Nucleotide passivated cadmium sulfide quantum dots†

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Semiconductor quantum dots are finding numerous applications in biological systems; in this paper, we report the simple *in situ* preparation of nucleotide capped cadmium sulfide (CdS) nanoparticles and investigate the interaction of the capping agent with the nanoparticle surface.

One of the most important recent applications of nanomaterials, specifically semiconductor quantum dots, is their use in biological systems.[1–6] Seminal work on the application of semiconducting nanoparticles for bioimaging was reported by Alivisatos *et al.* and Chan and Nie, who exchanged surface passivating agents on high quality CdSe–ZnS nanoparticles for biologically compatible ligands.[1,2] This work has been developed further and has led to production of high quality biological labels that have been used in numerous studies.[3–6] In all cases, the surface of the nanoparticles is made biologically active by using ligands with either pendant functional groups for further conjugation, or alternatively by the direct attachment of a biological agent such as a protein or related structure, such as cysteine or histidine.[7,8]

With all biological applications, the nature of the surface of the nanomaterial is of paramount importance. Properties such as emission intensity and solubility in the required solvent (water or buffer solution) are highly sensitive to the physicochemical characteristics of the surface. Recently, surfactant capping agents utilised during synthesis have been shown to be detrimental to biological systems,[9] therefore the coordination of one, clean biological capping agent during synthesis is desired. Moreover, successful attachment of the biological entity to be studied is critically dependent on availability of suitable functional sites. We have recently demonstrated that the nucleotide adenosine triphosphate (ATP) can be reverse-engineered and considered as a materials chemistry synthon.[10] In this paper, we report the use of a range of related nucleotides as capping agents and their coordination to nanoparticle surfaces during growth.¶

The basis for selection of suitable nucleotides for investigation was that each should possess the triphosphate and ribose groupings, with a DNA base as the pendant moiety. Hence the molecules chosen were adenosine 5′-triphoshate (ATP, adenine pendant base) and the complimentary thymidine 5′-triphosphate (TTP, thymine pendant base), guanosine 5′-triphosphate (GTP, guanine pendant base) and the complimentary cytidine 5′-triphosphate (CTP, cytosine pendant base).

The capping agents were chosen specifically in order to expose a DNA base in solution, assuming the nucleotide coordinated to the metal surface through the phosphate groups. Further more, It was envisaged that ATP capped nanoparticles should link to the TTP capped nanoparticles, whereas GTP passivated particles would be expected to coordinate to CTP capped particles. With the exception of one system, the synthetic route produced water-soluble materials. Only experiments where CTP was employed as a capping agent were unsuccessful. The use of GTP as a capping agent resulted in a large amount of precipitate, although a nanoparticle solution also formed. In these latter systems, bulk cadmium sulfide was formed immediately upon addition of sodium sulfide.

The origin of the solubility of nanoparticles is attributed to the capping agent. The capping groups bear some resemblance to sodium hexametaphosphate used as a stabiliser in the preparation of water soluble nanoparticles reported by the Henglein group.[11]

To investigate the coordination of the nucleotide on the surface, characterisation by FT-IR was undertaken on the free ligand and the capped nanoparticles.† In the case of ATP, we have previously reported that the molecule is clearly bound to the nanoparticles surface through at least two, and probably all three, phosphate groups as evidenced by broadening in the bending and stretching modes associated with the phosphate groups (between *ca.* 800 and 1300 cm^{-1}).[10] Surprisingly, we found the amine group on the adenine moiety was also coordinated to the nanoparticle's surface as demonstrated by a higher energy shift in the $-NH_2$ feature from 1706 cm^{-1} to 1645 cm^{-1}.

GTP is a purine-based nucleotide with both a pendant amine and carbonyl group. Investigations by FT-IR concerning water-soluble CdS–GTP displayed a clear defined shift in the amine feature, from 1692 cm^{-1} in the free nucleotide to 1645 cm^{-1}, suggesting the amine group coordinated to the particle surface. All the bends and stretches associated with the phosphate groups were observed.

In the case of TTP passivated CdS particles, the ν(N–H) features are not assigned to a pendant amine group, rather to a pyrimidine ring. The ν(N–H) features at 1692 and 1476 cm^{-1} in the free ligand were suppressed slightly, although not shifted, suggesting an interaction with the surface. The bends and stretches associated with the phosphate groups were again clearly visible.

CdS–CTP capped particles were insoluble in all solvents investigated. In the present study, the bending and stretching modes associated with phosphate groups were clearly visible on spectra taken from the CdS–CTP sample, confirming the presence

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of the nucleotide on the surface. By contrast, the features associated with the $-NH_2$ group at *ca.* 1721 and 1683 $cm^{-1}$are completely suppressed, suggesting that the amine group interacts with the surface. All features observed in FT-IR spectra for the CdS–CTP sample were broadened, which made further unambiguous assignment of peaks difficult. However, strong evidence for the presence of the molecule on the material's surface was obtained.

The difference between CTP and the other nucleotides is the heterocyclic ring attached to the ribose group, and hence, in the case of CdS–CTP the heterocycle must contribute to the rapid growth of the cadmium sulfide and its precipitation out of solution. We attribute the water solubility of the particles to the phosphate groups, but assign a certain degree of growth control to the actual heterocyclic constituent of the nucleotide, with the differing number and positions of Lewis bases affecting the coordination to the growing particle, either allowing rapid growth or inhibiting growth for long enough to form stable particles. It is also worth noting that in the systems with a purine-based heterocyclic ring (ATP and GTP capped CdS), the shift in the amine feature manifested itself as a notable distinct shift, not a suppression, as was the case for CTP and TTP capped CdS, where the heterocycle is pyrimidine-based.

This suggests that the purine-based nucleotides, which consist of a six and a five membered ring had clear coordination to the particle surface, whilst the single ring pyrimidines may have coordinated in a different manner, maybe coordinating parallel to the surface in a flat geometry.[12]

The water-soluble nanoparticles (capped with ATP, TTP or GTP) all exhibited absorption spectra consistent with nanosized CdS (Fig. 1), displaying band edge absorption at *ca.* 480 nm. As expected, the blue shift in all cases is modest due to the small exciton diameter in CdS (*ca.* 5.2 nm) and hence the particles show weak confinement effects. From the absorption data, it is hard to ascertain a definite band edge position and estimate a particle size.[13] Importantly, PL measurements provided no evidence for deep trap emission except for ATP capped particles. The relative band positions of emission are shown in Fig. 2. The shape and position of the emission (*ca.* 550 nm) for GTP and TTP capped CdS is strongly indicative of band edge photoluminescence for a

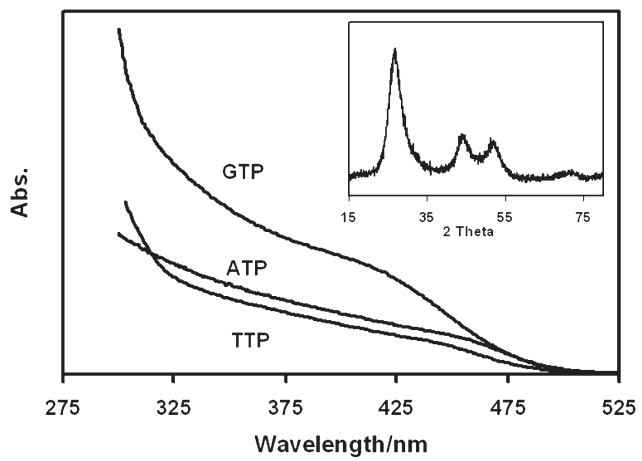

Fig. 1 UV spectrum of CdS nanoparticles capped with various nucleotides. Inset, a typical XRD pattern of nucleotide capped CdS.

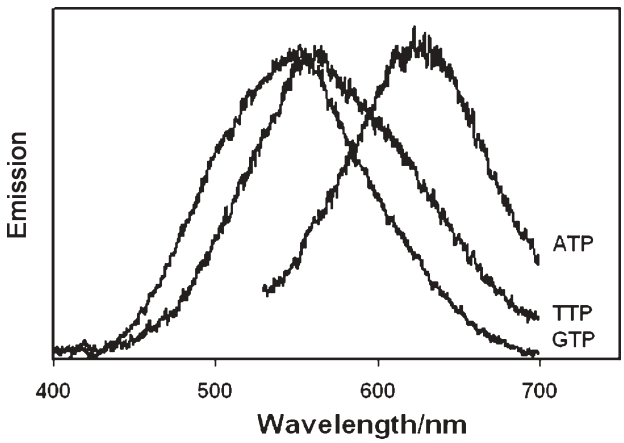

Fig. 2 Emission spectra of CdS nanoparticles capped with various nucleotides ($\lambda_{exc.}$ = 365 nm).

sample with a large size distribution, whilst the ATP capped material showed shifted emission in comparison to other samples (*ca.* 630 nm) suggesting deep trap emission. This observation suggests that ATP is a relatively poor capping agent. This was confirmed by measuring the particle size and size distribution for all particles, giving roughly similar results, suggesting the shift in emission in ATP capped particles is not due to particle size.

High-resolution microscopy (HR-TEM) experiments confirmed the capped samples to be irregularly shaped, approximately 3–5 nm diameter, with a broad size distribution (average particle diameter for ATP capped particles = 3.99 nm $\pm$ 12% standard deviation; TTP capped = 4.44 nm $\pm$ 14 %; GTP capped = 4.34 $\pm$ 27%). In all cases, the particles were free-standing and crystalline, with a tendency to cluster or cross-link (Fig. 3); it could be that the particles are more wire-like in character. The phenomenon may be associated with the multiple Lewis base sites on the nucleotide passivating agents. Although the nucleotides are bound to the nanoparticles through the polyphosphate group, the pendant amine groups may coordinate weakly to neighbouring particles. The crystals appear to posses a cubic core (as ascertained by X-ray diffraction) with evidence of twinning and a small number of particles possess a hexagonal crystalline core. A typical XRD pattern is shown in Fig. 1 (inset)

The pattern of results obtained in this study suggests that nanoparticles prepared as described are unlikely to be useful in cross-linking experiments, *i.e.* ATP capped nanoparticles cannot be linked with the complimentary TTP capped nanoparticles due

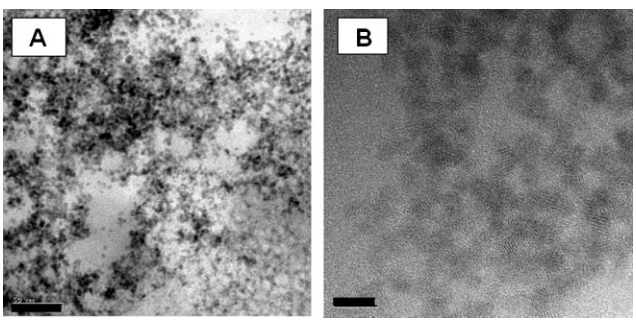

Fig. 3 Transmission electron microscope images of (a) TTP capped CdS; (b) ATP capped CdS. Scale bars = (a) 50 nm and (b) 10 nm.

to the coordination of the amine on the passivated particles. Similarly, CTP capped particles cannot be linked to GTP particles as the CTP particles precipitated out of solution and were found to be insoluble in all cases, and hence intractable for further studies. Despite the coordination of the heterocyclic ring to the nanoparticle surface, other points exist on a nucleotide where conjugation can occur; notably the ribose and the phosphate groups.[14] Mixing a solution of nanoparticles capped with differing nucleotides resulted in no observable interaction.

In conclusion, nucleotide passivated CdS nanoparticles have been prepared and their optical and structural characteristics investigated, along with the coordination geometry of the nucleotide with the particle surface. The differing Lewis bases characteristics contribute to the particle growth, whilst the phosphate groups impart a degree of water solubility. CTP is not suitable as a capping agent, whilst ATP appears to provide poor surface coverage as evidenced by trap-like emission. TTP and GTP both provided particles with band edge (albeit broad) emission, although the reaction yield for GTP capped particles is poor.

Notes and references

¶ Synthesis of nucleotide passivated nanoparticles. In a typical experiment, nucleotide-capped CdS nanoparticles were prepared as follows: a solution of the relevant nucleotide was prepared in deionised water (50 cm^3, 2×10^{-4} mol) to which cadmium acetate dihydrate (2×10^{-4} mol) was added and stirred until dissolution was complete. Subsequently the solution was modified by addition of a solution of sodium sulfide nonahydrate in 1 cm^3 deionised water (2×10^{-4} mol). The reaction was allowed to proceed for approximately 1 h. A large volume (*ca.* 100 cm^3) of isopropanol was then added to the reaction mixture, resulting in a precipitate that was isolated by centrifugation. The powder was readily redispersed in deionised water. The resultant colloidal solutions were determined to be stable for *ca.* 1–2 months. It should be noted that the reaction to prepare GTP capped CdS resulted in a large amount of bulk CdS precipitate, although a pale yellow solution was still obtained.

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