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Polymer-coated quantum dots

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Quantum Dots (QDs) are semiconductor nanocrystals with distinct photophysical properties finding applications in biology, biosensing, and optoelectronics. Polymeric coatings of QDs are used primarily to provide long-term colloidal stability to QDs dispersed in solutions and also as a source of additional functional groups used in further chemical derivatization of the nanoparticles. We review the coating methods, including multidentate and amphiphilic polymeric coatings, and grafting-to and grafting-from approaches. We highlight the most commonly used polymers and discuss how their chemical structure influences the coating properties.

Introduction

Semiconductor nanocrystals, so-called Quantum Dots (QDs), are experiencing booming scientific interest due to their unique optical properties, advances in synthetic approaches and availability of surface functionalization protocols.[1–3] These advances resulted in many applications in biology,[4–7] biosensing,[8–10] and optoelectronics,[11] gradually replacing other types of optical probes.[12–14] A diagnostic and therapeutic "QD tool-box" is being actively developed for live cells[15–24] and *in vivo*[4,25,26] imaging, down to the single nanoparticle level.[27]

The widespread application of QDs stems also from their electronic properties. When the size of the nanocrystals is decreased below a certain critical value, quantum confinement effects cause the energy bandgap of the QDs to increase, and the energy levels near the bandgap to become discreet. QDs made of the same semiconductor material with diameters ranging from 1 to 10 nm are obtained by a suitable choice of a synthetic protocol and by fine-tuning the reaction parameters like reaction temperature or time. Populations of QDs with narrow size distributions display emission spectra that are much narrower compared to conventional organic dyes. In contrast, the absorption spectra are broad, with absorption efficiency increasing toward the blue end of the electromagnetic spectrum. These features allow one to excite multiple QDs at one wavelength while collecting well-separated emission from multiple probes. Such multicolour imaging is often required to probe the complexity and dynamics within[28–31] or on the surface of cells.[32–34] Additionally, QDs exhibit reduced photobleaching rates, which allow for constant photoexcitation on time scales much longer and at excitation powers much larger compared to the commonly used organic chromophores. Indeed, QDs emerged as major contenders to become the labels of choice for biological imaging and long-term biosensing, and these were the biological applications of QDs that provided a major thrust for the scientific research. Before applying QDs as luminescent probes or as sensing elements, chemical identity of the QD surface has to be carefully addressed. Surface ligands have to interact directly with the QD inorganic surface and have functional groups that would provide colloidal stability in solution. To be able to visualize or probe biological processes the QDs need also to display functional groups that would bind to relevant biological molecules. The spectrum of functional groups that were successfully coupled to QDs is truly impressive and ranges from a variety of small organic molecules to functional peptides, bulky proteins, long and short chain polymers, or DNA. Integration of QDs into composite materials or functional devices also depends on the availability of reactive functional groups on the surface of the nanocrystals. The photophysical properties of QDs are influenced by the quality of the surface ligands and by the ligands' electronic properties.[35]

Although early research concentrated on small organic molecules, prevalently thiols, as the QD surface ligands, there has been considerable scientific and commercial success stemming from the application of polymeric molecules as QD surface coatings. It has been recognized that multivalent interactions between the polymer and the QDs result in more stable nanoparticles under complex and biologically relevant conditions such as a broad range of pH or ionic strengths, and in some instances the polymer provided additional barrier for leakage of toxic metal ions from the QDs to the environment. A polymeric coating provided also more flexibility in functionalization of the QDs and allowed tuning of the number of functional groups on the surface of the QDs. For optoelectronic applications, intimate contact of polymers with the surface of

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QDs translates directly into device performance and related studies are currently an active field of research.[11]

In this review we will summarize the research efforts concentrated on the chemical engineering of the QD surface with polymers.[36,37] The synthesis and photophysical properties of QDs are briefly reviewed followed by a description of surface modification strategies. In the following sections we focus on the polymeric surface coatings and on the direct modification of nanoparticle surfaces with polymers *via* hydrophobic and electrostatic interactions, multivalent passivation, and direct grafting. The application of amphiphilic polymers as a versatile and robust coating platform will be described. In the following we limit ourselves mostly to the prototypical CdSe nanocrystals; however most of the discussed topics can be applied to other types of QDs or nanoparticles.

Synthesis and properties of quantum dots

Quantum dots are nanocrystals made of semiconductor materials with characteristic size in the range between 1 and 20 nm. The most studied and applied QDs are made of elements from the II and VI groups (*e.g.* CdSe, PbSe, CdS, and ZnO), as well as, although less commonly, from the III and V groups (*e.g.* InAs, InSb, and GaAs) of the periodic table of elements. The chemical composition of the QDs and their size determine the QD electronic properties. As the size decreases, the confinement felt by the charge carriers in the semiconductor increases, and the energy difference between the valence and conduction bands, the energy bandgap, increases. Since luminescence originates from the recombination process of the photogenerated holes and electrons from the valence and conduction bands across the bandgap, the emission wavelength is related directly to the nanocrystals' size. For example, for the commonly used CdSe-based QDs the emission can be tuned over the entire visible part of the electromagnetic spectrum, from blue (for 2 nm QDs) to red (for 6 nm QDs) (Fig. 1a). Narrow emission spectra from an ensemble of nanocrystals can be obtained by using monodisperse QD solutions (Fig. 1b). The ability of synthesizing large quantities of monodisperse QDs is therefore important. In addition, defects at the nanocrystal surface, from which the electrons and holes may recombine, will cause the emission to shift to higher wavelengths or render the QDs nonemissive. Proper handling of the surface during the nanocrystal synthesis or during subsequent chemical manipulation is therefore essential to obtain well-defined and highly luminescent QDs.

Synthetic protocols for the preparation of semiconductor nanoparticles are readily available.[39,40] The seminal work of Bawendi and coworkers[41] deserves a special mention as it provided a relatively easy approach to obtain high quality, monodisperse QDs exhibiting high luminescence quantum yields (QY). Their method was based on high temperature decomposition of organometallic precursors in the presence of a coordinating solvent. By carefully tuning the reaction temperature and time one could obtain CdSe QDs with low size polydispersity (<5%) and quantum yields exceeding 50%. The resulting QDs were coated with a stabilizing surface ligand, usually trioctylphosphine oxide (TOPO) (Fig. 1c). The TOPO's

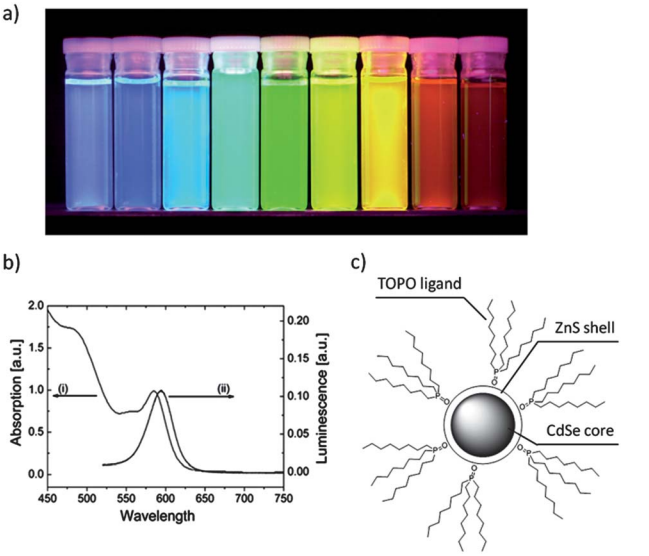

Fig. 1 (a) Luminescence from UV-illuminated solutions containing CdSe/ZnS QDs with diameters ranging from 2 nm (blue) to 6 nm (red). (b) Typically, (i) the absorption spectrum of QDs is broad with the absorbance increasing for shorter wavelengths while (ii) the emission spectrum is narrow. The position of the absorption and emission peaks is tunable *via* chemical composition and size of the QDs.[38] (c) Schematic structure of a prototypical CdSe/ZnS core/shell QD with TOPO ligands coated on the surface.

octyl groups stabilized the QDs in an organic solvent, like toluene, and rendered the QDs insoluble in water. Nowadays, using various synthetic schemes, QDs with emission spectra with full widths at half maximum (fwhm) values of 20 nm and luminescence QYs above 50% can be routinely synthesized. To improve the QY additional inorganic "shells" made of a different semiconductor material are grown on the initial QD core to passivate the surface and provide additional confinement.[42–45]

The high surface to volume ratio of the nanocrystals makes them colloidally unstable unless they are coated with suitable stabilizing ligands. The ligands interact also with the nanocrystal surface and strongly influence the optoelectronic and photoredox properties of the QDs by passivating surface sites that may act as traps for photoexcited electrons or holes. The importance of the appropriate choice of ligands increases when decreasing the nanocrystal size. The choice of the ligand is therefore crucial. Good passivating ligands such as TOPO make the QDs insoluble in water preventing the applications of TOPO-stabilized QDs in biology. In addition, charge transfer processes between the photogenerated charges and the ligand may significantly alter, enhance or quench, the optical emission from QDs – a topic, which has recently became a separate branch of QD research.

QD surface modification strategies

Chemical modifications of the surface of QDs are performed to provide good dispersibility in a given solvent, to avoid nanoparticle aggregation and precipitation, and to provide specific chemical functional groups suitable for further coupling.[5] The common strategy to render the QDs dispersible in water

includes exchanging the original hydrophobic ligands (*e.g.* TOPO) with ligands having one chemical group able to bind to the nanocrystal surface (*e.g.* thiols, amines, phosphines, carboxylic acids, and pyridines), and a polar head group (*e.g.* hydroxyl), directed towards water (Fig. 2). Another approach is based on preserving the original ligands and avoiding ligand exchange by coating the QDs with amphiphilic molecules. These amphiphilic coatings will have hydrophobic groups interacting with the original ligand and hydrophilic groups providing water solubility. Alternatively, one can coat the QDs with an inorganic silica shell[46–50] using the classical Stöber process (base-catalyzed hydrolysis of tetraethoxysilane and subsequent condensation of the monomers onto the existing nuclei)[51] or by synthesis in microemulsion.[52]

A distinction is usually made between the ligands based on the number of interaction sites they can make with the QDs (Fig. 2). Monodentate ligands, ligands that allow for only one interaction site, are usually simple low molecular weight organic molecules possessing one functional group able to bind to the QD surface. Thiol, amine, and phosphine-based ligands are most commonly used. Thiols are however relatively unstable against oxidation. The study performed by Aldana *et al.*[53,54] revealed that catalytic photooxidation of thiols to disulfides on the surface of QDs can occur under light illumination and that the ligands can detach at low pH values due to protonation of the thiolate. Multidentate ligands, on the other hand, can interact with the QD surface *via* multiple sites. Using multivalent interactions improves the overall stability of the QD/ligand interface. Bidentate thiols,[55–57] oligomeric phosphines[58,59] and amine or thiol containing polymers were shown to effectively passivate the surface of QDs.

Ligand exchange reactions are usually difficult to control and may result in QDs, which are colloidally less stable and of lower QY. To avoid ligand exchange, the original ligands can be covered with an additional coating layer *via* supramolecular interactions. For example, octyl alkyl groups of TOPO can interact with hydrophobic parts of other molecules.[60,61]

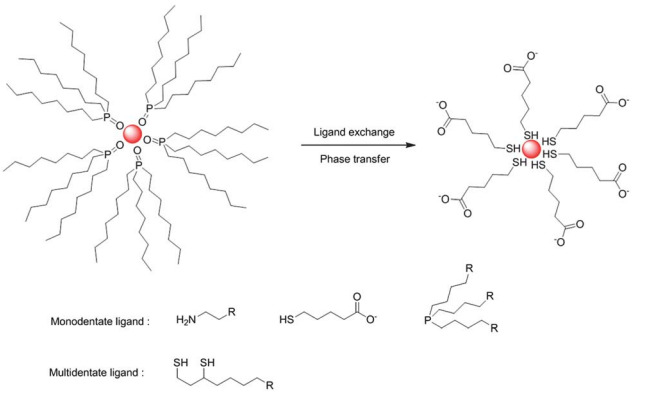

Fig. 2 During the ligand exchange reaction for phase transfer to water, the original TOPO ligands are displaced by molecules bearing a functional group able to bind to the QD surface, *e.g.* thiol or amine, and a polar head group, *e.g.* carboxy ion, for water dispersibility. The ligands can be monodentate or polydentate depending on the number of interaction sites each ligand is able to make with the surface of the QDs.

Cyclodextrines with hydrophobic pockets,[62,63] phospholipids,[64–69] and cone-shaped calixarene macrocycle derivatives with long alkyl chains[70] were used to coat and transfer the QDs to water. Among the phase transfer protocols a prominent position has coating of QDs with polymers *via* hydrophobic interactions. Such polymeric coatings have solved many problems encountered in ligand exchange procedures and provided a robust platform for QD functionalization. The hydrophobic bilayer is in general resistant to hydrolysis and enzymatic degradation even under *in vivo* conditions.[71] Currently, commercially available QDs are sold with a coating of amphiphilic polymers which are ready to be functionalized or which carry already some suitable functional groups. The ability to introduce multiple chemical functionalities onto the polymer backbone has contributed significantly to the success of the polymers as coatings of QDs. An amphiphilic coating approach can be also used for any other nanoparticles as long as there are hydrophobic groups displayed on the nanoparticle surface. In general, the size of the polymer coated QDs depends on the molar mass of the polymer, the coating method and polymer conformation in a solvent. The latter will depend on the chemical structure of the polymer and on the surface coverage.[72] For example, at high surface coverage, end-grafted polymers may adopt a brush-like extended conformation, much longer than the characteristic size of the polymer in solution.[72] Several recent studies have been devoted to the in-depth characterization of polymer-coated nanoparticles.[73,74]

Multidentate polymeric coatings

The ligands on the surface of the nanocrystals are in equilibrium with free ligands in solution. For weakly bound ligands, and without excess ligand present in the solution, desorption of the molecules from the QD surface leads to loss of functionality, deterioration of the optical properties, aggregation, and finally precipitation.[53,54] Ligands that are able to bind with more than one chemical group were shown to provide organic shells, which were much more stable under physiological conditions and during subsequent chemical functionalization.[75] These could be simple dithiol ligands, like dihydrolipoic acid,[57,76–78] carbodithioic acid,[79–81] dithiocarbamate,[82] polymers exhibiting functional side groups,[83–86] denaturated proteins like bovine serum albumin (BSA)[87] or hyperbranched polymers.[88] The functional groups interacting with the QD surface are most often thiols, amines, and carboxylic acids. Crosslinking the monodentate ligand shell may also result in a polymer-like multidentate shell,[89,90] however the crosslinking reaction is hard to control and a local excess of crosslinker results in polymeric shells of uneven thickness.[91]

Weiss and coworkers adopted a multidentate coating strategy based on designer peptides. Amphiphilic peptides with a hydrophobic domain composed of cysteine repeats flanked by hydrophobic 3-cyclohexylalanines or phenylalanines were able to displace the original TOPO ligands by the cysteine unit and provide solubility in water (Fig. 3).[92–94] As measured by SE-HPLC the coated QDs had small diameters of 11–14 nm, relatively narrow size distribution and did not aggregate. The peptide

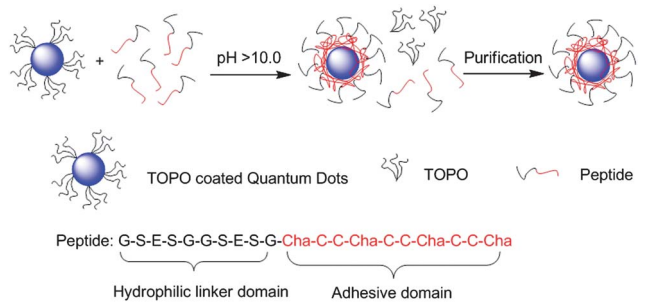

Fig. 3 Coating of CdSe/ZnS QDs with designer peptides bearing a hydrophilic domain for dispersibility in water and an adhesive domain for binding to the QD surface. The adhesive domain contains cysteine (C) units flanked by 3-cyclohexylalanine (Cha) units.[94]

ligand shell thickness can be reduced further by using hydrophilic cysteine-rich phytochelatin peptides. Xu *et al.* reported a peptide coating with a thickness of less than 1 nm.[95]

This remarkable result is believed to be due to better flexibility (and wrapping ability) of the peptide compared to previous studies. The tighter and denser coating with a higher number of interaction sites increased also the luminescence quantum yield. Recently, monofunctionalization of the peptide-coated QDs was demonstrated for single molecule assays.[96]

Polydentate ligands based on oligomeric phosphines (Fig. 4) efficiently passivate CdSe or CdSe/ZnS QDs. One type of oligomeric phosphines is synthesized by reacting monomeric trishydroxypropylphosphine with diisocyanatohexane. The unreacted OH groups can be further functionalized by reaction with isocyanates.[58] Bawendi *et al.* showed that polymers consisting of phosphine oxide and a poly(ethylene glycol) (PEG) linker (Fig. 4c) can efficiently stabilize various nanoparticles, including CdSe/ZnS QDs in water.[59]

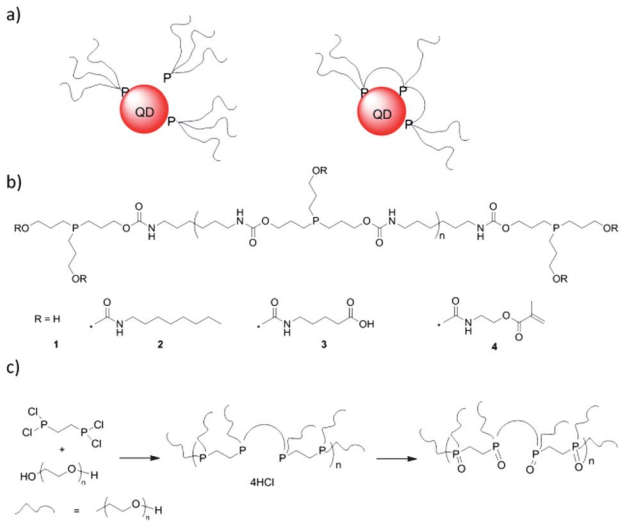

Fig. 4 (a) Schematic concept of the oligomeric phosphine coating. Multivalent interactions between the oligomeric phosphines and the QD surface result in a more stable coating compared to a coating made of monovalent alkyl phosphines.[58] (b) Free OH groups can be used for further coupling to different linkers bearing various functional groups.[58] (c) Synthesis of the phosphine oxide polymer with PEG bridges.[59]

Hydrophilic polymers incorporating multiple thiol groups, PEG chains and carboxylic acids or amines in the side groups were reported by Yildiz *et al.* (Fig. 5).[86] The thiol groups interacted with the surface of the QDs, while the PEG chain rendered the QDs stable in water over a broad range of pH values and salt concentrations. The free amine and carboxylic acid groups were used for further functionalization of the coating with *e.g.* dyes.[85]

Mattoussi *et al.* used a low molecular weight poly(acrylic acid) backbone to which methoxy, amine, azide and thioctic acid functionalized PEG was attached. While the thioctic acid reduced to a dihydrolipoic acid was previously found to bind efficiently to the ZnS surface, PEG provided also good dispersibility of the nanocrystals in water and the azide and amine groups could be used for further functionalization.[84]

Peptide–polymer hybrid macromolecules are a new class of materials, which can be used as effective multidentate QD coatings. The peptide imparts biocompatibility and stability in aqueous environments and provides multiple functional groups for further derivatization.[97] The length of the denatured protein is well defined and the number and location of functional groups along the chain is known. After denaturation and reduction of the protein disulfide bridges, PEG chains, amino functionality, and thioctic acid groups could be introduced by reacting with free thiol and amine groups on the peptide (Fig. 6). Thioctic acid bound efficiently to the QD surface while PEG provided stability in water.

A grafted polycationic PEG–polypeptide copolymer was used as multivalent coating of QDs. The polymer was obtained from cationized serum albumin obtained by reaction of a diamine linker with carboxylic groups on the protein. Denaturation of the protein and reduction of disulfide bridges provided additional thiol groups to which PEG chains were coupled using maleimide chemistry. Finally, thioctic acid groups were introduced by reacting succinimide-activated thioctic acid to lysine residues.[22] The positively charged ligand shell displayed efficient cellular uptake, stability under intracellular conditions and low cytotoxicity. Moreover, the shell could form complexes with DNA for gene delivery applications.

Poly(dimethylaminoethyl methacrylate) (PDMA)[98] or polyacrylic acids derivatized with diamine and monoamine linkers[99] were found to be efficient multidentate ligands for QDs

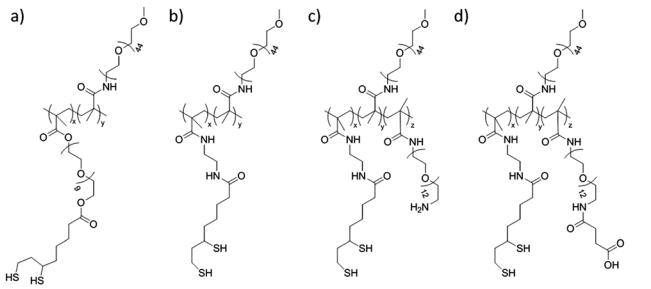

Fig. 5 (a–d) Chemical structures of hydrophilic polythiols based on a polymethacrylate backbone with pendant thiol groups and PEG chains. The thiol groups can be appended using a long (a) or short (b) linker. Additional functional groups such as amines (c) or carboxylic acids (d) can be incorporated into the coating and used for further derivatization.[85,86]

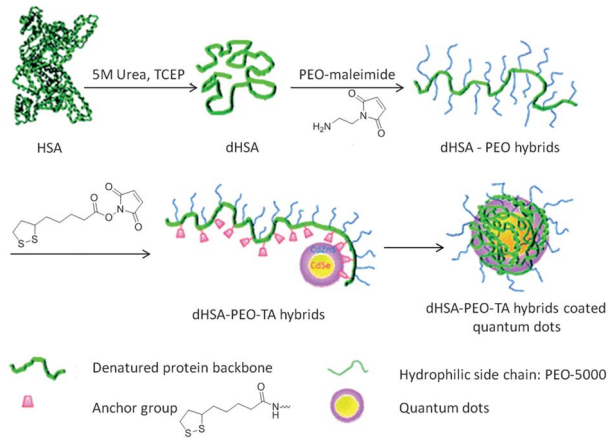

Fig. 6 Modified proteins are obtained by denaturation, disulfide bridge reduction, and reaction of the resulting thiol groups on the polypeptide with maleimide linkers. Linkers bearing thioctic acid are used to provide anchoring groups to the surface of the QDs and linkers bearing polyethylene oxide (PEO) provide solubility in water for the assembly. Reprinted with permission from ref. 97. Copyright (2010) American Chemical Society.

(Fig. 7a–c). PDMA was shown to interact strongly with the QD surface and the resulting QD dispersions were stable in solvents like toluene or methanol with no visible aggregation and only a modest decrease in the luminescence quantum yield. On average twelve polymer chains were bound to each of the 4 nm QDs and five polymer chains were bound to a 3.4 nm QD, with the polymer corona thickness being proportional to the length of the polymer chain.[98,100] Unfortunately, even though the polymer is water-soluble, the polymer coated QDs could not be dissolved in water. However, these polymer-coated QDs could be transferred to water by adding small excess of a methylating agent methyl iodide. It was stipulated that the increased solubility in aqueous solution was due to the reaction of methyl iodide with unbound dimethylamino groups and their conversion to alkyltrimethylammonium groups.[101] However, when using a PEG-*b*-PDMA copolymer (Fig. 7c) the PDMA block binds to the QD surface and the PEG block provides direct dispersibility in water without the need for ammonium groups.[102] The quantum yield is however reported to be lower upon transfer to water. A remedy for this was adding water-soluble primary amines like 3-amino-1-propanol.[103]

Smith and Nie have demonstrated that a mixed composition of functional groups, amines and thiols, grafted to a polyacrylic acid results in a much thinner and more stable coating presumably due to the coating adopting a very specific conformation on the surface of the QDs.[104] Interestingly, for a specific surface coverage, the QDs displayed increased QY and improved stability.

Polyhistidine motifs bind efficiently to the surface of QDs and copolymers with pendant imidazole groups were thought to exhibit similar binding affinity. Random copolymers incorporating PEG side chains and imidazole side groups were obtained by radical addition–fragmentation chain transfer (RAFT) reaction (Fig. 8).[105] The copolymer efficiently exchanged TOPO, the imidazole groups interacted with the QD surface, and the PEG chains provided stability in aqueous buffers. This multidentate polymeric ligand did not cause a decrease of the QY of the QDs. Introducing amino end-functionalized PEG allowed for further coupling to biomolecules. For example, norbornene functionalized QDs can efficiently react with tetrazine functionalized molecules.[106]

The synthesis of nanoparticles,[107] including QDs,[108] using hyperbranched polymers as surface ligands, or directly in individual dendrimers is established. Dendrimers are effective multidentate ligands due to the high density of functional groups (usually amines) at their periphery and throughout the branched structure. Hyperbranched polyethylenimines (PEI) of low (800 D) and high (25 kD) molecular weight were used to transfer hydrophobic QDs to water *via* ligand exchange (Fig. 9a), however some quenching of the QDs by photooxidation was reported.[88]

PEG-functionalized PEI coatings (Fig. 9b) were found to provide the QDs with good dispersibility in water, ability to penetrate the cell membrane and escape the endosomes due to the presence of a large number of amine groups on the surface, and due to the proton sponge effect.[109] PEG chains

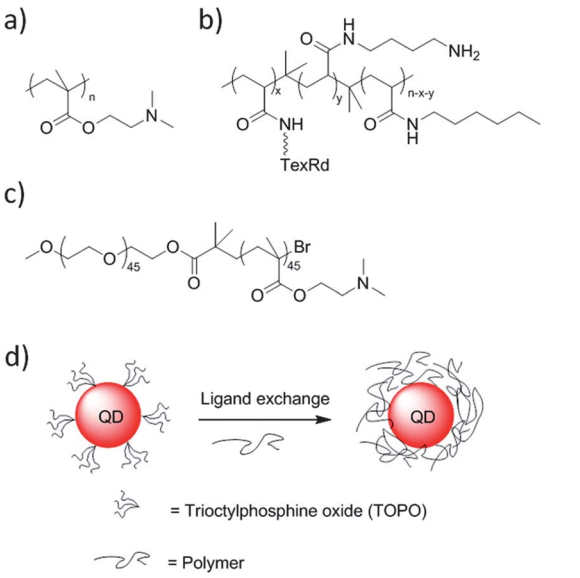

Fig. 7 (a) Poly(dimethylaminoethyl methacrylate) (PDMA) or (b) polyacrylic acids derivatized with diamine and monoamine linkers[99] displace TOPO ligands on the surface of the QDs and provide a stable multidentate polymeric coating.[100] (d) Ligand exchange reaction with a PEG-*b*-PDMA block copolymer (c) leads to QDs, which are dispersible in aqueous solutions. While PDMA binds to the QD surface, the PEG provides dispersibility in water.[102]

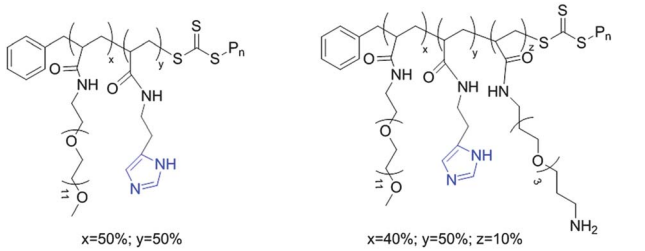

Fig. 8 Chemical structures of imidazole-based random copolymer ligands.[105]

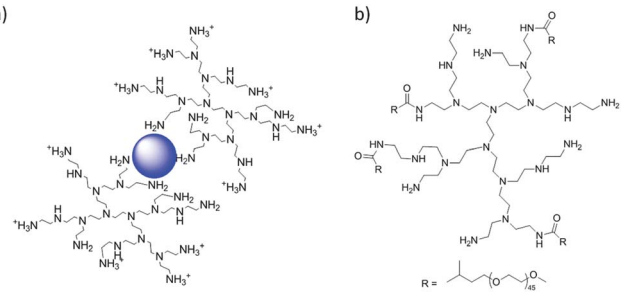

Fig. 9 (a) A hyperbranched polyethylenimine (PEI) coating of QDs.[88] (b) Chemical structure of polyethylene glycol grafted polyethylenimine (PEG-*g*-PEI).[109]

decreased also the cytotoxic effect of the PEI. Poly(amido amine) (PAMAM) dendrimers modified with aliphatic chains at their periphery were shown to be good QD ligands. The internal amine groups could interact with the QD surface while the aliphatic chains extended into the solvent. This was possible because of the amphiphilic character of the modified PAMAM.[110] Generation-4 PAMAM exhibiting 64 amine groups at the periphery was functionalized with thiol groups by reacting with 3-mercaptopropionic acid, resulting in 1–2 thiol groups per dendrimer. Such modified dendrimers effectively exchanged TOPO as ligands and provided solubility in aqueous buffers.[111]

Amphiphilic polymeric coatings

Amphiphilic polymeric coatings are made of polymers, which present hydrophobic and hydrophilic parts. While the hydrophobic parts interact strongly with the hydrophobic ligands on the QD surface, the hydrophilic parts allow for the transfer of the QDs from nonpolar to polar solvents. The availability from commercial sources of polymeric backbones, such as poly(acrylic acid) or various polymeric anhydrides, which may be readily functionalized, made the amphiphilic polymeric coatings very popular. The functionalization of the amphiphilic polymers can be carried out before or after the coating procedure and multiple functional groups can be introduced onto the surface of the QDs without compromising water dispersibility. The ability to functionalize the polymeric coatings with multiple different functional groups allowed for the preparation of complex nanoparticles for signal multiplexing and multimodal signal detection.[112] The main disadvantage of this method is that it results in QDs with substantially increased diameters compared to those coated with simple organic ligands.[113,114] However, the QDs seem to be more resistive to photooxidation, and their suspensions are colloidally stable over prolonged periods. QDs coated with amphiphilic polymers showed also lower cytotoxicity compared to QDs coated with, *e.g.*, mercaptopropionic acid, by providing additional barrier for diffusion of toxic Cd^{2+} ions. However, polymer coated QDs were also found to precipitate on the cell surface increasing the cell cytotoxicity.[115] It should be noted that the research on the cytotoxicity of nanoparticles is ongoing and currently available results are still controversial due to the lack of standard QD preparation and toxicity protocols.[116]

Dubertret *et al.*[65] encapsulated QDs within the core of phospholipid block copolymer micelles and their DNA conjugates (Fig. 10). The micelles were composed of 40% 1,2-dipalmitoyl-*sn-glycero*-3-phosphoethanolamine-*N*-[methoxy-(polyethylene glycol)-2000] and 60% of 1,2-dipalmitoyl-*sn-glycero*-3-phosphocholine. The percentage contribution of the polymer-modified lipid was adjusted for the molecules to form spherical micelles with hydrophobic cores and hydrophilic PEG chains extending into the water phase. The resulting QD-micelles were between 10 and 15 nm large.[113] Amine-functionalized micelles conjugated with single stranded DNA served as *in vitro* probes for the hybridization to complementary sequences. Phospholipid block copolymer-coated QDs were also stable, nontoxic, and displayed low photobleaching rates when injected into *Xenopus* embryos. The QDs could be followed to the tadpole stage, allowing lineage-tracing experiments in embryogenesis.[65] A detailed protocol for the encapsulation of QDs within phospholipid micelles is available.[64]

Gao *et al.*[71] developed multifunctional QD probes by encapsulating the QDs in an amphiphilic triblock copolymer and further coupling specific ligands to the polymeric shell (Fig. 11). The polymer consisted of a poly(butylacrylate) part (hydrophobic), a poly(ethylacrylate) part (hydrophobic), and a poly(methacrylic acid) part (hydrophilic). This high molar mass polymer (M_w = 100 kg mol^{-1}) is commercially available and to increase its interactions with the TOPO layer 25% of the carboxylic acid group were modified with *n*-octylamine. The coating could be further modified by reaction with amine-functionalized PEG (M_w = 5 kg mol^{-1}), diagnostic and therapeutic agents.[117] In general, attaching PEG would improve the water solubility of the assembly and single QD fluorescence and TEM images showed indeed that the particles did not aggregate in solution. On average, the shell consisted of 4–5 block copolymer chains with 5–6 grafted PEG chains each. The hydrodynamic radius of the coated QDs increased up to 10–15 nm as determined by Dynamic Light Scattering, which corresponded to a 2 nm amphiphilic polymer shell wrapping the QDs (without the PEG chains). The optical properties of the QDs were stable at a broad range of pH values (1–14), salt concentrations (0.01 to 1 M) and even after treatment with 1.0 M hydrochloric acid.

Poly(maleic anhydride-*alt*-1-tetradecene),[118] poly(maleic anhydride-*alt*-1-octadecene),[119,120] poly(maleic anhydride-*alt*-1-decene),[121]

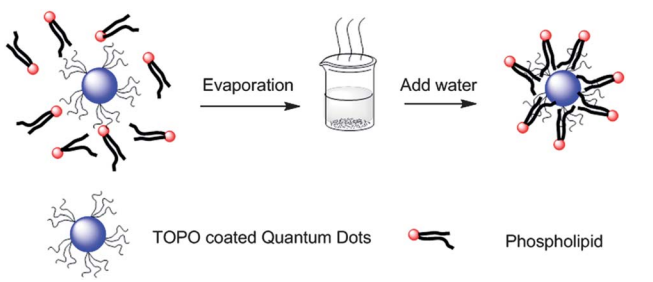

Fig. 10 Formation of phospholipid block copolymer-coated QDs. The phospholipids are functionalized with PEG chains, which provide good dispersibility in water for the assembly, while the hydrophobic parts of the lipids interact with the hydrophobic groups on the surface of the QDs.[65]

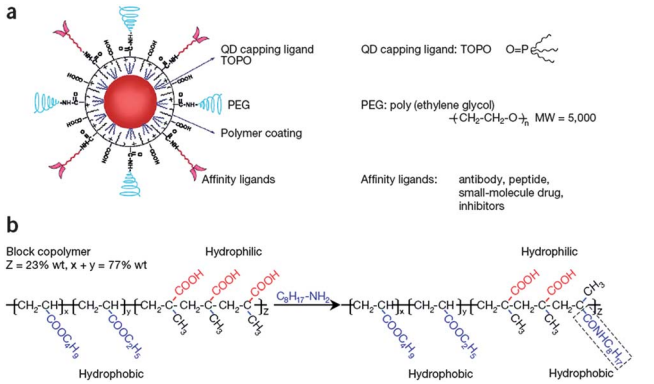

Fig. 11 (a) Scheme of a QD coated with a multifunctional amphiphilic triblock copolymer. (b) Chemical structure of the amphiphilic polymer used in (a). Adapted by permission from Macmillan Publishers Ltd., copyright (2004).[71]

and their derivatives were often used as coatings (Fig. 12). The maleic acid anhydride, once hydrolyzed, results in hydrophilic carboxylic acid groups. These groups allow for further functionalization and facile crosslinking of the coating.[122] The crosslinking improves the coating stability and can be performed with, *e.g.*, bis(6-aminohexyl)amine.

In the procedure first described by Pellegrino *et al.*[118] the QDs are coated with the unmodified polyanhydride in chloroform, and then crosslinked (Fig. 13). After evaporation of chloroform, the coated QDs are dissolved under sonication in an aqueous buffer at pH = 9. Under these conditions the unreacted anhydride groups hydrolyze to two carboxy ions each, rendering the whole QD–polymer assembly highly soluble in water. The unbound polymer could be removed by size-exclusion chromatography. This procedure is highlighted as it represents a prototypical protocol for using amphiphilic anhydride-based polymers to coat QDs. Subsequently reported protocols displayed some variation regarding this procedure depending on the length of the alkyl side chains and the molar mass of the amphiphilic polymer.[119]

Amphiphilic polymers may be obtained by functionalization of polyacrylic acid. In general, the performance of the coating will be determined by the appended alkyl chain length, *e.g.*, octylamine, dodecylamine, hexadecylamine or octadecylamine, by the grafting density, and the phase transfer protocol for QDs of a given size and surface functionality.[123] QDs linked to immunoglobin G (IgG) and streptavidin for labeling of cellular components[30] were prepared by coating the QDs with 40% octylamine modified polyacrylic acid. Further cross-linking and functionalization could be performed by EDC-mediated coupling to lysine (or PEG-lysine) and then coupling to

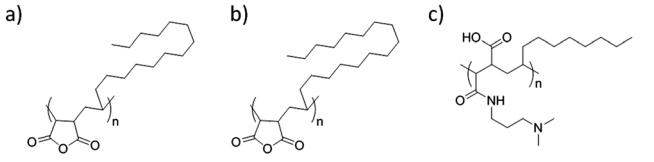

Fig. 12 Chemical structures of (a) poly(maleic anhydride-*alt*-1-tetradecene),[118] (b) poly(maleic anhydride-*alt*-1-octadecene),[119,120] and (c) poly(maleic anhydride-*alt*-1-decene) modified with dimethylamino propylamine.[121]

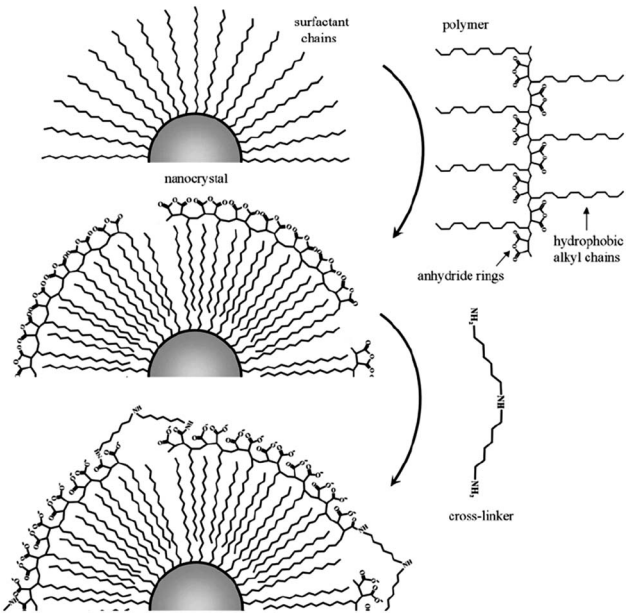

Fig. 13 Schematic illustration of the QD coating procedure. The unreacted polyanhydride coats the QDs *via* hydrophobic interactions between the alkyl side groups and hydrophobic ligands on the surface of the QDs. After coating, a crosslinker is added to improve the stability of the assembly. Upon transferring the QDs to water the remaining anhydride units are opened providing carboxy ions and rendering the whole assembly highly water-soluble. Reprinted with permission from ref. 118. Copyright (2004) American Chemical Society.

streptavidin or antibodies.[29] These coated QDs were successfully used in *in vivo* multiphoton fluorescence imaging.[124] The coating did not affect the two-photon cross-sections for the same size QDs. The size of the polymer-coated water-soluble QDs was estimated to be 14 nm and larger than that of dry QDs, indicating some interactions between the polymeric coating and the solvent. Luccardini *et al.*[125] randomly grafted hydrophobic octylamine (25% of carboxy groups) and isopropylamine (40% of carboxy group) to PAA in the presence of a dicyclohexylcarbodiimide activating agent (Fig. 14). The remaining hydrophilic carboxylic acid groups were turned into their basic form using sodium methanoate.

In amphiphilic polymeric coatings the alkyl chains can be substituted by other highly hydrophobic groups, like a phenyl ring. It was shown that low molar mass poly(styrene-*co*-maleic anhydride) (1700 g mol^{-1}, PSMA) effectively coated the surface of TOPO-coated QDs (Fig. 15). The functionalization of the coating can be performed the same way as for other maleic anhydride-based amphiphilic polymers, *i.e.*, by reaction with amine functionalized molecules. Reacting the anhydrides on

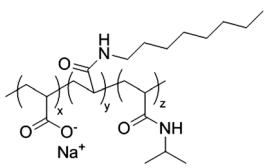

Fig. 14 Chemical structure of poly(acrylic acid) randomly grafted with hydrophobic octylamine and isopropylamine.[125]

the coated QDs with ethanolamine or polyetheramine (a PEG derivative) renders the coating amphiphilic and the QDs can be transferred to water.[122,126] The coating resulted in QDs with diameter between those of QDs coated by DHLA–PEG and poly(maleic anhydride-*alt*-1-octadecene). Grafting molecules with triethoxysilane groups allowed growth of thin silica layers onto the QDs.[48]

The amphiphilic polymer coatings provide a large number of carboxylic units on the surface of the QDs which can be further used for attachment of biomolecules, dyes,[127] PEG, *etc.* Functionalization of the coating is usually performed using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC). However, the original anhydride units are highly reactive towards primary amines without the addition of any coupling agents.

Another type of polymer, which was successfully applied by us,[21,38,129–132] and by others[133–139] as efficient and versatile coating of QDs was based on poly(isobutylene-*alt*-maleic anhydride). To render the polymer amphiphilic, different molecules can be grafted to the anhydride unit. The molecules can be amine or carboxyl-terminated and react with the anhydride to form amide or ester bonds. For each anhydride unit one obtains two carboxylic groups, where one carboxylic group takes part in the new bond formation. The general structure of the resulting amphiphilic polymer consists of hydrophobic alkyl side chains for interaction with TOPO, and hydrophilic carboxylic groups, which render the whole assembly water-soluble (Fig. 16a).

The anhydride can be also opened without attaching any molecule, resulting in two carboxylic groups per monomer. It was immediately recognized that the anhydride approach provides great flexibility and control over the ratio of hydrophobic to hydrophilic units, the number of functional groups for further derivatization, and that it provides a versatile scaffold for the conjugation of functional groups at the stage of the amphiphilic polymer synthesis (therefore not requiring post-coating functionalization reactions). Comparing to functionalization of polyacrylic acid-type polymers, each monomer unit will always contain a minimum of one carboxylic group after the anhydride opening. This ensures that the hydrophilic groups are distributed throughout the polymer chain. This allows in turn to couple highly hydrophobic ligands, such as acetylene groups for "click" chemistry (Fig. 16b), to the polymer backbone while preserving the amphiphilic character of the polymer.

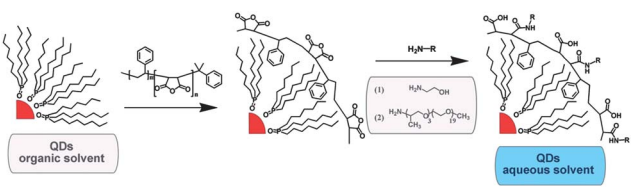

Fig. 15 Transfer of QDs from the organic solvent to water using a poly(styrene-*co*-maleic anhydride) coating. The coating can be further functionalized by reacting amine-terminated linkers with unopened anhydride units. Reprinted with permission from ref. 126. Copyright (2009) American Chemical Society.

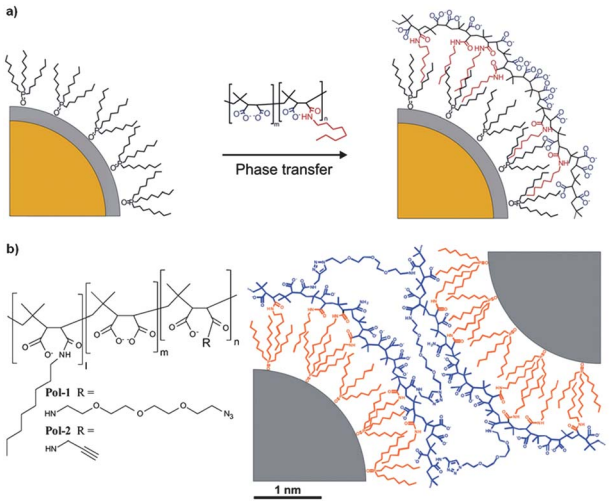

Fig. 16 Amphiphilic QD coatings based on poly(isobutylene-*alt*-maleic anhydride) are obtained by grafting amine-functionalized groups to a polyanhydride backbone. (a) Alkylamine chains of various lengths interact with the TOPO layer *via* hydrophobic interactions, while the opened anhydride units provide carboxy ions resulting in stable QD suspensions in water.[38] (b) Functionalization of the amphiphilic polymer before the coating procedure allows one to introduce additional functional groups. For example, hydrophobic acetylene groups can be used in "click" reactions with azide-functionalized coatings. Adapted from ref. 128 with permission from The Royal Society of Chemistry.

Functionalization of the amphiphilic polymeric coating

The amphiphilic polymer can be functionalized before and after coating the QDs. The pre-coating procedure includes polymerization of functional polymers or post-polymerization modifications. It was demonstrated by using electrophoresis as the separation method that the number of functional groups on the polymeric coating could be in principle controlled down to a single functional group.[140] The coatings are typically functionalized with PEG, which not only improves the stability of the QDs in solution, but it also minimizes nonspecific interactions of the QDs with cell membranes. Thus, such functionalization is often performed for biological applications.

A popular functionalization strategy is to modify the coating before encapsulating the QDs.[122,134,141] A primary requirement is that the polymer retains its amphiphilic character after functionalization; otherwise phase transfer of the hydrophobic QDs to water would not be possible. Functional groups or molecules can be introduced during the polymer synthesis or *via* modifications of the polyacrylic acid or polyanhydrides. For example, Chen *et al.* have synthesized a polyacrylic acid *via* Reversible Addition–Fragmentation Chain Transfer (RAFT) reaction. After modification with octylamine the polymer became amphiphilic but the advantage of using RAFT, besides obtaining well-defined polymers, became apparent by coupling a dye to the thiol-functionalized chain-end of the polymer (the thiol functionality being a left over from the RAFT agent).[142] Zhou *et al.* have coupled octylamine chains and diamine PEG to polyacrylic acid. The resulting polymer effectively coated QDs in water and

provided free NH_2 groups that could be linked *via* a crosslinker to thiol-functionalized peptides. This strategy allowed coupling of peptides in which the free amines participated in ligand–receptor interactions, and therefore could not be coupled to carboxylic groups on the polyacrylic acid.[143]

Polyanhydrides and their copolymers are a versatile platform for coupling of organic molecules modified with nucleophilic groups.[132] The reaction is very efficient and compared to other methods no coupling agents, such as EDC, are needed. A variety of functional groups has been used ranging from small organic molecules through larger and bulkier groups like aza rings, galactopyranoside, dyes, to polymers like PEG or PNIPAM.[144,145] Poly(maleic anhydride-*alt*-1-decene) modified with dimethylamino propylamine results in an amphiphilic polymer which is positively charged at neutral pH.[121] The zwitterionic coating was shown to bind siRNA[121] and deliver it into cells.[146]

Post-coating functionalization is usually more challenging due to the stability of the amphiphilic coating during functionalization. EDC coupling has been shown to be problematic in some cases and to decrease the quantum yield and cause irreversible precipitation of the QDs. Novel carbodiimide coupling agents were therefore researched and successfully used for the functionalization of the amphiphilic polymeric coating.[147] The coating is usually functionalized with PEG chains of various lengths.[148,149] For example, methoxy or carboxy terminated PEG chains with molar masses ranging from 750 to 5000 g mol^{-1} were conjugated to an amphiphilic poly(acrylic acid) coating *via* EDC coupling. PEG chains change circulation lifetimes *in vivo*, and show decreased nonspecific absorption in live animal models[148] and in different cell lines.[149] The coating can be also functionalized *via* electrostatic interactions using procedures developed for simple ligands. Mattoussi *et al.* described how to coat carboxy functionalized QDs with proteins fused to a positively charged leucine zipper domain. This domain binds electrostatically to the QD surface ligands.[76] Antibodies were also coupled to the amphiphilic coatings *via* reaction with EDC.[150]

Coating QDs with polymers *via* the grafting-to and grafting-from approaches

Bringing the polymer close to the QDs

In most of electronic applications of QDs there is a requirement that the organic electroactive molecules are in close proximity to the nanocrystal surface. This is needed for charge separation in photovoltaic devices or charge injection and recombination in light emitting devices. To achieve this, one can attach a pre-synthesized end-functionalized polymer chain to the surface of the QDs, or grow the polymer chain directly from the surface of the QDs. These methods are often referred to in the literature as the polymer "grafting to" and the "grafting from" methods, respectively.

Grafting polymers to the QD surface

In the "grafting to" method the pre-synthesized polymer needs to be end-functionalized with suitable chemical groups. One can make use of the well-known strong binding groups such as pyridine,[151] pyridyl,[152] thiols[72,153] or phosphonic acids.[154] By grafting water-soluble polymers to the QD surface, *e.g.*, pyridine-terminated PEG[151] (Fig. 17), the QDs can be rendered soluble in polar solvents. Thiol terminated DNA was successfully attached to QDs stabilized by mercaptopropionic acid. The DNA could hybridize with complementary strands present on other nanoparticles[153] and telomerization could be followed in real time by using dye labeled dNTPs and unlabelled dNTPs in the presence of telomerase. The latter experiment would therefore also constitute real time observation of surface initiated polymerization of a macromolecular chain.[155]

The main advantage of the grafting-to method is the use of monodisperse polymers either synthesized in the lab or procured from commercial sources. The main disadvantage is the lack of control over the number of attached macromolecules; the ligand exchange process is a stochastic process and long polymer chains sterically hinder the attachment of subsequent macromolecules.

Most ligands are electrical insulators with large bandgaps and a more intimate contact between an electroactive matrix and the QDs is therefore needed. Alkyl-substituted 3-hexyl oligothiophenes (P3HT) with a phosphonic acid group at the chain end were shown to exchange TOPO from the surface of QDs (Fig. 18a). The alkyl side chains provided good dispersibility in nonpolar solvents.[154] Pyridyl-functionalized poly(3-hexylthiophenes) were also shown to attach to CdSe QDs (Fig. 18b). The presence of the polymer directly on the QD surface improved dispersibility in a poly(3-hexylthiophene) matrix.[152] P3HT grafted QDs were also obtained by grafting vinyl functionalized polythiophene to [(4-bromophenyl)methyl]dioctylphosphine oxide-functionalized CdSe QDs (Fig. 18c).[156]

A range of different bidentate ligands coupled to PEG chains obtained by attaching the polymer directly to dihydrolipoic acid were developed.[55,77,157] These ligands were shown to provide water solubility to the QDs and to broaden the range of pH and ionic strength conditions at which the nanoparticles did not precipitate from water.[57] For PEG chain molar mass higher than 400 g mol^{-1} aggregate-free suspensions were obtained which could be stored over prolonged time. The PEG end-functionalized with

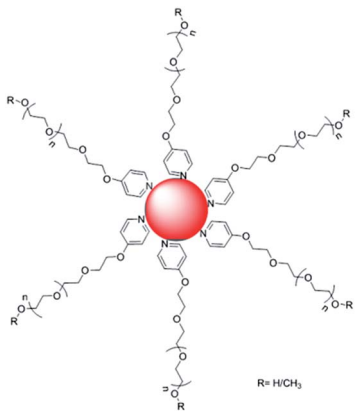

Fig. 17 Pyridine-terminated PEG grafted to QDs results in an assembly, which is soluble in aqueous solutions.[151]

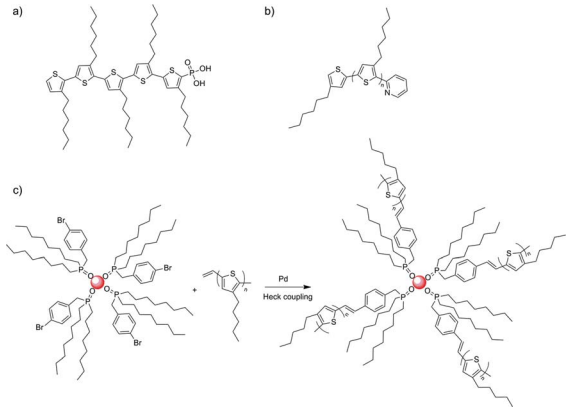

Fig. 18 Chemical structures of (a) phosphonic acid functionalized oligothiophenes[154] and (b) pyridyl functionalized poly(3-hexylthiophene).[152] (c) Grafting vinyl end-functionalized poly(3-hexylthiophene) to [(4-bromophenyl)methyl]dioctylphopshine oxide-functionalized CdSe QDs.[156]

hydroxy groups could be further derivatized to provide a range of functional groups like amine, or carboxylic acid for coupling to *e.g.* dyes, peptides or proteins (Fig. 19).[56,158,159]

Peng and coworkers presented a method to graft to the surface of CdSe/CdS QD dendrons thiol-functionalized at the focal point.[160–162] Even though the dendron shell is only 1–2 nm thick, the QDs were more resistant towards oxidation compared to the QDs coated with simple thiol ligands. The dendron shell could be crosslinked to improve the photochemical and thermal stability of the QDs. If vinyl functionalized dendrons are used, the crosslinking reaction can be performed through ring-closing metathesis (RCM) reaction.[161] Water-soluble QDs are obtained when using hydroxy-functionalized dendrons, which could be crosslinked with amine-functionalized generation-two dendrimers. The resulting amine rich surface could be further coupled to other molecules.[162] Hydroxy-terminated dendrons with two primary amines at their focal points were shown to coat QDs in water. Although the amines provide weaker bonding to the surface of ZnS the bidentate character of the ligand resulted in stable dendron-coated QDs without the need for crosslinking the shell.[163]

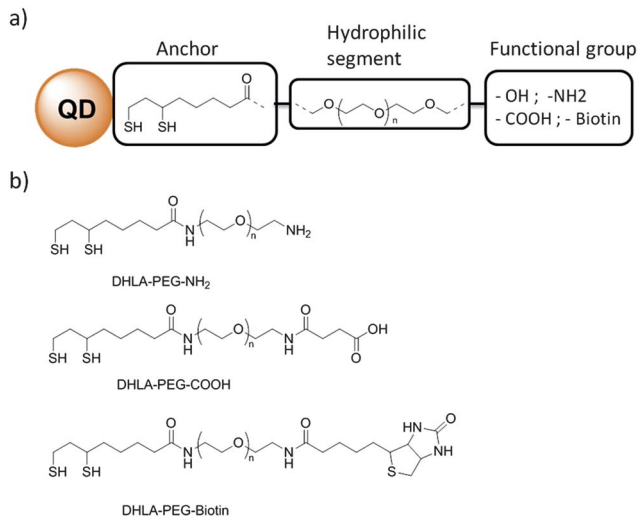

Fig. 19 (a) Scheme for grafting of PEG to the surface of QDs using bidentate ligands. (b) The polymers are end-functionalized with various chemical groups suitable for further derivatization.[56]

Grafting polymers from the surface of QDs

It is arguably much more difficult to perform polymerization from the QD surface compared to grafting end-functionalized polymers to the QDs. The main problems are associated with harsh polymerization conditions and availability of suitable surface initiators. To maintain the optical properties of the QDs the initiators should passivate well the surface of the QDs while providing a sterically unhindered polymerization initiation group directed towards the solution. Most commonly used polymerization reactions were based on ring-opening reactions[164] or controlled radical polymerizations such as atom transfer radical polymerization (ATRP)[165] or reversible addition–fragmentation chain transfer polymerization (RAFT). The suitable initiators can be introduced onto the QD surface by ligand exchange or directly during the synthesis by using ligands that are stable at high temperatures. Despite its challenging requirements, the "grafting from" method offers some exciting opportunities. Control over the surface concentration of the initiators results in a controlled number of polymer chains per nanoparticle and the nature of the polymerization protocols allows one to grow block copolymers.

A number of strategies to obtain polymer coated QDs based on surface initiated polymerization was developed by the group of Todd Emrick. These include the design of surface ligands (Fig. 20), which can be used as initiators of polymerization and provide good passivation and stability to the nanocrystals. For example, Skaff *et al.* described functional phosphine oxide ligands that could be transformed into a metathesis catalyst by carbene exchange (Fig. 20a).[166] Ruthenium-catalyzed ring-opening metathesis polymerization (ROMP) of a number of cyclic olefin monomers such as cyclooctene, dicyclopentadiene and oxanorbornene was demonstrated (Fig. 21).

Surface grafted polystyrene and poly(styrene-*r*-methyl methacrylate) block copolymers could be obtained by nitroxide-mediated controlled free radical polymerization.[167] To this end, a nitroxide containing phosphine oxide ligand (Fig. 20b) was synthesized and coated onto CdSe QDs *via* ligand exchange. A ligand used during the synthesis of the QDs based on

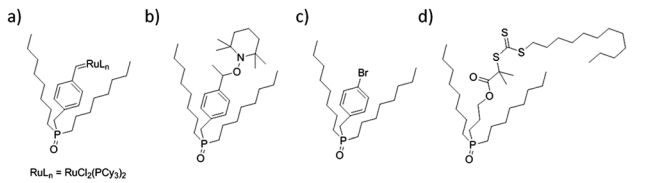

Fig. 20 Chemical structures of polymerization-initiating ligands for grafting polymers from the QD surface. The ligands are based on phosphine oxide functionalized with (a) ruthenium,[166] (b) 2,2,6,6-tetramethylpiperidinyloxy,[167] (c) bromide,[168] and (d) trithiocarbonate.[169]

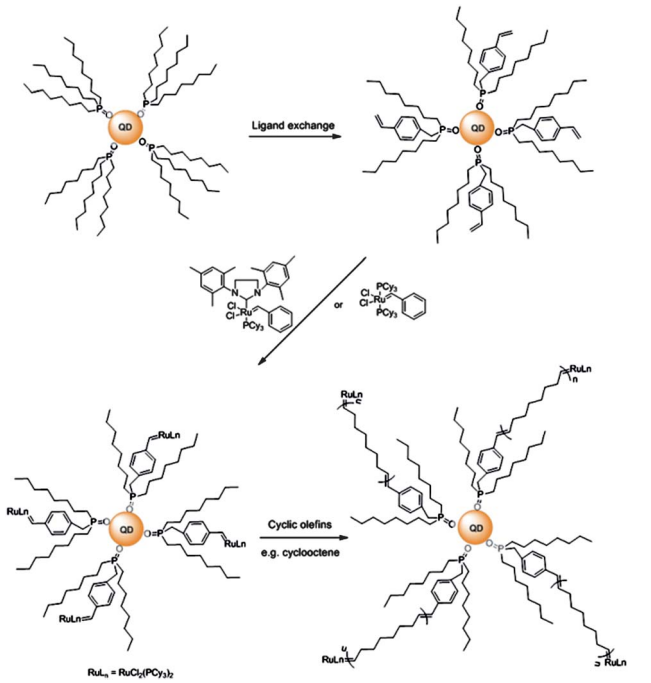

Fig. 21 Scheme describing the grafting of cyclic olefins from the surface of QDs functionalized with a ruthenium-based catalyst for ring-opening metathesis polymerization (ROMP).[166]

p-bromobenzyl-di-*n*-octyl phosphine oxide (Fig. 20c)[168] was used for the polymerization of poly(*para*-phenylene-vinylene) (PPV) by copolymerization of 1,4-divinylbenzene with 1,4-dibromobenzene derivatives by palladium-catalyzed Heck-type coupling reaction.[168] The polymer chains were relatively short – primarily trimers and tetramers were obtained. This however allowed the QDs to be well dispersed in a PPV matrix and resulted in materials with novel optoelectronic properties. Single QD measurements showed that the intimate contact of the conjugated polymer with the QD surface results in hybrid electronic materials.[170] Most notably, QDs coated with oligo-PPV exhibited modified fluorescence intermittency, which at high ligand coverage was completely suppressed on the 1 s time scale.[171] Finally, reversible addition–fragmentation chain-transfer (RAFT) polymerization from the QD surface was performed by employing ligands with trithiocarbonate functionality (Fig. 20d).[169] Living polymerization conditions allowed for polymerization of homopolymers as well as random and block copolymers such as polystyrene, poly(butyl acrylate) or poly(styrene-*b*-butyl acrylate) with relatively low polydispersity of 1.17 to 1.32 and molar masses ranging from 9 kg mol^{-1} to 49 kg mol^{-1}.

Other examples of the grafting-from strategy include hyperbranched polyglycerol, which could be obtained by anionic ring-opening polymerization of glycidol from the surface of CdTe QDs[172] and the synthesis of a thermoresponsive polymer poly(2-(dimethylamino)ethyl methacrylate) from the surface of CdTe QDs by surface-initiated oxyanionic vinyl polymerization. The latter QDs were soluble in water and organic solvents and were therefore called amphibious. Upon heating the QD solution above the lower critical solution temperature of the polymer (between 32 and 38 °C, depending on the grafted polymer fraction on the QD) the grafted chains collapsed and the QDs aggregated.[173]

Conclusions

We have reviewed surface modifications of QDs based on different macromolecular coatings. The short ligands on the surface of the QDs resulting from the QD synthetic protocols can be readily exchanged by polymeric ligands bearing functional groups, which are able to interact strongly with the nanocrystals' surface. Polymeric coating strategies include using polymers as multidentate ligands, where multiple side groups interact with the QD surface, using hydrophobic interactions between the polymeric coating and the hydrophobic ligands on the QDs, and by attaching the polymers by their chain ends. The latter could be achieved by growing polymers directly from the surface of the QDs or by attaching an end-functionalized polymer to the QD surface or to the surface ligands. Overall, most of the polymer-coated QDs display enhanced colloidal stability in solution and provide a robust platform for chemical derivatization. The choice of a suitable coating method is dictated primarily by the final application of the QDs. Taking advantage of the availability of functional groups, polymer-coated QDs have found applications in biology and biosensing as luminescent tags and probes, while the ability to introduce polymers close to the QD surface was used in optoelectronic applications.

The control of the number of functional groups on the surface of the QDs remains relatively unexplored with current methods being based primarily on purification procedures (and therefore low yields). Spatial distribution of multiple functional groups was to our knowledge not addressed. We believe that these topics will gain more attention in the near future as such materials would allow performing quantitative biological experiments and will help to understand the electronic interactions between the polymeric shell and the QDs.

Acknowledgements

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References

1 W. R. Algar, K. Susumu, J. B. Delehanty and I. L. Medintz, *Anal. Chem.*, 2011, **83**, 8826.
2 N. Erathodiyil and J. Y. Ying, *Acc. Chem. Res.*, 2011, **44**, 925.
3 A. P. Alivisatos, W. W. Gu and C. Larabell, *Annu. Rev. Biomed. Eng.*, 2005, **7**, 55.
4 X. H. Gao, L. L. Yang, J. A. Petros, F. F. Marshal, J. W. Simons and S. M. Nie, *Curr. Opin. Biotechnol.*, 2005, **16**, 63.
5 T. Pellegrino, S. Kudera, T. Liedl, A. M. Javier, L. Manna and W. J. Parak, *Small*, 2005, **1**, 48.
6 F. Pinaud, S. Clarke, A. Sittner and M. Dahan, *Nat. Methods*, 2010, **7**, 275.

7 A. R. Lowe, J. J. Siegel, P. Kalab, M. Siu, K. Weis and J. T. Liphardt, *Nature*, 2010, **467**, 600.
8 J. Riegler and T. Nann, *Anal. Bioanal. Chem.*, 2004, **379**, 913.
9 C. Y. Zhang, H. C. Yeh, M. T. Kuroki and T. H. Wang, *Nat. Mater.*, 2005, **4**, 826.
10 H. Q. Yao, Y. Zhang, F. Xiao, Z. Y. Xia and J. H. Rao, *Angew. Chem., Int. Ed.*, 2007, **46**, 4346.
11 L. Zhao and Z. Q. Lin, *Adv. Mater.*, 2012, **24**, 4353.
12 I. L. Medintz, H. T. Uyeda, E. R. Goldman and H. Mattoussi, *Nat. Mater.*, 2005, **4**, 435.
13 X. Michalet, F. F. Pinaud, L. A. Bentolila, J. M. Tsay, S. Doose, J. J. Li, G. Sundaresan, A. M. Wu, S. S. Gambhir and S. Weiss, *Science*, 2005, **307**, 538.
14 U. Resch-Genger, M. Grabolle, S. Cavaliere-Jaricot, R. Nitschke and T. Nann, *Nat. Methods*, 2008, **5**, 763.
15 W. R. Algar, A. J. Tavares and U. J. Krull, *Anal. Chim. Acta*, 2010, **673**, 1.
16 V. Biju, T. Itoh and M. Ishikawa, *Chem. Soc. Rev.*, 2010, **39**, 3031.
17 M. Dahan, S. Levi, C. Luccardini, P. Rostaing, B. Riveau and A. Triller, *Science*, 2003, **302**, 442.
18 D. Maysinger, J. Lovric, A. Eisenberg and R. Savic, *Eur. J. Pharm. Biopharm.*, 2007, **65**, 270.
19 S. Pathak, E. Cao, M. C. Davidson, S. H. Jin and G. A. Silva, *J. Neurosci.*, 2006, **26**, 1893.
20 T. Pons and H. Mattoussi, *Ann. Biomed. Eng.*, 2009, **37**, 1934.
21 N. Tomczak, D. Janczewski, D. Dorokhin, M. Y. Han and G. J. Vancso, Enabling biomedical research with designer quantum dots, in *Nanotechnology in regenerative medicine*, ed. M. Navarro and J. A. Planell, Humana Press, New York, 2012, pp. 245–265.
22 Y. Z. Wu, K. Eisele, M. Doroshenko, G. gara-Siller, U. Kaiser, K. Koynov and T. Weil, *Small*, 2012, **8**, 3465.
23 P. Zrazhevskiy, M. Sena and X. H. Gao, *Chem. Soc. Rev.*, 2010, **39**, 4326.
24 J. K. Oh, *J. Mater. Chem.*, 2010, **20**, 8433.
25 S. Kim, Y. T. Lim, E. G. Soltesz, A. M. De Grand, J. Lee, A. Nakayama, J. A. Parker, T. Mihaljevic, R. G. Laurence, D. M. Dor, L. H. Cohn, M. G. Bawendi and J. V. Frangioni, *Nat. Biotechnol.*, 2004, **22**, 93.
26 H. Mattoussi, G. Palui and H. B. Na, *Adv. Drug Delivery Rev.*, 2012, **64**, 138.
27 M. P. Bruchez, *Curr. Opin. Chem. Biol.*, 2011, **15**, 775.
28 J. K. Jaiswal, H. Mattoussi, J. M. Mauro and S. M. Simon, *Nat. Biotechnol.*, 2003, **21**, 47.
29 L. C. Mattheakis, J. M. Dias, Y. J. Choi, J. Gong, M. P. Bruchez, J. Q. Liu and E. Wang, *Anal. Biochem.*, 2004, **327**, 200.
30 X. Y. Wu, H. J. Liu, J. Q. Liu, K. N. Haley, J. A. Treadway, J. P. Larson, N. F. Ge, F. Peale and M. P. Bruchez, *Nat. Biotechnol.*, 2003, **21**, 41.
31 M. V. Yezhelyev, A. Al-Hajj, C. Morris, A. I. Marcus, T. Liu, M. Lewis, C. Cohen, P. Zrazhevskiy, J. W. Simons, A. Rogatko, S. Nie, X. Gao and R. M. O'Regan, *Adv. Mater.*, 2007, **19**, 3146.
32 I. Chen, Y. A. Choi and A. Y. Ting, *J. Am. Chem. Soc.*, 2007, **129**, 6619.
33 B. C. Lagerholm, M. M. Wang, L. A. Ernst, D. H. Ly, H. J. Liu, M. P. Bruchez and A. S. Waggoner, *Nano Lett.*, 2004, **4**, 2019.
34 D. S. Lidke, P. Nagy, R. Heintzmann, D. J. rndt-Jovin, J. N. Post, H. E. Grecco, E. A. Jares-Erijman and T. M. Jovin, *Nat. Biotechnol.*, 2004, **22**, 198.
35 K. E. Knowles, M. T. Frederick, D. B. Tice, A. J. Morris-Cohen and E. A. Weiss, *J. Phys. Chem. Lett.*, 2012, **3**, 18.
36 A. Quarta, A. Curcio, H. Kakwere and T. Pellegrino, *Nanoscale*, 2012, **4**, 3319.
37 F. Zhang, E. Lees, F. Amin, P. R. Gil, F. Yang, P. Mulvaney and W. J. Parak, *Small*, 2011, **7**, 3113.
38 N. Tomczak, D. Janczewski, O. Tagit, M. Y. Han and G. J. Vancso, Surface engineering of Quantum dots with designer ligands, in *Surface design: Applications in bioscience and nanotechnology*, ed. R. Forch, H. Schonherr and A. T. A. Jenkins, Wiley-VCH, Weinheim, 2009, pp. 341–361.
39 M. Green and P. O'Brien, *Chem. Commun.*, 1999, 2235.
40 T. Trindade, P. O'Brien and N. L. Pickett, *Chem. Mater.*, 2001, **13**, 3843.
41 C. B. Murray, D. J. Norris and M. G. Bawendi, *J. Am. Chem. Soc.*, 1993, **115**, 8706.
42 A. R. Clapp, I. L. Medintz, J. M. Mauro, B. R. Fisher, M. G. Bawendi and H. Mattoussi, *J. Am. Chem. Soc.*, 2004, **126**, 301.
43 B. O. Dabbousi, J. RodriguezViejo, F. V. Mikulec, J. R. Heine, H. Mattoussi, R. Ober, K. F. Jensen and M. G. Bawendi, *J. Phys. Chem. B*, 1997, **101**, 9463.
44 M. A. Hines and P. Guyot-Sionnest, *J. Phys. Chem.*, 1996, **100**, 468.
45 X. G. Peng, M. C. Schlamp, A. V. Kadavanich and A. P. Alivisatos, *J. Am. Chem. Soc.*, 1997, **119**, 7019.
46 M. Bruchez, M. Moronne, P. Gin, S. Weiss and A. P. Alivisatos, *Science*, 1998, **281**, 2013.
47 M. A. Correa-Duarte, M. Giersig and L. M. Liz-Marzan, *Chem. Phys. Lett.*, 1998, **286**, 497.
48 P. D. McNaughter, J. C. Bear, D. C. Steytler, A. G. Mayes and T. Nann, *Angew. Chem., Int. Ed.*, 2011, **50**, 10384.
49 P. Mulvaney, L. M. Liz-Marzan, M. Giersig and T. Ung, *J. Mater. Chem.*, 2000, **10**, 1259.
50 W. J. Parak, D. Gerion, D. Zanchet, A. S. Woerz, T. Pellegrino, C. Micheel, S. C. Williams, M. Seitz, R. E. Bruehl, Z. Bryant, C. Bustamante, C. R. Bertozzi and A. P. Alivisatos, *Chem. Mater.*, 2002, **14**, 2113.
51 W. Stober, A. Fink and E. Bohn, *J. Colloid Interface Sci.*, 1968, **26**, 62.
52 M. Darbandi, R. Thomann and T. Nann, *Chem. Mater.*, 2005, **17**, 5720.
53 J. Aldana, N. Lavelle, Y. J. Wang and X. G. Peng, *J. Am. Chem. Soc.*, 2005, **127**, 2496.
54 J. Aldana, Y. A. Wang and X. G. Peng, *J. Am. Chem. Soc.*, 2001, **123**, 8844.
55 B. C. Mei, K. Susumu, I. L. Medintz and H. Mattoussi, *Nat. Protoc.*, 2009, **4**, 412.
56 K. Susumu, B. C. Mei and H. Mattoussi, *Nat. Protoc.*, 2009, **4**, 424.

57 H. T. Uyeda, I. L. Medintz, J. K. Jaiswal, S. M. Simon and H. Mattoussi, *J. Am. Chem. Soc.*, 2005, **127**, 3870.
58 S. Kim and M. G. Bawendi, *J. Am. Chem. Soc.*, 2003, **125**, 14652.
59 S. W. Kim, S. Kim, J. B. Tracy, A. Jasanoff and M. G. Bawendi, *J. Am. Chem. Soc.*, 2005, **127**, 4556.
60 F. Boulmedais, P. Bauchat, M. J. Brienne, I. Arnal, F. Artzner, T. Gacoin, M. Dahan and V. Marchi-Artzner, *Langmuir*, 2006, **22**, 9797.
61 H. Y. Fan, *Chem. Commun.*, 2008, 1383.
62 J. Feng, S. Y. Ding, M. P. Tucker, M. E. Himmel, Y. H. Kim, S. B. Zhang, B. M. Keyes and G. Rumbles, *Appl. Phys. Lett.*, 2005, **86**, 033108.
63 Y. Wang, J. F. Wong, X. W. Teng, X. Z. Lin and H. Yang, *Nano Lett.*, 2003, **3**, 1555.
64 O. Carion, B. Mahler, T. Pons and B. Dubertret, *Nat. Protoc.*, 2007, **2**, 2383.
65 B. Dubertret, P. Skourides, D. J. Norris, V. Noireaux, A. H. Brivanlou and A. Libchaber, *Science*, 2002, **298**, 1759.
66 H. Y. Fan, E. W. Leve, C. Scullin, J. Gabaldon, D. Tallant, S. Bunge, T. Boyle, M. C. Wilson and C. J. Brinker, *Nano Lett.*, 2005, **5**, 645.
67 I. Geissbuehler, R. Hovius, K. L. Martinez, M. Adrian, K. R. Thampi and H. Vogel, *Angew. Chem., Int. Ed.*, 2005, **44**, 1388.
68 M. Lalancette-Hebert, A. Moquin, A. O. Choi, J. Kriz and D. Maysinger, *Mol. Pharm.*, 2010, **7**, 1183.
69 J. B. Liu, X. H. Yang, K. M. Wang, Y. He, P. F. Zhang, H. N. Ji, L. X. Jian and W. Liu, *Langmuir*, 2012, **28**, 10602.
70 F. Osaki, T. Kanamori, S. Sando, T. Sera and Y. Aoyama, *J. Am. Chem. Soc.*, 2004, **126**, 6520.
71 X. H. Gao, Y. Y. Cui, R. M. Levenson, L. W. K. Chung and S. M. Nie, *Nat. Biotechnol.*, 2004, **22**, 969.
72 K. M. Krueger, A. M. Al-Somali, M. Mejia and V. L. Colvin, *Nanotechnology*, 2007, **18**, 475709.
73 D. N. Benoit, H. G. Zhu, M. H. Lilierose, R. A. Verm, N. Ali, A. N. Morrison, J. D. Fortner, C. Ayendano and V. L. Colvin, *Anal. Chem.*, 2012, **84**, 9238.
74 R. A. Sperling, T. Liedl, S. Duhr, S. Kudera, M. Zanella, C. A. J. Lin, W. H. Chang, D. Braun and W. J. Parak, *J. Phys. Chem. C*, 2007, **111**, 11552.
75 E. Giovanelli, E. Muro, G. Sitbon, M. Hanafi, T. Pons, B. Dubertret and N. Lequeux, *Langmuir*, 2012, **28**, 15177.
76 H. Mattoussi, J. M. Mauro, E. R. Goldman, G. P. Anderson, V. C. Sundar, F. V. Mikulec and M. G. Bawendi, *J. Am. Chem. Soc.*, 2000, **122**, 12142.
77 M. H. Stewart, K. Susumu, B. C. Mei, I. L. Medintz, J. B. Delehanty, J. B. Blanco-Canosa, P. E. Dawson and H. Mattoussi, *J. Am. Chem. Soc.*, 2010, **132**, 9804.
78 N. Anikeeva, T. Lebedeva, A. R. Clapp, E. R. Goldman, M. L. Dustin, H. Mattoussi and Y. Sykulev, *Proc. Natl. Acad. Sci. U. S. A.*, 2006, **103**, 16846.
79 C. Querner, A. Benedetto, R. Demadrille, P. Rannou and P. Reiss, *Chem. Mater.*, 2006, **18**, 4817.
80 C. Querner, P. Reiss, S. Sadki, M. Zagorska and A. Pron, *Phys. Chem. Chem. Phys.*, 2005, **7**, 3204.
81 C. Querner, P. Reiss, J. Bleuse and A. Pron, *J. Am. Chem. Soc.*, 2004, **126**, 11574.
82 Y. Li, B. Shen, L. Liu, H. Xu and X. H. Zhong, *Colloids Surf., A*, 2012, **410**, 144.
83 L. Liu, X. H. Guo, Y. Li and X. H. Zhong, *Inorg. Chem.*, 2010, **49**, 3768.
84 G. Palui, H. B. Na and H. Mattoussi, *Langmuir*, 2012, **28**, 2761.
85 I. Yildiz, E. Deniz, B. McCaughan, S. F. Cruickshank, J. F. Callan and F. M. Raymo, *Langmuir*, 2010, **26**, 11503.
86 I. Yildiz, B. McCaughan, S. F. Cruickshank, J. F. Callan and F. M. Raymo, *Langmuir*, 2009, **25**, 7090.
87 Q. Wang, Y. C. Kuo, Y. W. Wang, G. Shin, C. Ruengruglikit and Q. R. Huang, *J. Phys. Chem. B*, 2006, **110**, 16860.
88 T. Nann, *Chem. Commun.*, 2005, 1735.
89 P. F. Zhang and H. X. Han, *Colloids Surf., A*, 2012, **402**, 72.
90 Y. G. Zheng, Z. C. Yang, Y. Q. Li and J. Y. Ying, *Adv. Mater.*, 2008, **20**, 3410.
91 W. Jiang, S. Mardyani, H. Fischer and W. C. W. Chan, *Chem. Mater.*, 2006, **18**, 872.
92 G. Iyer, X. Michalet, Y. P. Chang, F. F. Pinaud, S. E. Matyas, G. Payne and S. Weiss, *Nano Lett.*, 2008, **8**, 4618.
93 G. Iyer, F. Pinaud, J. Tsay and S. Weiss, *Small*, 2007, **3**, 793.
94 F. Pinaud, D. King, H. P. Moore and S. Weiss, *J. Am. Chem. Soc.*, 2004, **126**, 6115.
95 J. M. Xu, P. Ruchala, Y. Ebenstain, J. J. Li and S. Weiss, *J. Phys. Chem. B*, 2012, **116**, 11370.
96 S. Clarke, F. Pinaud, O. Beutel, C. J. You, J. Piehler and M. Dahan, *Nano Lett.*, 2010, **10**, 2147.
97 Y. Z. Wu, S. Chakrabortty, R. A. Gropeanu, J. Wilhelmi, Y. Xu, K. S. Er, S. L. Kuan, K. Koynov, Y. Chan and T. Weil, *J. Am. Chem. Soc.*, 2010, **132**, 5012.
98 X. S. Wang, T. E. Dykstra, M. R. Salvador, I. Manners, G. D. Scholes and M. A. Winnik, *J. Am. Chem. Soc.*, 2004, **126**, 7784.
99 I. Potapova, R. Mruk, C. Hubner, R. Zentel, T. Basche and A. Mews, *Angew. Chem., Int. Ed.*, 2005, **44**, 2437.
100 M. F. Wang, T. E. Dykstra, X. D. Lou, M. R. Salvador, G. D. Scholes and M. A. Winnik, *Angew. Chem., Int. Ed.*, 2006, **45**, 2221.
101 M. F. Wang, J. K. Oh, T. E. Dykstra, X. D. Lou, G. D. Scholes and M. A. Winnik, *Macromolecules*, 2006, **39**, 3664.
102 M. F. Wang, N. Felorzabihi, G. Guerin, J. C. Haley, G. D. Scholes and M. A. Winnik, *Macromolecules*, 2007, **40**, 6377.
103 M. F. Wang, M. Zhang, J. S. Qian, F. Zhao, L. Shen, G. D. Scholes and M. A. Winnik, *Langmuir*, 2009, **25**, 11732.
104 A. M. Smith and S. Nie, *J. Am. Chem. Soc.*, 2008, **130**, 11278.
105 W. H. Liu, A. B. Greytak, J. Lee, C. R. Wong, J. Park, L. F. Marshall, W. Jiang, P. N. Curtin, A. Y. Ting, D. G. Nocera, D. Fukumura, R. K. Jain and M. G. Bawendi, *J. Am. Chem. Soc.*, 2010, **132**, 472.
106 H. S. Han, N. K. Devaraj, J. Lee, S. A. Hilderbrand, R. Weissleder and M. G. Bawendi, *J. Am. Chem. Soc.*, 2010, **132**, 7838.
107 R. M. Crooks, M. Q. Zhao, L. Sun, V. Chechik and L. K. Yeung, *Acc. Chem. Res.*, 2001, **34**, 181.

108 B. I. Lemon and R. M. Crooks, *J. Am. Chem. Soc.*, 2000, **122**, 12886.
109 H. W. Duan and S. M. Nie, *J. Am. Chem. Soc.*, 2007, **129**, 3333.
110 C. X. Zhang, S. O'Brien and L. Balogh, *J. Phys. Chem. B*, 2002, **106**, 10316.
111 A. C. Wisher, I. Bronstein and V. Chechik, *Chem. Commun.*, 2006, 1637.
112 Z. Ali, A. Z. Abbasi, F. Zhang, P. Arosio, A. Lascialfari, M. F. Casula, A. Wenk, W. Kreyling, R. Plapper, M. Seidel, R. Niessner, J. Knoll, A. Seubert and W. J. Parak, *Anal. Chem.*, 2011, **83**, 2877.
113 T. Pons, H. T. Uyeda, I. L. Medintz and H. Mattoussi, *J. Phys. Chem. B*, 2006, **110**, 20308.
114 A. M. Smith, H. W. Duan, M. N. Rhyner, G. Ruan and S. M. Nie, *Phys. Chem. Chem. Phys.*, 2006, **8**, 3895.
115 C. Kirchner, T. Liedl, S. Kudera, T. Pellegrino, A. M. Javier, H. E. Gaub, S. Stolzle, N. Fertig and W. J. Parak, *Nano Lett.*, 2005, **5**, 331.
116 M. Bottrill and M. Green, *Chem. Commun.*, 2011, **47**, 7039.
117 Y. Xing, Q. Chaudry, C. Shen, K. Y. Kong, H. E. Zhau, L. WChung, J. A. Petros, R. M. O'Regan, M. V. Yezhelyev, J. W. Simons, M. D. Wang and S. Nie, *Nat. Protoc.*, 2007, **2**, 1152.
118 T. Pellegrino, L. Manna, S. Kudera, T. Liedl, D. Koktysh, A. L. Rogach, S. Keller, J. Radler, G. Natile and W. J. Parak, *Nano Lett.*, 2004, **4**, 703.
119 R. Di Corato, A. Quarta, P. Piacenza, A. Ragusa, A. Figuerola, R. Buonsanti, R. Cingolani, L. Manna and T. Pellegrino, *J. Mater. Chem.*, 2008, **18**, 1991.
120 W. W. Yu, E. Chang, J. C. Falkner, J. Y. Zhang, A. M. Al-Somali, C. M. Sayes, J. Johns, R. Drezek and V. L. Colvin, *J. Am. Chem. Soc.*, 2007, **129**, 2871.
121 L. F. Qi and X. H. Gao, *ACS Nano*, 2008, **2**, 1403.
122 B. W. Muir, B. A. Moffat, P. Harbour, G. Coia, G. L. Zhen, L. Waddington, J. Scoble, D. Krah, S. H. Thang, Y. K. Chong, P. Mulvaney and P. Hartley, *J. Phys. Chem. C*, 2009, **113**, 16615.
123 R. E. Anderson and W. C. W. Chan, *ACS Nano*, 2008, **2**, 1341.
124 D. R. Larson, W. R. Zipfel, R. M. Williams, S. W. Clark, M. P. Bruchez, F. W. Wise and W. W. Webb, *Science*, 2003, **300**, 1434.
125 C. Luccardini, C. Tribet, F. Vial, V. Marchi-Artzner and M. Dahan, *Langmuir*, 2006, **22**, 2304.
126 E. E. Lees, T. L. Nguyen, A. H. A. Clayton, P. Mulvaney and B. W. Muir, *ACS Nano*, 2009, **3**, 1121.
127 P. T. Snee, R. C. Somers, G. Nair, J. P. Zimmer, M. G. Bawendi and D. G. Nocera, *J. Am. Chem. Soc.*, 2006, **128**, 13320.
128 D. Janczewski, N. Tomczak, S. H. Liu, M. Y. Han and G. J. Vancso, *Chem. Commun.*, 2010, **46**, 3253.
129 D. Janczewski, N. Tomczak, M. Y. Han and G. J. Vancso, *Macromolecules*, 2009, **42**, 1801.
130 D. Janczewski, N. Tomczak, Y. W. Khin, M. Y. Han and G. J. Vancso, *Eur. Polym. J.*, 2009, **45**, 3.
131 D. Janczewski, N. Tomczak, J. Song, H. Long, M. Y. Han and G. J. Vancso, *J. Mater. Chem.*, 2011, **21**, 6487.
132 D. Janczewski, N. Tomczak, M. Y. Han and G. J. Vancso, *Nat. Protoc.*, 2011, **6**, 1546.
133 M. T. Fernandez-Arguelles, A. Yakovlev, R. A. Sperling, C. Luccardini, S. Gaillard, A. S. Medel, J. M. Mallet, J. C. Brochon, A. Feltz, M. Oheim and W. J. Parak, *Nano Lett.*, 2007, **7**, 2613.
134 C. A. J. Lin, R. A. Sperling, J. K. Li, T. Y. Yang, P. Y. Li, M. Zanella, W. H. Chang and W. G. J. Parak, *Small*, 2008, **4**, 334.
135 A. V. Yakovlev, F. Zhang, A. Zulqurnain, A. zhar-Zahoor, C. Luccardini, S. Gaillard, J. M. Mallet, P. Tauc, J. C. Brochon, W. J. Parak, A. Feltz and M. Oheim, *Langmuir*, 2009, **25**, 3232.
136 T. Niebling, F. Zhang, Z. Ali, W. J. Parak and W. Heimbrodt, *J. Appl. Phys.*, 2009, **106**, 104701.
137 F. Amin, D. A. Yushchenko, J. M. Montenegro and W. J. Parak, *ChemPhysChem*, 2012, **13**, 1030.
138 S. A. Diaz, G. O. Menendez, M. H. Etchehon, L. Giordano, T. M. Jovin and E. A. Jares-Erijman, *ACS Nano*, 2011, **5**, 2795.
139 S. A. Diaz, L. Giordano, T. M. Jovin and E. A. Jares-Erijman, *Nano Lett.*, 2012, **12**, 3537.
140 R. A. Sperling, T. Pellegrino, J. K. Li, W. H. Chang and W. J. Parak, *Adv. Funct. Mater.*, 2006, **16**, 943.
141 Y. Yan, S. H. Wang, Z. W. Liu, H. Y. Wang and D. J. Huang, *Anal. Chem.*, 2010, **82**, 9775.
142 Y. Chen, R. Thakar and P. T. Snee, *J. Am. Chem. Soc.*, 2008, **130**, 3744.
143 M. Zhou, E. Nakatani, L. S. Gronenberg, T. Tokimoto, M. J. Wirth, V. J. Hruby, A. Roberts, R. M. Lynch and I. Ghosh, *Bioconjugate Chem.*, 2007, **18**, 323.
144 O. Tagit, D. Janczewski, N. Tomczak, M. Y. Han, J. L. Herek and G. J. Vancso, *Eur. Polym. J.*, 2010, **46**, 1397.
145 O. Tagit, N. Tomczak, A. Jafarpour, D. Janczewski, M. Y. Han, G. J. Vancso and J. L. Herek, *Nanotechnology*, 2011, **22**, 265701.
146 M. V. Yezhelyev, L. F. Qi, R. M. O'Regan, S. Nie and X. H. Gao, *J. Am. Chem. Soc.*, 2008, **130**, 9006.
147 H. Y. Shen, A. M. Jawaid and P. T. Snee, *ACS Nano*, 2009, **3**, 915.
148 B. Ballou, B. C. Lagerholm, L. A. Ernst, M. P. Bruchez and A. S. Waggoner, *Bioconjugate Chem.*, 2004, **15**, 79.
149 E. L. Bentzen, I. D. Tomlinson, J. Mason, P. Gresch, M. R. Warnement, D. Wright, E. Sanders-Bush, R. Blakely and S. J. Rosenthal, *Bioconjugate Chem.*, 2005, **16**, 1488.
150 M. T. Fernandez-Arguelles, J. M. Costa-Fernandez, R. Pereiro and A. Sanz-Medel, *Analyst*, 2008, **133**, 444.
151 H. Skaff and T. Emrick, *Chem. Commun.*, 2003, 52.
152 W. M. Kochemba, *Chem. Mater.*, 2012, **24**, 4459.
153 G. P. Mitchell, C. A. Mirkin and R. L. Letsinger, *J. Am. Chem. Soc.*, 1999, **121**, 8122.
154 D. J. Milliron, A. P. Alivisatos, C. Pitois, C. Edder and J. M. J. Frechet, *Adv. Mater.*, 2003, **15**, 58.
155 F. Patolsky, R. Gill, Y. Weizmann, T. Mokari, U. Banin and I. Willner, *J. Am. Chem. Soc.*, 2003, **125**, 13918.
156 J. Xu, J. Wang, M. Mitchell, P. Mukherjee, M. Jeffries-EL, J. W. Petrich and Z. Q. Lin, *J. Am. Chem. Soc.*, 2007, **129**, 12828.

157 W. Liu, M. Howarth, A. B. Greytak, Y. Zheng, D. G. Nocera, A. Y. Ting and M. G. Bawendi, *J. Am. Chem. Soc.*, 2008, **130**, 1274.
158 K. Susumu, H. T. Uyeda, I. L. Medintz, T. Pons, J. B. Delehanty and H. Mattoussi, *J. Am. Chem. Soc.*, 2007, **129**, 13987.
159 B. C. Mei, K. Susumu, I. L. Medintz, J. B. Delehanty, T. J. Mountziaris and H. Mattoussi, *J. Mater. Chem.*, 2008, **18**, 4949.
160 Y. A. Wang, J. J. Li, H. Y. Chen and X. G. Peng, *J. Am. Chem. Soc.*, 2002, **124**, 2293.
161 W. H. Guo, J. J. Li, Y. A. Wang and X. G. Peng, *J. Am. Chem. Soc.*, 2003, **125**, 3901.
162 W. Z. Guo, J. J. Li, Y. A. Wang and X. G. Peng, *Chem. Mater.*, 2003, **15**, 3125.
163 Y. L. Zhao, Y. P. Li, Y. T. Song, W. Jiang, Z. Y. Wu, Y. A. Wang, J. H. Sun and J. Y. Wang, *J. Colloid Interface Sci.*, 2009, **339**, 336.
164 G. Carrot, D. Rutot-Houze, A. Pottier, P. Degee, J. Hilborn and P. Dubois, *Macromolecules*, 2002, **35**, 8400.
165 A. C. C. Esteves, L. Bombalski, T. Trindade, K. Matyjaszewski and A. Barros-Timmons, *Small*, 2007, **3**, 1230.
166 H. Skaff, M. F. Ilker, E. B. Coughlin and T. Emrick, *J. Am. Chem. Soc.*, 2002, **124**, 5729.
167 K. Sill and T. Emrick, *Chem. Mater.*, 2004, **16**, 1240.
168 H. Skaff, K. Sill and T. Emrick, *J. Am. Chem. Soc.*, 2004, **126**, 11322.
169 H. Skaff and T. Emrick, *Angew. Chem., Int. Ed.*, 2004, **43**, 5383.
170 M. Y. Odoi, N. I. Hammer, K. Sill, T. Emrick and M. D. Barnes, *J. Am. Chem. Soc.*, 2006, **128**, 3506.
171 N. I. Hammer, K. T. Early, K. Sill, M. Y. Odoi, T. Emrick and M. D. Barnes, *J. Phys. Chem. B*, 2006, **110**, 14167.
172 L. Zhou, C. Gao, W. J. Xu, X. Wang and Y. H. Xu, *Biomacromolecules*, 2009, **10**, 1865.
173 L. Zhou, C. Gao and W. J. Xu, *J. Mater. Chem.*, 2009, **19**, 5655.