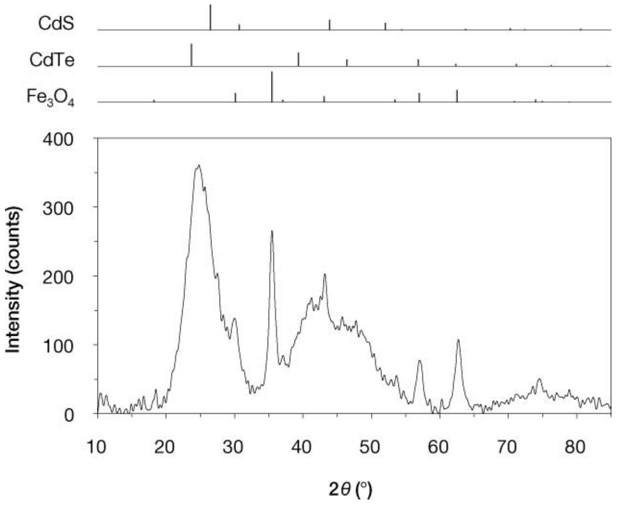


Fig. 3 Powder X-ray diffraction pattern for the nanocomposite material, with reference patterns for CdTe, CdS and Fe_3O_4.

Microscopy

Electron microscopy of the nanocomposite material (Fig. 4) showed the attachment of QDs to the surface of Fe_3O_4. The nanocomposite particles were about 15–20 nm in size. Elemental image maps of the nanocomposite, obtained using energy-filtered TEM, also indicated the presence of both Fe and Cd species. Lattice spacings measured from Fourier transforms of Fe and Cd regions of high resolution TEM images agreed with both PXRD and previously measured data. A TEM overview of the composite sample is shown in the supporting information.†

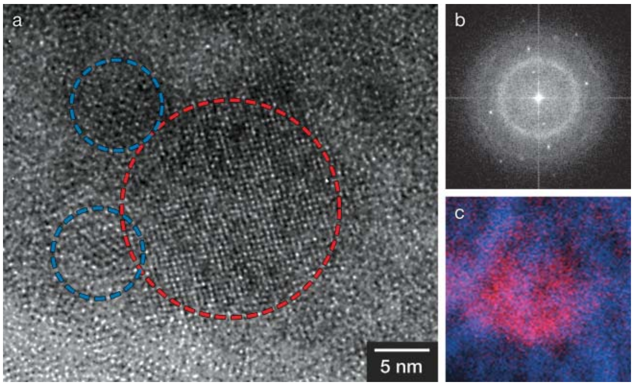


Fig. 4 (a) TEM image of the nanocomposite material, highlighting one Fe_3O_4 particle and two QDs, (b) FFT of the image, and (c) corresponding elemental map for iron (red) and cadmium (blue).

Magnetometry

Magnetisation *versus* applied field measurements at room temperature indicated zero coercivity and remanence of the nanocomposite material (Fig. 5). The magnetic behaviour was consistent with the expected superparamagnetic properties owing to the small size of the magnetic cores. We measured a representative specific saturation magnetisation of 9.2 emu g^{-1} for the nanocomposite, and based on Atomic Absorption Spectroscopy (AAS) analysis for iron content, a normalised value of 76 ± 5 emu g^{-1} for Fe_3O_4 in the composite alone. This value was close to the specific saturation magnetisation of bare 8–10 nm Fe_3O_4 nanoparticles prepared by co-precipitation as reported in earlier publications,[27] and similar to the value we measured by SQUID for the as-prepared magnetite particles (see supporting information†). This confirmed that the combination of the QDs with Fe_3O_4 did not significantly alter the magnetic behaviour of the latter.

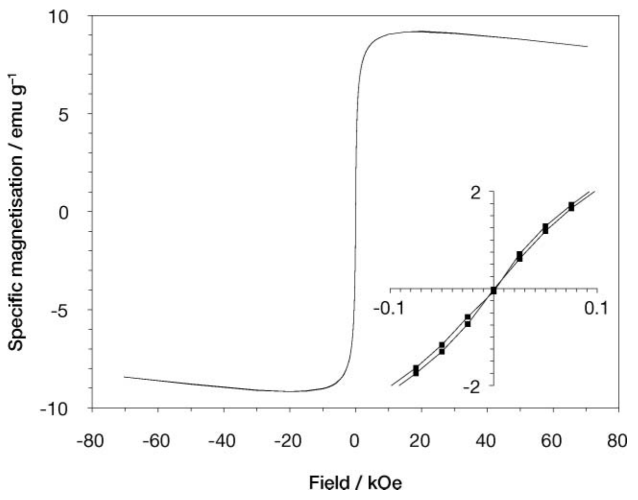


Fig. 5 Magnetisation curve for the nanocomposite material, showing specific magnetisation *vs.* applied field, and (inset) detail at the origin.

Experimental methods

Chemicals used in this work were as follows: cadmium nitrate tetrahydrate (Analar, 99%), L-glutathione (Fluka, 97%), tellurium (Fluka, 99.999%), 3-mercaptopropanoic acid (Aldrich, 99%), iron(II) chloride tetrahydrate (Fluka, 98%), iron(III) chloride (Fluka, 98%). All other chemicals were of analytical grade purity. Degassed Milli-Q water (>18 MΩ cm) was used in all preparations, and samples were stored under argon.

Magnetite preparation

Magnetite was prepared using the coprecipitation technique, described elsewhere. Concentrated ammonia solution (1 mL) was added to 50 mL degassed aqueous solution of Fe^{2+} (10 mM) and Fe^{3+} (20 mM) with stirring. Magnetic separation was used to wash the black Fe_3O_4 particles, which were subsequently resuspended in 10 mL degassed Milli-Q water.

Cadmium telluride preparation

CdTe was prepared using a published microwave technique.[13] Under argon, Te (20 mg) was reduced in water (3 mL) using excess $NaBH_4$ with heating, to yield a colourless solution of NaHTe, which was transferred with stirring to 150 mL aqueous cadmium nitrate (4 mM) and L-glutathione (10 mM). The pH of the solution was adjusted to 8.0 with 1 M HCl or NaOH solution. Subsequent heating formed CdTe nanoparticles, using any desired combination of temperature (110–140 °C) and heating time (5–45 min) to achieve different fluorescence emission wavelengths. The microwave reactor (CEM Discovery) used an 80 mL glass vessel, the headspace of which was purged with argon prior to heating. The maximum microwave power ranged from 200–300 W, depending on the volume of solution to be heated.

Magnetic–fluorescent composite preparation

In a typical preparation, 10 mL colloidal CdTe solution prepared as described above was precipitated by addition of 50 μL 3-mercaptopropanoic acid. The precipitate was collected by centrifugation, washed several times, and resuspended in several millilitres of degassed milli-Q water. Aqueous magnetite suspension (250 μL) was added with stirring. After 24 h, a magnetic, fluorescent material was collected by the application of a magnetic field. Samples were freeze-dried prior to powder X-ray diffraction and magnetic analysis.

Instrumentation

Magnetometric measurements were made on a Quantum Design 7 T MPMS instrument, using approximately 5 mg samples. Fluorescence spectra were recorded using a Varian Cary Eclipse spectrophotometer. Quantum yields were measured against Rhodamine 6G as a standard (95%), and corrected for absorbance. For atomic absorption spectroscopy, the iron content of nanocomposite samples was measured using a Varian SpectrAA 100 instrument, using a 1 : 1 mixture of air/acetylene. A commercially available standard solution of iron (1000 ± 3 mg mL^{-1} Fe, in 2% HCl) was used to calibrate the instrument. Powder X-ray diffraction patterns were obtained at 300 K on a Siemens D5000 diffractometer, using Ni-filtered Cu-Kα radiation (λ = 1.54056 Å, operated at 40 kV and 35 mA). Transmission electron micrographs were acquired using a JEOL 3000F microscope operated at 300 kV.

Conclusions

We have demonstrated a simple route to self-assemble cadmium telluride nanoparticles on the surface of superparamagnetic magnetite nanoparticles. The nanocomposite combines the properties of its constituents; namely, superparamagnetism and size-tunable luminescence. The procedure was carried out in its entirety in aqueous solution, which we believe will assist in overcoming physiological solubility issues, and furthermore, the resulting particles remain within the nano size regime and are therefore likely to be more readily usable in subcellular labelling applications. We expect that the combination of magnetic and luminescent functions will offer the ability to magnetically position the nanosystem with respect to an anatomical reference, and the fluorescence of the semiconductor quantum dots will facilitate tracking the distribution of the nanosystem at the subcellular level. This synthetic route promotes the design of smaller materials, where a thick polymer or silica coating to achieve a sufficient incorporation of QDs is unnecessary.

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