Synthesis of nanoparticles for biomedical applications

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This review summarises the advances in synthetic methods of nanoparticles (NPs) for biomedical applications published in 2009.

Highlights

The highlights of this review comprise the syntheses of magnetic NPs with tuneable shapes using simple procedures and by employing different reaction conditions.[7] Efforts have been made to modify the coating of NPs to allow them to respond to external stimuli.[9,10,49–53,126] Hollow structures[27–31] and NPs composed of noble metals[44] continue to be of interest. High quantum yield has been achieved in CdTe/CdSe semiconductor quantum dots.[99] Multimodal NPs with optical and magnetic properties continue to attract great interest and have been further developed.[125–130,132–134]

1. Introduction

Significant interest has arisen in the research of NPs during the last decade, in particular for biomedical applications. The integration of nanotechnology into the field of medical science has opened new possibilities. Working with nanomaterials has allowed a better understanding of molecular biology. As a consequence, there is the potential of providing novel methods for the treatment of diseases which were previously difficult to target due to size restrictions. For biomedical applications, the synthesis of biofunctional NPs is very important, and it has recently drawn the attention of numerous research groups, making this area constantly evolve.

Currently there is a vast extent of materials and chemical synthesis techniques that are being investigated for biomedical applications. In this review of the publications in 2009, we will focus only on the research of the NP synthesis which include magnetic, noble metals and semiconducting materials.

2. Magnetic nanoparticles

The applications of magnetic NPs in biomedicine have been reviewed.[1] Water dispersable ultrasmall superparamagnetic iron oxide (USPIO) NPs have been obtained by a post synthesis ligand exchange step. Small α-hydroxyacids such as

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citric or tartaric acid have been reported to enable high colloidal stability in 4 nm maghemite NPs when introduced after synthesis by high-temperature hydrolysis of chelated iron(II) and (III) diethylene glycol alkoxide complexes.[2] An iron(III)-oleate complex derived from dissolution of hematite in oleic acid (OA) was used as an alternative iron source for the synthesis of maghemite NPs. Control over particle size was achieved by modifying the hematite : fatty acid ratio.[3] L-Ascorbic acid functionalised 6.5 nm magnetite NPs were obtained using a flow-through supercritical hydrothermal microreactor. L-ascorbic acid was used both as reducing agent and stabiliser, generating water dispersable NPs with high biocompatibility enabling a saturation magnetisation of 23 emu g^{-1}.[4] L-Arginine has also been used as both reducing agent and stabilising ligand for iron oxide NPs. L-arginine was reported as a possible initiator for the nucleation process due to iron hydrolysis. The size of the NPs can be controlled from 9 to 15 nm by Fe : arginine ratio. This synthetic approach was extended to the synthesis of manganese and cobalt ferrite NPs.[5] Tri(ethyleneglycol) was used as both solvent and stabilising agent due to its adsorption on the NP surface for the synthesis of magnetite NPs by reducing iron(III) acetylacetonate.[6] Variation of the nature of the reagents used for the synthesis of FePt, FePd and FePtPd NPs was reported to affect the kinetics of particle growth and the symmetry of the nuclei leading to NPs of different shape (sphere, cube, octopod/cube, star, rod, bilobe, tetrahedron, and multipods) (Fig. 1).[7] A solvent-free approach was reported for the synthesis of maghemite NPs by an isothermal oxidation of iron(II) acetate treated by initial grinding leading to quasi monodisperse (15–20 nm) NPs.[8]

Magnetite NPs with a pH-sensitive polymer coating were obtained by post synthetic addition of poly(2-dimethylamino) ethyl methacrylate *via* atom transfer radical polymerisation to α-bromoisobutyric acid functionalised magnetite NPs yielding a saturation magnetisation of 53.4 emu g^{-1}.[9] A thermo-responsive polymer based on poly(*N*-isopropylacrylamide) containing a co-monomer of acrylamide or acrylic acid was introduced to 8 nm OA functionalised maghemite or Co NPs, respectively, by ligand exchange.[10]

A high pressure polyol method was used for the synthesis of citrate functionalised magnetite nanoparticles promoting the formation of 40–300 nm magnetite clusters

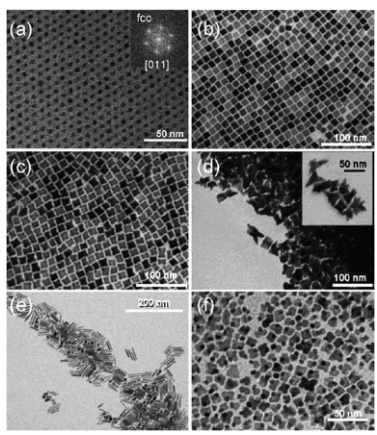

Fig. 1 TEM images of (a) spherical, (b) cubic, (c) octopod-cubic, (d) star, (e) rod and (f) bilobar Fe–Pt NPs.[7]

from USPIOs under homogenously induced basic conditions from the release of ammonia due to the decomposition of urea. Ferric ions were reduced to ferrous by ethylene glycol and hence accelerated the formation of magnetite.[11] Magnetite clusters were obtained by co-precipitation methods in the presence of a double hydrophilic block copolymer polyethylene oxide-*b*-polyacrylic acid (PEO_{45}-*b*-PAA_{70}). The obtained particles were homogeneous in size but the final cluster size could not be controlled.[12] Formation of NP clusters has been also exploited for the synthesis of USPIOs by the "*Flocculation-redispersion*" method. Carboxyl dextran-functionalised NPs were obtained in the presence of polyvinyl alcohol (PVA) leading to the formation of large clusters with the potential for redispersion in solution as a result of electrostatic repulsion by addition of citric acid in solution.[13] Carboxyl dextran was reported for the coating of Mn/Zn ferrite NPs which make them stable under physiological conditions (0.15 M NaCl, pH = 7.0).[14]

Functionalisation of NPs has been exploited for the incorporation of biomolecules and the improvement of NP colloidal stability. The use of an alcohol-based ligand was shown to improve ligand exchange due to bond lability when incorporated in the synthesis of ferrite NPs from transition-metal acetate precursors.[15] Alternatively, mpolyethylene glycol 2000 (mPEG2000) and dimercaptosuccinic acid (DMSA) were used as coating agents for 9 nm iron oxide NPs. It has been shown that DMSA could be used as anchoring point for biomolecules such as proteins due to the presence of thiol groups.[16] Air stable Co NPs were obtained by thermal decomposition of the carbonyl precursor in the presence of the silane coupling agent 3-aminopropyl-triethoxysilane. Siloxane functionalised NPs were air stable due to the presence of a thin oxide shell obtained by controlled oxidation with synthetic air, and water soluble due to silane polymer coating.[17] An oligo(phenylene vinylene)-based prodendritic ligand was used for the biofunctionalisation of magnetite NPs. The obtained coated NPs enable ferromagnetic behaviour at room temperature as well as luminescent properties due to the chromophore on the ligand moiety.[18] A widely applicable functionalisation approach was reported by incorporation of adipoyl chloride onto nickel–zinc ferrite NPs in the presence of 4-methylmorpholine as a Lewis base. The highly reactive acyl chloride terminal moiety provided an efficient approach for further functionalisation.[19] Introduction of polyether functionalisation from triammonium amphiphilic poly(propylene oxide-*b*-ethylene oxide) copolymer to magnetite NPs, was achieved by sonication.[20] Functionalisation of 100 nm magnetite NPs with chitosan was approached by a reverse microemulsion method enabling 5-fluoroacil upload.[21] Gram-scale synthesis of monodisperse mesoporous poly(methacrylic acid) (PMMA) coated magnetite NPs were obtained by a solvothermal method leading to a saturation magnetisation of 65 emu g^{-1}.[22]

Carbon coated Fe, Co and Ni NPs were obtained by high pressure chemical vapour deposition using metallocenes as precursors. The obtained NPs were investigated for their potential applications in hyperthermia.[23] Triblock poly(ethylene oxide)-*b*-poly(propylene oxide)-*b*-poly(ethylene oxide) copolymer $EO_{106}PO_{70}EO_{106}$ (Pluronic P127) was used as carbon precursor for the self-template synthesis of iron oxide/carbon NPs. Silica assembly from tetraethylorthosilicate (TEOS) onto P127 micelles was reported prior to thermal treatment yielding 4 nm carbon coated iron oxide NPs.[24] A magnetite shell was grown onto iron–core NPs by means of an air-controlled oxidation. The final *cannonball* structure was reported to induce higher saturation magnetisation than manganese ferrite NPs.[25] *n*-Butyllithium in diphenyl ether was used as a strong reducing agent to obtain air stable 13 nm α-manganese NPs with a thin 3 nm amorphous layer of a OA stabilised manganese oxide.[26]

There has been a lot of interest in the generation of hollow structures due to their high surface area to volume ratio and large pore volume. Synthesis and biomedical applications of hollow nanostructures have been reviewed.[27,28] A one-pot co-precipitation method was used to obtain magnetite-based clusters in the presence of nonylphenyl ether (NFE, 4-$(C_9H_{19})C_6H_4(OCH_2CH_2)_nOH$) and cyclodextrin for coating and stabilising the magnetite NPs. A hollow structure with a saturation magnetisation of 105–115 emu g^{-1} was produced when long-chain NFE was used.[29] Surfactant template assisted growth was used for the hydrothermal synthesis of hollow Co NPs of 50–200 nm with a wall thickness of 10–20 nm using cetyltrimethyl ammonium bromide as surfactant (Fig. 2a).[30] Template assisted CoPt hollow NPs were obtained by a reduction method in the presence of long-chain thiol polymer ligands and a short peptide.[31] 20 nm water-dispersible hollow porous manganese oxide NPs were obtained from core–shell MnO/Mn_3O_4 by selective core removal with phthalate buffer solution. It was reported that the relaxation time T_1 and T_2 of the hollow structures are shorter than those obtained for solid hollow manganese oxide NPs when the same concentration of Mn was used.[32] Porous hollow NPs of magnetite of 16 nm were recently obtained by thermal decomposition in the presence of oleylamine (OLA). Selective core removal from Fe/Fe_3O_4 NPs was aided by trimethylammonium-*N*-oxide.[33]

Hollow structures can also be obtained by template-free approaches. Hollow Fe/C chitosan functionalised NPs were generated by acid etching and conjugation of chitosan within a microemulsion formed with AOT (aerosol optical thickness, sodium dioctyl sulfosuccinate) and they were used for hyperthermia experiments.[34] The hydrothermal synthesis of hollow magnetite NPs was reported in the presence of sodium acetate and ethylene glycol. Water-solubility of the obtained clusters was achieved by sonication in polyacrylic acid.[35] Magnetite hollow NPs were obtained by initial solid state reaction of $FeCl_3$ with urea by mechanical grinding to obtain the corresponding complex. Ethylene glycol was used as stabilising agent and solvent for the solvothermal synthesis of hollow spheres.[36] A chain-like array of hollow Fe_3O_4 NPs was produced by a reduction method in the presence of cetyltrimethyl-ammonium bromide. 1–3 micron chains of 80–100 nm hollow NPs were achieved by slow gas exposition oxidation. Shell thickness could be controlled by oxidation exposition time (Fig. 2b).[37]

Magnetic particles presenting hollow structures have also been reported using particle loading within a polymeric structure. OA—magnetite NPs were adhered to 500 nm hydroxymethyl-functionalised poly(3,4-ethylenedioxythiophene) poly(EDOT-OH) hollow spheres. Hydroxyl groups on the surface permitted water-dispersability

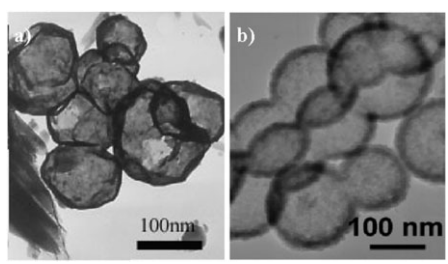

Fig. 2 TEM images of (a) surfactant templated synthesis of Co NPs,[30] (b) template-free synthesis of Fe_3O_4 NPs.[37]

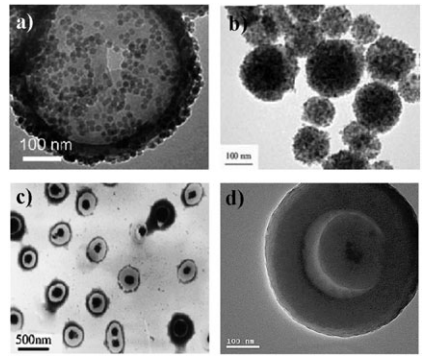

Fig. 3 TEM images of Fe_3O_4 NPs loaded on polymeric structures (a) poly(EDOT-OH) nanospheres,[38] (b) cross-linked pNIPAM with MBA,[39] (c) polystyrene[41] and (d) poly-(MBAAm-co-MAA).[42]

without further treatment. The polymeric structure exhibited a 20 nm diameter hole that could be potentially used for loading small molecules (Fig. 3a).[38] Polymeric cages of 400–1000 nm constituted by a thermoresponsive polymer poly-(*N*-isopropylacrylamide) (pNIPAM) cross-linked with *N*,*N*′-methylenebisacrylamide (MBA) were used for OA-Fe_3O_4 loading. These composites showed a saturation magnetisation of 18 emu g^{-1}. The cross-linked polymer experienced conformational changes above the lower critical solution temperature (LCST) resulting in the release of the polymeric cage content (Fig. 3b).[39] Maghemite NPs were incorporated into polyorganosiloxane core–shell nanospheres from dimethyldimethoxysilane, methyltrimethoxysilane and *p*-chloromethylphenyltrimethoxysilane. The obtained networked structures allowed the diffusion of small NPs into the nanospheres.[40] Incorporation of NPs onto polymeric structures could be also carried out *in situ* within polymer cage synthesis. OA functionalised magnetite NPs were depositied onto polystyrene spheres *via* miniemulsion polymerisation (Fig. 3c).[41] A poly-(*N*,*N*′-methylenebisacrylamide-*co*-methacrylic acid) (poly(MBAAm-co-MAA)) polymer mixture was used for the generation of pH-sensitive hollow microspheres with silica-coated magnetite NPs. Polymer synthesis was carried out by distillation precipitation copolymerisation onto a previously synthesised magnetic core (Fig. 3d).[42] Oxide-free Co NPs were trapped in PVA cross-linked-polymer cages leading to the formation of self-standing magnetic films. Encapsulation was achieved by suspension of the Co powder into the polymer solution which was thereafter dried under vacuum on a ceramic tile.[43]

3. Noble metal nanoparticles

Synthesis of noble metal NPs has been attempted by a wide range of synthetic approaches. A general method has been reported based on the reduction of the metal ions transferred from an aqueous phase by dodecylamine (Fig. 4).[44]

Applications of Au NPs in nanomedicine have been reviewed.[45] Monodisperse Au NPs were obtained in a range of 50–175 nm when using hydroxyquinone as reducing agent.[46] The response of particle coating to external stimuli has been exploited to expand the applicability of Au NPs. Thermo responsive Au NPs were obtained by polymer functionalisation with copoly(oligoethylene oxide) acrylates using reversible addition-fragmentation chain transfer polymerisation.[47] The thermally reversible

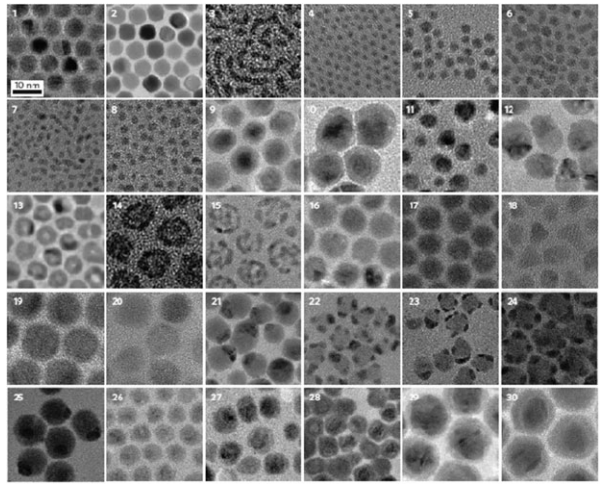

Fig. 4 TEM images of metal NPs. (1) Ag, (2) Au, (3) worm-like Pd and (4) Pt. Alloy NPs of (5) AgAu, (6) PdPt, (7) PtRh and (8) PtRu. Core–shell NPs of (9) 7.4 nm Au@Ag, (10) 12.7 nm Au@Ag, (11) Pt@Ag and (12) Pt@Ag, (13) Ag@Au and (14) Ag@Pt (15) Pt hollow spheres (16) AgPd. Semiconductor nanocrystals of (17) Ag_2S, (18) CdS, (19) HgS and (20) PbS. Hybrid NPs of (21) Ag_2S–Au, (22) CdS–Au, (23) CuS–Au, (24) PbS–Au, (25) Ag_2S–Ag, (26) CdS–Ag, (27) CuS–Ag and (28) PbS–Ag. Core–shell NPs of Au@Ag_2S synthesised with Au : Ag_2S precursor molar ratios of (29) 1 : 1 and (30) 1 : 3. The scale of each image is identical.[44]

assembly of Au NPs functionalised with dithiolthreitol and monothiol DNA was developed for the colorimetric detection of DNA sequences.[48] pH-sensitive Au NPs were obtained by the introduction of a bulky thiolamide moiety by ligand exchange. The bulky coating enabled colloidal stability above pH = 7 whereas electrostatic particle attraction led to induced aggregation under acidic conditions. Selective photothermal therapy could be applied after aggregation.[49] pH-sensitive switchable moieties were employed for the introduction of amine-based functionalisation into 2 nm Au NPs.[50] Multilayered pH-responsive hydrogen microcapsules have been used for the *in situ* synthesis of Au NPs in the presence of a borate buffer under ambient temperature and pressure conditions. The PMMA capsules constituted from hydrogen–bonded (PMMA/poly-*N*-cinylpyrrolidone) (PMMA/PVPON) precursors cross-linked with ethylenediamine (EDA) allowed amine groups to be readily available within the cross-linked structure. Amine protonation was controlled by solution pH.[51] Functionalisation of Au NPs with zwitterionic thiol ligands was reported to promote the entrapment of hydrophobic small molecules due to the formation of ''*hydrophobic pockets*'' from the alkyl segments in the thiol ligand chains. The solvent displacement method was used for NPs payload. This feature was exploited for membrane-mediated diffusion of the *pocket* content.[52] Self-assembled photocleavable ligands were applied in conjunction with zwitterionic thiol ligands to coat 2 nm Au NPs. Particle exposition to UV-Vis yielded photoregulated release of fluoroacil (5-FU) linked to photoresponsive *o*-nitrobenzyl on NPs capping.[53] Biologically active Au and Ag NPs were reported using heparin and hyaluronan as reducing and stabilising agents. NPs functionalised with 2,6-diaminopyridinyl heparin enabled anticoagulant and anti-inflammatory properties yet allowing further functionalisation.[54]

Synthesis of water soluble Au NPs of 18 nm has been reported using folic acid as reducing and stabilising agent.[55] The one-pot green synthesis in the presence of chitosan allowed Au NPs to be tuneable in size and morphology depending on the reaction temperature.[56] In the presence of OLA it was possible to obtain the Au NPs of 2, 11 or 13 nm with different $HAuCl_4$ concentration.[57] The stability of the OLA/Au intermediate complex was investigated.[58] A similar approach was attempted in the presence of polyvinylpyrrolidone (PVP); however, NaOH was needed as reduction initiator. The size varied from 6.8 to 16.5 nm depending on the $HAuCl_4$: PVP ratio.[59] Photocatalytic reduction of Au salts in the presence of visible light promoted the formation of 8 nm Au NPs capped with PVP in presence of a tin(IV) electron donor complex and a source of long-lived radical ions. This method was also applied to the synthesis of 5 nm Ag NPs.[60] Water soluble Au and Ag NPs were achieved using an imidazol based polymer, constituted by 2,4,6-tris(bromomethyl)mesitylene and 1,4-dibromo-2,3-butanediol as monomers for the inverse microemulsion polymerisation. This method was also used for the stabilisation of semiconductor NPs.[61]

Femtosecond laser-based ablation and seed growth was used as an alternative synthetic method for Au NPs. The size of the NPs was varied by the concentration and nature of the present biopolymer within the solution synthesis. Chitosan, α,ω-dithiol poly(*N*-isopropylacrylamide), PEG and dextran were used in order to obtain a variety of functionalised NPs with different moieties.[62] The nature of the buffer in Au NPs synthesis has been found to have an impact on particle growth. Depending upon a reducing buffer (*e.g.* 4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid (HEPES)) or a non-reducing buffer (*e.g.* borate buffer), the growth of NPs could be controlled and separated from the nucleation steps.[63]

New approaches in Au NP synthesis have focused on the utilisation of reagents extracted from natural sources. Starch from potatoes or carrots was reported as a suitable biocompatible stabilising agent using glucose as reducing agent to obtain 4 nm Au NPs. Size and colloidal stability was highly dependent on the starch concentration.[64] Starch has also been extracted from *Cinnamomum zeylanicum* leaf broth. Terpenoids and sugars contained in leaf broth were believed to induce particle reduction. Particle morphology was dependent on the concentration of the broth leaf extract containing the reducing agent, leading to a mixture of Au nanoprisms and spheres at lower concentrations whereas predominantly spherical particles were obtained at high concentration.[65] Similar morphologies were found when *Magnolia kobus* and *Diopyros kaki* leaf extracts were used for the reduction of Au NPs and the NPs conversion was above 90%.[66] Apigenin-7-apiosyl-glucoside (apiin) extracted from Henna leaves was used as reducing and stabilising agent for the synthesis of the Ag and Au NPs. The obtained particle morphology was dependent on appin concentration leading to nanoprisms at low concentration and spherical particles when concentration was increased.[67]

Noble metal NPs have been synthesised *in situ* on the membrane of a variety of micro organisms. Au NPs were synthesised *in situ* on the *R. oryzae Mycelia* cell membrane from $HAuCl_4$ at pH = 3 in the presence of potato dextrose.[68] Ag NPs were obtained by microbial reduction using *Bacillus sp*[69] and *Alternaria alternata* fungus[70] from $AgNO_3$. Incubation of $AgNO_3$ solution with *Fusarium solani*, an aerobic fungus, yielded 16 nm Ag NPs. Colloidal stability was reported to be achieved by conjugation with amide moieties from the fungal extract.[71]

Green chemistry synthesis and antimicrobial properties of Ag NPs were reviewed.[72] Green synthesis of Ag and Au NPs by microwave heating in the presence

of mung bean starch vermicelli as the template was reported and the helical conformation present by the starch allowed size and shape control.[73] Chemical reduction with sodium ascorbate and photocatalytic reduction of $AgNO_3$ was carried out in the presence of a peptide library. Generation of the NPs was performed with a split-and-mix peptide library in order to identify those peptides that induced Ag NP generation.[74] Polyphenols and flavonoids from black tea leaf extract were used for the green chemistry reduction synthesis of 20 nm Au and Ag NPs from $HAuCl_4$ and $AgNO_3$.[75] *Bryophyllum*, *Cyperus* and *Hydrilla* plant extracts were alternatively used for the reduction synthesis of Ag NPs from $AgNO_3$ under mild heating conditions of 40 °C. Reduction of silver ions is known to happen due to reaction with metabolites such as quinones or catechol/protocatacheuic acid; however, the exact cause of NP formation is unknown.[76] Leaf extract from pine, magnolia, persimmon, ginkgo and platanus were successfully used as reducing agents for $AgNO_3$ under heat treatment at 95 °C to yield high conversion.[77] Latex extracted from *Jatropha curcas* was found to enable high colloidal stability when used as reducing and stabilising agent.[78] Ag NPs were obtained from silver nitrate using quercetin-3-rutinoside (rutin), a citrus flavonoid glycoside, as reducing and stabilising agent. The obtained flower-like shaped NPs were readily soluble in water. Particle shape and morphology was found to be dependent on rutin : Ag ratio.[79] Desert rose-like shaped structure was observed for Ag NPs when enzymatic reduction with horseradish peroxidase was carried out.[80] Ag NPs were prepared from a silver acetate precursor by lysozyme enzymatic reduction in methanol, acting as reducing and nucleating agent. Moreover, lysozyme acted as a capping agent to stabilise the colloidal suspension and limit agglomeration.[81]

Non-capped Ag NPs were obtained by direct thermal decomposition of an acetate precursor under Ar atmosphere. Colloidal stability was maintained by the negatively charged surface due to the presence of residual hydroxyl groups.[82] Ketyl radicals generated under UV light from 1-[4-(2-hydroxyethoxy)phenyl]-2-hydroxy-2-methyl-1-propan-1-one (I-2959) enable rapid generation of 3.4 nm Ag NPs. Hexadecylamine capped Ag NPs stable in toluene gave high fluorescence while having lower toxicity than the conventially used QDs.[83] Biotinylated Ag-dendrimer nanocomposite was obtained by $NaBH_4$ reduction from a silver nitrate solution in the presence of the biotinylated functionalised poly(amidoamine) (PAMAM) dendrimers. When a PEG spacer was added to the biotin moiety, a higher degree of Ag NP aggregation was observed.[84] Chitosan coated Ag NPs could be alternatively obtained by γ-ray irradiation for the photocatalytic reduction of $AgNO_3$ in the presence of an acetic acid chitosan solution. NPs size was found to be affected by γ-ray intensity and exposition time.[85]

Ag/Au alloy NPs were obtained by solvothermal synthesis in the presence of OLA as reducing agent and stabilising surfactant. The NPs were obtained by metal diffusion from an initial Ag/Au core–shell structure, generated by Au deposition onto 13 nm Ag NPs.[86] When using sodium citrate as reducing agent and stabilising capping, 25 nm Ag/Au alloy NPs were obtained through a one-step reduction synthesis.[87]

Pd NPs have been obtained using a thermal and chemically stable protein extracted from *populous tremula* plant as template. The template is not affected after NPs deposition therefore it can undergo further biofunctionalisation for site-specific targeting.[88] Synthesis of phthalocyanine stabilised Rh NPs was carried out for the biosensing of cytochrome C. Rh NPs were obtained by reduction with $NaBH_4$ from the halogen precursor in dimethyl sulfoxide.[89]

4. Semiconductor nanoparticles

Synthesis and functionalisation of semiconductor QDs and their biomedical applications have been reviewed.[90,91] Thereafter, open air synthesis of 3-mercaptopropionic acid (MPA) functionalised CdSe QDs was reported using a hydrazine hydrate–Se complex as a source of highly reactive selenium ions; subsequently, further reaction with the cadmium present in solution occurred. The resulting water soluble, air stable particles enabled a maximum 40% quantum yield (QY).[92] A green approach for the synthesis of CdSe QDs has been reported using *N*,*N*-dimethyloleoyl amide as an alternative to replace trioctylphoshine (TOP) for Se powder solution, using OA as primary capping ligand, and benzophenone as secondary ligand.[93] Microwave-assisted synthesis of OA–CdSe QDs was carried out with diesel as an alternative solvent.[94] Water solubility of tri-*n*-octylamine and OA coated CdSeS QDs was achieved by a two step phase-transfer of sodiumdodecyl sulphate and *n*-octyltrimethoxysilane leading to the formation of a thin 0.3–0.4 nm silica shell. The obtained 4.4 nm particles showed water solubility and a maximum 49% QY.[95] Control over particle size and photoluminescence efficiency within CdSe and CdTe QDs was reported when working under supersaturation conditions.[96]

Improvement of the synthetic methods used for CdTe and its derivatives has drawn great interest. Glutathione (GSH) and thioglycolic acid cadmium complex in aqueous solution was used as a Cd source. Water soluble 2–3 nm CdTe QDs were generated under mild heating conditions with up to 63% QY. The presence of carboxylic acid and amino moieties on the capping surface permitted further functionalisation.[97] Silica embedded into CdTe QDs was applied to promote water solubility by a reverse microemulsion method, using TEOS as the silica source.[98] GSH was reported as stabiliser and sulphur source for the one-pot synthesis of CdTe/CdSe QDs. Mild heat treatment after the synthesis of the CdTe core led to partial hydrolysis of GSH, increasing the efficiency of CdSe shell formation and giving a final 3 nm particle size with up to 83% QY.[99] Amphiphilic CdTe QDs were directly obtained by *in situ* capping with thiolated methoxypolyethylene glycol. QDs were readily recovered in water from toluene by phase-transfer, needless of surface modification, and thereafter transferred to chloroform thus showing promising applications for cross cell membrane transport.[100] Amphiphilic thermoresponsive CdTe QDs were obtained by functionalisation with PDMAEMA *via* direct surface-initiated oxyanionic vinyl polymerisation. The obtained QDs were further functionalised by adhesion onto silica nanospheres by a layer-by-layer approach with sodium polyacrylate. Fluorescent properties were nonetheless inferior.[101] *N*-acetyl-L-cysteine was used as stabiliser for the hydrothermal synthesis of 4.3 and 5.3 nm water soluble CdTe/CdSe QDs (maximum 62% QY) using $NaBH_4$ as reducing agent.[102] Cysteine was used as a stabiliser for the aqueous phase synthesis of CdTe/ZnTe QDs. The use of cadmium and tellurium perchlorate reagents resulted in the generation of 3–5 nm QDs with QY of 52%.[103] $[Zn(NH_3)_4]Cl_2$ has been reported as an alternative zinc precursor over conventionally used zinc perchlorate for the synthesis of water soluble CdSe/ZnS stabilised with MPA.[104]

Water soluble CdTeSe QDs one-pot synthesis was achieved by consequential injection of the reagents under oxygen free conditions. A L-cysteine (thiol) capping ligand was added as an initial reagent.[105] One-pot synthesis of water soluble ZnCdSe QDs stabilised with MPA was achieved using $Cd(ClO_4)_2$ and $Zn(ClO_4)_2$ with NaHSe as precursors leading to emission of white light.[106] The conventionally used cadmium carboxylate precursor was substituted by cadmium tetradecylphosphonic

acid ($Cd(TDPA)_2$) giving higher control over particle size for the synthesis of TOP and OA stabilised CdTeSe/CdZnS. A maximum QY of 20% was found after PEG encapsulation.[107] One-pot synthesis of CdTe/CdS/ZnS was reported from the initial formation of CdTe core. CdS was formed by addition of thiourea as sulphur precursor in excess that later on reacted with the zinc precursor to form the ZnS shell.[108] Water dispersability of highly luminescent near infrared-emitting QDs developed through constructing CdTe/CdSe/ZnS nanostructure was achieved by ligand exchange with MPA.[109]

MPA was used as stabiliser for the nucleation-doping synthetic method in aqueous solution of 4 nm Mn : ZnSe QDs. Manganese-doped particles were believed to yield higher photostability due to the protection that the ZnSe shell offers to the QD core against UV photobleaching.[110] Dihydrolipoic acid (DHLA), a non-toxic biocompatible capping agent, was used as stabiliser for the synthesis of 2.3–4 nm water soluble PbS QDs.[111] DHLA and DHLA-PEG*n* have been applied as capping agents for the synthesis of 3.2 nm InAs/ZnS QDs with up to 20% QY.[112] Facile room temperature synthesis of water soluble 4 nm SnS near-infrared QDs was reported.[113] The NPs were synthesised in solution using ionic starting materials $SnBr_2$ and Na_2S in the presence of ethanolamines with three (triethanolamine), two (*N*-methyldiethanolamine), or one hydroxyl group (*N*,*N*-dimethylethanolamine) in ethylene glycol.

Silicon QDs have been reported as alternative non-toxic high photoluminescent NPs. Si–NPs of 13 nm and a 1–2 nm oxide shell were obtained by microwave plasma synthesis following pyrolysis of silane with posterior acid etching. Further functionalisation of these NPs with alkenes was then induced.[114]

QD composites have also been reported using particle loading within a polymeric structure. Two copolymers of poly(lactide)-vitamin E TPGS (PLA-TPGS) and vitamin E TPGS-carboxyl (TPGS-COOH) were synthesised. These were blended at various weight ratios to make QD-loaded NPs decorated with folate for targeted and sustained imaging.[115]

NPs of semiconductor ZnO and TiO_2 also have interesting applications within the biomedical field. Synthesis of TiO_2 NPs has a great interest for biomedical applications due their known antibacterial properties.[116] Biosynthesis of TiO_2 NPs was carried out using *lactobacillus sp.* and *Sachharomyces cerevisae*. Synthesis was believed to be a consequence of the oxido-reductases found on the cell membrane.[117]

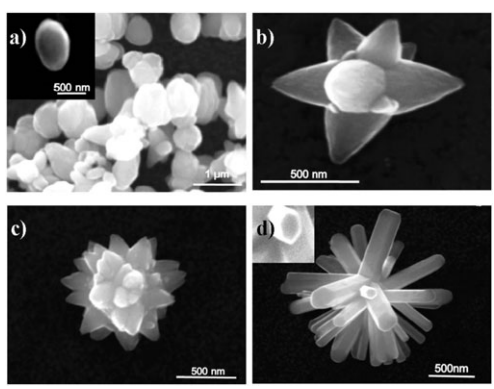

Fig. 5 TEM images of ZnO NPs synthesised under different concentration of NaOH (a) 0.175 M, (b) 0.3 M, (c) 0.5 M, (d) 4 M.[121]

Bio-templated synthesis of ordered mesoporous TiO_2 NPs was achieved on the cell membrane of yeast cells. The accumulation of NPs on the surface was related to the electrostatic attraction between the negatively charged cell surface and the positively charged titanium ions.[118]

One-pot polyol hydrolysis method was reported for the synthesis of water soluble ZnO for cell labelling applications.[119] Synthesis of ZnO from zinc acetate precursor *via* a precipitation synthetic method lead to positively charged ZnO NPs. These were studied for their potential application for DNA biosensors as a result of the electrostatic interaction between the positively charged NPs and the negatively charged DNA chain.[120] Polyaniline coated Au (Au/PANI) NPs were used as seeds for the growth of ZnO NPs in the presence of PVP as coating agent. NP morphology was dependent upon NaOH concentration leading to a variety of nanostructures (Fig. 5).[121]

5. Multimodal or composite nanoparticles

Multimodal or composite NPs present a combination of functionalities or building blocks that enable them to be analysed by different techniques yet enhancing their detection sensitivity and broadening the field of application. The biomedical applications of multimodal NPs have been reviewed.[122–124] Reductive decomposition of $Au(O_2CCH_3)$ in the presence of OLA and surfactants was carried out with FePt NPs leading to 10 nm FePt/Au core–shell NPs with a saturation magnetisation of 15 emu g^{-1}. Water dispersability was achieved by 11-mercaptoundecanoic acid coating.[125] The combination of Au NPs with magnetic entities has also been attempted by formation of dumbbell-like structures. Such structures could be used as both magnetic and optical probes. 8 nm/18 nm Au–Fe_3O_4 complex NPs were functionalised by ligand exchange from OA/OLA to dopamine and thiol linked surfactants. The pH-dependent release of cisplatin was achieved by a pH-sensitive thiol anchored ligand to the Au entity.[126] Immuno–Fe_2O_3/Au NPs for bioseparation were achieved by incubation of the antihuman immunoglobulin G (IgG) with borate buffer and blocked with bovine serum albumin.[127] Au-shell magnetite NPs were obtained by initial synthesis of $Fe(OH)_2$ cubic NPs in the presence of polyethyleneimine (PEI) as stabilising agent. An Au shell was incorporated by initial reduction with $NaBH_4$. The subsequent Au shells were grown by iterative reduction of Au onto Au–PEI-coated magnetite NPs.[128] Catalytic growth of a nickel shell onto Au NPs was reported to yield thermoresponsive NPs that enable both optical and magnetic detection. The Au core was obtained by a seeded growth method upon diffusion through poly(*N*-isopropylacrylamide) shell. Ni/NiO shell was obtained by Ni Pt-catalysed reduction in the presence of hydrazine.[129] Raspberry-like hierarchical Au/Pt NPs were obtained by a three step synthetic approach involving the initial synthesis of TiO_2 spheres, followed by Au deposition by interaction with the amino functionalised NPs. Thereafter, heat treatment in the presence of H_2PtCl_6 as Pt precursor and ascorbic acid as reducing agent was carried out.[130] DNA functionalised 13 nm Au NPs were conjugated with Gd chelates as a new platform for magnetic resonance imaging. Click chemistry was employed for the incorporation of Gd to thiol modified DNA strands that were thereafter conjugated to Au NPs.[131]

Multimodal probes based on QDs and magnetic NPs have also been investigated. A pH sensitive CdS–iron oxide fluorescent–magnetic nanocomposite was achieved by reaction of Cd : Fe (10 : 1) and 3-mercaptopropyltrimethoxysilane (MPS) (MPS : Fe, 1 : 1) under acidic conditions (pH = 2). The 200–500 nm nanocomposite

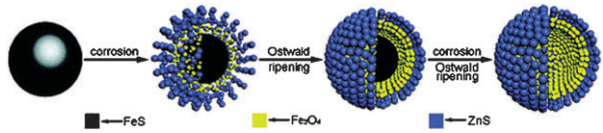

Fig. 6 Formation of Fe_3O_4/ZnS hollow nanospheres.[134]

presented a maximum QY of 20% and saturation magnetisation of 55 emu g^{-1}.[132] Sequential co-precipitation from iron chloride salts on Re sulfide NPs yielded ReS_2/Fe_3O_4 NPs.[133] *Corrosion-aided* Ostwald ripening was utilised to obtain 97 nm superparamagnetic fluorescent Fe_3O_4/ZnS hollow NPs. FeS NPs were used as source of iron and sulphur for shell growing in the presence of zincacetylacetonate and PVP. The obtained water soluble hollow NPs presented a maximum QY of 13% (Fig. 6).[134]

Hybrid magnetite-silica-NiO superstructure was obtained by initial growth of silica coating onto magnetite NPs, followed by conjugation of NiO NPs by incubation of NiO NPs functionalised with (3-aminopropyl)-trimethoxylsilane (APTMS) with the amino functionalised silica coated magnetite NPs. Water solubility was achieved by APTMS calcination and PEG conjugation.[135] Multifunctional core–shell magnetite NPs with a terbium doped silica coating were obtained as a simultaneous magnetic and optical probe. Terbium was incorporated into the silica shell *via* chelation by the presence carboxylic groups within the silane precursor.[136]

6. Conclusions

Great efforts have been made for the incorporation of biomolecules into the synthesis of NPs to increase their colloidal stability in biological media and to enable specific targeting. Work has been done to improve particle coating in order to reduce their toxicity while avoiding the reduction of their physical properties such as magnetization and quantum yield, among others. Current achievements in this field, although promising, need further work to fully harness the potential of NPs for biomedical applications and to enable their incorporation into clinical practice.

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References

1 Q. A. Pankhurst, N. K. T. Thanh, S. K. Jones and J. Dobson, *J. Phys. D: Appl. Phys.*, 2009, **42**, 224001.
2 G. Goloverda, B. Jackson, C. Kidd and V. Kolesnichenko, *J. Magn. Magn. Mater.*, 2009, **321**, 1372.
3 C. J. Chen, H. Y. Lai, C. C. Lin, J. S. Wang and R. K. Chiang, *Nanoscale Res. Lett.*, 2009, **4**, 1343.
4 K. Sue, H. Hattori, T. Sato, T. Komoriya, A. Kawai-Nakamura, S. Tanaka, T. Hiaki, S. Kawasaki, Y. Takebayashi, S. Yoda and T. Furuya, *Chem. Lett.*, 2009, **38**, 792.
5 Z. J. Wang, H. Zhu, X. L. Wang, F. Yang and X. R. Yang, *Nanotechnology*, 2009, **20**, 465606.
6 D. Maity, S. N. Kale, R. Kaul-Ghanekar, J. M. Xue and J. Ding, *J. Magn. Magn. Mater.*, 2009, **321**, 3093.

7 D. Ung, L. D. Tung, G. Caruntu, D. Delaportas, I. Alexandrou, I. A. Prior and N. T. K. Thanh, *CrystEngComm*, 2009, **11**, 1309.
8 K. Kluchova, R. Zboril, J. Tucek, M. Pecova, L. Zajoncova, I. Safarik, M. Mashlan, I. Markova, D. Jancik, M. Sebela, H. Bartonkova, V. Bellesi, P. Novak and D. Petridis, *Biomaterials*, 2009, **30**, 2855.
9 L. L. Zhou, J. Y. Yuan, W. Z. Yuan, X. F. Sui, S. Z. Wu, Z. L. Li and D. Z. Shen, *J. Magn. Magn. Mater*., 2009, **321**, 2799.
10 I. Robinson, C. Alexander, L. D. Tung, D. G. Fernig and N. T. K. Thanh, *J. Magn. Magn. Mater*., 2009, **321**, 1421.
11 C. M. Cheng, Y. H. Wen, X. F. Xu and H. C. Gu, *J. Mater. Chem*., 2009, **19**, 8782.
12 R. Sondjaja, T. A. Hatton and M. K. C. Tam, *J. Magn. Magn. Mater*., 2009, **321**, 2393.
13 C. M. Cheng, G. Kou, X. L. Wang, S. H. Wang, H. C. Gu and Y. J. Guo, *J. Magn. Magn. Mater*., 2009, **321**, 2663.
14 M. Latorre-Esteves, A. Cortes, M. Torres-Lugo and C. Rinaldi, *J. Magn. Magn. Mater*., 2009, **321**, 3061.
15 S. Adireddy, C. K. Lin, V. Palshin, Y. M. Dong, R. Cole and G. Caruntu, *J. Phys. Chem. C*, 2009, **113**, 20800.
16 L. Maurizi, H. Bisht, F. Bouyer and N. Millot, *Langmuir*, 2009, **25**, 8857.
17 A. Gorschinski, G. Khelashvili, D. Schild, W. Habicht, R. Brand, M. Ghafari, H. Bonnemann, E. Dinjus and S. Behrens, *J. Mater. Chem*., 2009, **19**, 8829.
18 S. Buathong, D. Ung, T. J. Daou, C. Ulhaq-Bouillet, G. Pourroy, D. Guillon, L. Ivanova, I. Bernhardt, S. Begin-Colin and B. Donnio, *J. Phys. Chem. C*, 2009, **113**, 12201.
19 M. Brzozowska and P. Krysinski, *Electrochim. Acta*, 2009, **54**, 5065.
20 W. C. Miles, J. D. Goff, P. P. Huffstetler, C. M. Reinholz, N. Pothayee, B. L. Caba, J. S. Boyd, R. A. Davis and J. S. Riffle, *Langmuir*, 2009, **25**, 803.
21 L. Z. Zhu, J. W. Ma, N. Q. Jia, Y. Zhao and H. B. Shen, *Colloids Surf., B*, 2009, **68**, 1.
22 S. J. Guo, D. Li, L. M. Zhang, J. Li and E. K. Wang, *Biomaterials*, 2009, **30**, 1881.
23 A. A. El-Gendy, E. M. M. Ibrahim, V. O. Khavrus, Y. Krupskaya, S. Hampel, A. Leonhardt, B. Buchner and R. Klingeler, *Carbon*, 2009, **47**, 2821.
24 S. M. Zhu, D. Zhang, Z. X. Chen and Y. M. Zhang, *J. Mater. Chem*., 2009, **19**, 7710.
25 H. Lee, T. J. Yoon and R. Weissleder, *Angew. Chem., Int. Ed*., 2009, **48**, 5657.
26 J. F. Bondi, K. D. Oyler, X. L. Ke, P. Schiffer and R. E. Schaak, *J. Am. Chem. Soc*., 2009, **131**, 9144.
27 K. An and T. Hyeon, *Nano Today*, 2009, **4**, 359.
28 Q. Zhang, W. S. Wang, J. Goebl and Y. D. Yin, *Nano Today*, 2009, **4**, 494.
29 H. B. Xia, P. Foo and J. B. Yi, *Chem. Mater*., 2009, **21**, 2442.
30 C. L. Jiang and Y. F. Wang, *Mater. Chem. Phys*., 2009, **113**, 531.
31 T. L. Lu, L. D. Tung, J. Long, D. G. Fernig and N. T. K. Thanh, *J. Mater. Chem*., 2009, **19**, 6023.
32 J. M. Shin, R. M. Anisur, M. K. Ko, G. H. Im, J. H. Lee and I. S. Lee, *Angew. Chem., Int. Ed*., 2009, **48**, 321.
33 K. Cheng, S. Peng, C. J. Xu and S. Sun, *J. Am. Chem. Soc*., 2009, **131**, 10637.
34 F. R. Li, W. H. Yan, Y. H. Guo, H. Qi and H. X. Zhou, *Int. J. Hyperthermia*, 2009, **25**, 383.
35 S. H. Liu, R. M. Xing, F. Lu, R. K. Rana and J. J. Zhu, *J. Phys. Chem. C*, 2009, **113**, 21042.
36 N. N. Guan, Y. T. Wang, D. J. Sun and J. Xu, *Nanotechnology*, 2009, **20**, 105603.
37 J. Huang, W. M. Chen, W. Zhao, Y. Q. Li, X. G. Li and C. P. Chen, *J. Phys. Chem. C*, 2009, **113**, 12067.
38 S. C. Luo, J. Jiang, S. S. Liour, S. J. Gao, J. Y. Ying and H. H. Yu, *Chem. Commun*., 2009, 2664.
39 L. B. Chen, F. Zhang and C. C. Wang, *Small*, 2009, **5**, 621.
40 S. Utech, C. Scherer and M. Maskos, *J. Magn. Magn. Mater*., 2009, **321**, 1386.
41 F. Yan, J. Li, J. J. Zhang, F. Q. Liu and W. S. Yang, *J. Nanopart. Res*., 2009, **11**, 289.
42 G. Y. Liu, H. Wang and X. L. Yang, *Polymer*, 2009, **50**, 2578.
43 S. Hatamie, S. D. Dhole, J. Ding and S. N. Kale, *J. Magn. Magn. Mater*., 2009, **321**, 2135.
44 J. Yang and J. Y. Ying, *Nat. Mater*., 2009, **8**, 683.
45 E. Boisselier and D. Astruc, *Chem. Soc. Rev*., 2009, **38**, 1759.
46 S. D. Perrault and W. C. W. Chan, *J. Am. Chem. Soc*., 2009, **131**, 17042.
47 C. Boyer, M. R. Whittaker, M. Luzon and T. P. Davis, *Macromolecules*, 2009, **42**, 6917.
48 J. Y. Kim and J. S. Lee, *Nano Lett*., 2009, **9**, 4564.

49 J. Nam, N. Won, H. Jin, H. Chung and S. Kim, *J. Am. Chem. Soc.*, 2009, **131**, 13639.
50 C. P. Chak, S. H. Xuan, P. M. Mendes, J. C. Yu, C. H. K. Cheng and K. C. F. Leung, *ACS Nano*, 2009, **3**, 2129.
51 V. Kozlovskaya, E. Kharlampieva, S. Chang, R. Muhlbauer and V. V. Tsukruk, *Chem. Mater.*, 2009, **21**, 2158.
52 C. K. Kim, P. Ghosh, C. Pagliuca, Z.-J. Zhu, S. Menichetti and V. M. Rotello, *J. Am. Chem. Soc.*, 2009, **131**, 1360.
53 S. S. Agasti, A. Chompoosor, C. C. You, P. Ghosh, C. K. Kim and V. M. Rotello, *J. Am. Chem. Soc.*, 2009, **131**, 5728.
54 M. M. Kemp, A. Kumar, S. Mousa, T. J. Park, P. Ajayan, N. Kubotera, S. A. Mousa and R. J. Linhardt, *Biomacromolecules*, 2009, **10**, 589.
55 G. P. Li, D. Li, L. X. Zhang, J. F. Zhai and E. K. Wang, *Chem.-Eur. J.*, 2009, **15**, 9868.
56 M. Potara, D. Maniu and S. Astilean, *Nanotechnology*, 2009, **20**, 315602.
57 L. Polavarapu and Q. H. Xu, *Nanotechnology*, 2009, **20**, 185606.
58 A. Kisner, S. Lenk, D. Mayer, Y. Mourzina and A. Offenhausser, *J. Phys. Chem. C*, 2009, **113**, 20143.
59 M. Zhou, B. X. Wang, Z. Rozynek, Z. H. Xie, J. O. Fossum, X. F. Yu and S. Raaen, *Nanotechnology*, 2009, **20**, 505606.
60 P. Quaresma, L. Soares, L. Contar, A. Miranda, I. Osorio, P. A. Carvalho, R. Franco and E. Pereira, *Green Chem.*, 2009, **11**, 1889.
61 N. R. Jana, P. K. Patra, A. Saha, S. K. Basiruddin and N. Pradhan, *J. Phys. Chem. C*, 2009, **113**, 21484.
62 S. Besner, A. V. Kabashin, F. M. Winnik and M. Meunier, *J. Phys. Chem. C*, 2009, **113**, 9526.
63 S. Diamanti, A. Elsen, R. Naik and R. Vaia, *J. Phys. Chem. C*, 2009, **113**, 9993.
64 C. Engelbrekt, K. H. Sorensen, J. D. Zhang, A. C. Welinder, P. S. Jensen and J. Ulstrup, *J. Mater. Chem.*, 2009, **19**, 7839.
65 S. L. Smitha, D. Philip and K. G. Gopchandran, *Spectrochim. Acta, Part A*, 2009, **74**, 735.
66 J. Y. Song, H. K. Jang and B. S. Kim, *Process Biochem.*, 2009, **44**, 1133.
67 J. Kasthuri, S. Veerapandian and N. Rajendiran, *Colloids Surf., B*, 2009, **68**, 55.
68 S. K. Das, A. R. Das and A. K. Guha, *Langmuir*, 2009, **25**, 8192.
69 N. Pugazhenthiran, S. Anandan, G. Kathiravan, N. K. U. Prakash, S. Crawford and M. Ashokkumar, *J. Nanopart. Res.*, 2009, **11**, 1811.
70 M. Gajbhiye, J. Kesharwani, A. Ingle, A. Gade and M. Rai, *Nanomed.: Nanotechnol., Biol. Med.*, 2009, **5**, 382.
71 A. Ingle, M. Rai, A. Gade and M. Bawaskar, *J. Nanopart. Res.*, 2009, **11**, 2079.
72 V. K. Sharma, R. A. Yngard and Y. Lin, *Adv. Colloid Interface Sci.*, 2009, **145**, 83.
73 S. Chairam, C. Poolperm and E. Somsook, *Carbohydr. Polym.*, 2009, **75**, 694.
74 K. Belser, T. V. Slenters, C. Pfumbidzai, G. Upert, L. Mirolo, K. M. Fromm and H. Wennemers, *Angew. Chem., Int. Ed.*, 2009, **48**, 3661.
75 A. V. Singh, R. Patil, M. B. Kasture, W. N. Gade and B. L. V. Prasad, *Colloids Surf., B*, 2009, **69**, 239.
76 A. K. Jha, K. Prasad and A. R. Kulkarni, *Colloids Surf., B*, 2009, **73**, 219.
77 J. Y. Song and B. S. Kim, *Bioprocess Biosyst. Eng.*, 2009, **32**, 79.
78 H. Bar, D. K. Bhui, G. R. Sahoo, P. Sarkar, S. R. De and A. Misra, *Colloids Surf., A*, 2009, **339**, 134.
79 B. K. Jena, B. K. Mishra and S. Bohidar, *J. Phys. Chem. C*, 2009, **113**, 14753.
80 T. Schuler, A. Steinbruck, G. Festag, R. Moller and W. Fritzsche, *J. Nanopart. Res.*, 2009, **11**, 939.
81 D. M. Eby, N. M. Schaeublin, K. E. Farrington, S. M. Hussain and G. R. Johnson, *ACS Nano*, 2009, **3**, 984.
82 S. Giuffrida, G. Ventimiglia and S. Sortino, *Chem. Commun.*, 2009, 4055.
83 L. Maretti, P. S. Billone, Y. Liu and J. C. Scaiano, *J. Am. Chem. Soc.*, 2009, **131**, 13972.
84 J. Maly, H. Lampova, A. Semeradtova, M. Stofik and L. Kovacik, *Nanotechnology*, 2009, **20**, 385101.
85 R. Yoksan and S. Chirachanchai, *Mater. Chem. Phys.*, 2009, **115**, 296.
86 C. Wang, S. Peng, R. Chan and S. H. Sun, *Small*, 2009, **5**, 567.
87 A. Pal, S. Shah, V. Kulkarni, R. S. R. Murthy and S. Devi, *Mater. Chem. Phys.*, 2009, **113**, 276.

88 S. Behrens, A. Heyman, R. Maul, S. Essig, S. Steigerwald, A. Quintilla, W. Wenzel, J. Burck, O. Dgany and O. Shoseyov, *Adv. Mater.*, 2009, **21**, 3515.
89 K. S. Lokesh, Y. Shivaraj, B. P. Dayananda and S. Chandra, *Bioelectrochemistry*, 2009, **75**, 104.
90 N. Tomczak, D. Janczewski, M. Y. Han and G. J. Vancso, *Prog. Polym. Sci.*, 2009, **34**, 393.
91 S. F. Lee and M. A. Osborne, *ChemPhysChem*, 2009, **10**, 2174.
92 M. N. Kalasad, A. K. Rabinal and B. G. Mulimani, *Langmuir*, 2009, **25**, 12729.
93 C. Wang, Y. Jiang, L. L. Chen, S. Y. Li, G. H. Li and Z. P. Zhang, *Mater. Chem. Phys.*, 2009, **116**, 388.
94 M. Q. Zhu, Z. Gu, J. B. Fan, X. B. Xu, J. Cui, J. H. Liu and F. Long, *Langmuir*, 2009, **25**, 10189.
95 R. C. Han, M. Yu, Q. Zheng, L. J. Wang, Y. K. Hong and Y. L. Sha, *Langmuir*, 2009, **25**, 12250.
96 A. Priyam, S. Ghosh, S. C. Bhattachcarya and A. Saha, *J. Colloid Interface Sci.*, 2009, **333**, 195.
97 J. N. Tian, R. J. Liu, Y. C. Zhao, Q. Xu and S. L. Zhao, *J. Colloid Interface Sci.*, 2009, **336**, 504.
98 C. Wang, Q. Ma, W. C. Dou, S. Kanwal, G. N. Wang, P. F. Yuan and X. G. Su, *Talanta*, 2009, **77**, 1358.
99 Y. F. Liu and J. S. Yu, *J. Colloid Interface Sci.*, 2009, **333**, 690.
100 A. Dubavik, V. Lesnyak, W. Thiessen, N. Gaponik, T. Wolff and A. Eychmuller, *J. Phys. Chem. C*, 2009, **113**, 4748.
101 L. Zhou, C. Gao and W. J. Xu, *J. Mater. Chem.*, 2009, **19**, 5655.
102 D. Zhao, Z. K. He, W. H. Chan and M. M. F. Choi, *J. Phys. Chem. C*, 2009, **113**, 1293.
103 W. C. Law, K. T. Yong, I. Roy, H. Ding, R. Hu, W. W. Zhao and P. N. Prasad, *Small*, 2009, **5**, 1302.
104 W. Schumacher, A. Nagy, W. J. Waldman and P. K. Dutta, *J. Phys. Chem. C*, 2009, **113**, 12132.
105 G. X. Liang, M. M. Gu, J. R. Zhang and J. J. Zhu, *Nanotechnology*, 2009, **20**, 415103.
106 C. C. Shen and W. L. Tseng, *Inorg. Chem.*, 2009, **48**, 8689.
107 T. Pons, N. Lequeux, B. Mahler, S. Sasnouski, A. Fragola and B. Dubertret, *Chem. Mater.*, 2009, **21**, 1418.
108 M. Green, P. Williamson, M. Samalova, J. Davis, S. Brovelli, P. Dobson and F. Cacialli, *J. Mater. Chem.*, 2009, **19**, 8341.
109 W. J. Zhang, G. J. Chen, J. Wang, B. C. Ye and X. H. Zhong, *Inorg. Chem.*, 2009, **48**, 9723.
110 C. Wang, X. Gao, Q. Ma and X. G. Su, *J. Mater. Chem.*, 2009, **19**, 7016.
111 D. W. Deng, W. H. Zhang, X. Y. Chen, F. Liu, J. Zhang, Y. Q. Gu and J. M. Hong, *Eur. J. Inorg. Chem.*, 2009, 3440.
112 H. S. Choi, B. I. Ipe, P. Misra, J. H. Lee, M. G. Bawendi and J. V. Frangioni, *Nano Lett.*, 2009, **9**, 2354.
113 Y. Xu, N. Al-Salim, C. W. Bumby and R. D. Tilley, *J. Am. Chem. Soc.*, 2009, **131**, 15990.
114 A. Gupta, M. T. Swihart and H. Wiggers, *Adv. Funct. Mater.*, 2009, **19**, 696.
115 J. Pan and S. S. Feng, *Biomaterials*, 2009, **30**, 1176.
116 F. R. Marciano, D. A. Lima-Oliveira, N. S. Da-Silva, A. V. Diniz, E. J. Corat and V. J. Trava-Airoldi, *J. Colloid Interface Sci.*, 2009, **340**, 87.
117 A. K. Jha, K. Prasad and A. R. Kulkarni, *Colloids Surf., B*, 2009, **71**, 226.
118 J. J. Cui, W. He, H. T. Liu, S. J. Liao and Y. Z. Yue, *Colloids Surf., B*, 2009, **74**, 274.
119 X. S. Tang, E. S. G. Choo, L. Li, J. Ding and J. M. Xue, *Langmuir*, 2009, **25**, 5271.
120 R. Wahab, Y. S. Kim, I. H. Hwang and H. S. Shin, *Synth. Met.*, 2009, **159**, 2443.
121 D. Krishnan and T. Pradeep, *J. Cryst. Growth*, 2009, **311**, 3889.
122 C. Fang and M. Q. Zhang, *J. Mater. Chem.*, 2009, **19**, 6258.
123 J. H. Gao, H. W. Gu and B. Xu, *Acc. Chem. Res.*, 2009, **42**, 1097.
124 L. E. Jennings and N. J. Long, *Chem. Commun.*, 2009, 3511.
125 K. Yano, V. Nandwana, G. S. Chaubey, N. Poudyal, S. Kang, H. Arami, J. Griffis and J. P. Liu, *J. Phys. Chem. C*, 2009, **113**, 13088.
126 C. J. Xu, B. D. Wang and S. H. Sun, *J. Am. Chem. Soc.*, 2009, **131**, 4216.
127 F. Bao, J. L. Yao and R. A. Gu, *Langmuir*, 2009, **25**, 10782.
128 I. Y. Goon, L. M. H. Lai, M. Lim, P. Munroe, J. J. Gooding and R. Amal, *Chem. Mater.*, 2009, **21**, 673.

129 A. Sanchez-Iglesias, M. Grzelczak, B. Rodriguez-Gonzalez, P. Guardia-Giros, I. Pastoriza-Santos, J. Perez-Juste, M. Prato and L. M. Liz-Marzan, *ACS Nano*, 2009, **3**, 3184.
130 S. J. Guo, S. J. Dong and E. K. Wang, *J. Phys. Chem. C*, 2009, **113**, 5485.
131 Y. Song, X. Y. Xu, K. W. MacRenaris, X. Q. Zhang, C. A. Mirkin and T. J. Meade, *Angew. Chem., Int. Ed.*, 2009, **48**, 9143.
132 D. Thakur, S. Deng, T. Baldet and J. O. Winter, *Nanotechnology*, 2009, **20**, 485601.
133 N. M. Tang and W. X. Tu, *J. Magn. Magn. Mater.*, 2009, **321**, 3311.
134 Z. X. Wang, L. M. Wu, M. Chen and S. X. Zhou, *J. Am. Chem. Soc.*, 2009, **131**, 11276.
135 K. S. Lee, M. H. Woo, H. S. Kim, E. Y. Lee and I. S. Lee, *Chem. Commun.*, 2009, 3780.
136 Z. Y. Ma, D. Dosev, M. Nichkova, R. K. Dumas, S. J. Gee, B. D. Hammock, K. Liu and I. M. Kennedy, *J. Magn. Magn. Mater.*, 2009, **321**, 1368.