REVIEW

Fluorescent, magnetic and plasmonic—Hybrid multifunctional colloidal nano objects

Nadja C. Bigall, Wolfgang J. Parak, Dirk Dorfs

Fachbereich Physik and WZMW, Philipps Universität Marburg, Marburg, Germany
Institute of Physical Chemistry and Electrochemistry, Leibniz University Hannover, Callinstr. 3A, D-30167 Hannover, Germany

Received 1 May 2012; received in revised form 18 June 2012; accepted 25 June 2012
Available online 20 July 2012

KEYWORDS
Nanoparticles; Multifunctional; Fluorescent; Plasmonic; Magnetic

Summary Progress in colloidal nanochemistry has been tremendous in the last decades. Nowadays a large variety of materials, sizes and shapes are accessible via colloid chemical methods. In the recent past research on colloidal nanocrystals has more and more focused on combining more than one functionality in one hybrid system. Fluorescent nanoparticles, magnetic nanoparticles and plasmonic nanoparticles are the three most common nanoparticles when looking at the particle functionality. Hence, in this review we summarize the most recent efforts undertaken in order to combine at least two of these properties in a hybrid system. Possible interactions in such hybrid systems are discussed together with possible synergetic effects giving rise to potential applications.

Introduction

Amongst many other rapidly advancing techniques for the fabrication of nanometer sized objects, colloidal chemistry is one promising technique which has experienced tremendous progresses in the last three decades regarding not only the amount of synthesizable materials (today a large variety of metals [1,2], semiconductors [3] and oxide based materials can be produced) but also complex shape and composition control [4]. Apart from (quasi) spherical nanoparticles (NPs), nowadays, e.g. rods [5], seeded rods [6], hollow NPs [7], concave NPs [8] and also controlled branched NPs [9,10] from one or more materials can be synthesized using colloidal techniques. The most advanced synthetic concepts yield samples with remarkable narrow size and shape distributions [11]. Furthermore, also the functionalization of colloidal NPs via their usually present ligand shell has also made large progress, allowing, e.g. selective binding in biological and other applications [12].

Colloidal NPs show many fascinating properties. Amongst the most widely investigated properties which also fundamentally and significantly differ from the properties of the corresponding bulk materials are fluorescence properties (e.g. quantum dots [13] and rare earth doped NPs [14], magnetic properties (e.g. superparamagnetic iron oxide NCs) [15–18] and plasmonic properties (e.g. mostly noble metal NCs) [19]. Each of these research topics is nowadays an extremely wide field by itself and they all have been reviewed several times in the past.

However, in the recent past, more and more researchers started to combine these research topics by synthesizing
and studying hybrid objects which combine at least two of the above mentioned properties in one system [20]. Meanwhile, the combination of several of the unique plasmonic, fluorescence and magnetic properties within a single system has become a whole research area being motivated mainly by biomedical multitasking applications, like e.g. sensing and manipulation, [21–23] but also motivated from a fundamental point of view for investigating fortification or weakening effects. As a consequence, a large variety of publications address the challenge to get control over those synergistic effects offering many different solution strategies. Hence, this review tries to summarize the recent efforts to produce hybrid and multifunctional objects from colloidal building blocks. Consequently, the following is divided into four parts, three of them dealing with systems exhibiting two of the three properties, respectively (thus fluorescent/magnetic systems, fluorescent/plasmonic systems, and magnetic/plasmonic systems), and one part focusing on systems combining all three properties. Each section summarizes the most recent advances with a specific focus on possible benefits from the combination of two or three of the respective properties. The first part focuses on the advantages of combining magnetic and plasmonic properties within a single system, highlighting possible applications, in e.g. plasmonic heating combined with magnetic targeting. The second part gives an overview about the advances in magnetic and fluorescent nano objects, which is mainly of interest for biomedical imaging and manipulation. Especially the optimization of both properties within a single particle is in focus, since in a lot of cases the improvement of one of both properties seems to impair the other (like e.g. fluorescence quenching). Solutions around these problems are discussed. In the third part, the partially synergetic effects of fluorescent and plasmonic domains in close proximity like a single nanoobject are discussed with a special focus on fluorescence enhancement due to plasmonic domains in the proximity. And in the last part, recent developments on nanoobjects with all three functionalities are presented and a motivation for further works on developing such multifunctional nanoobjects is given.

Magnetic and plasmonic objects

To date, the combination of magnetic and plasmonic NPs is the least investigated one amongst the three possible property combinations. The reason for this presumably lies in the not so obvious application possibilities as well as the not so obvious interactions between these two properties. However, in our opinion, indeed their combination has great potential for applications, like e.g. in biomedicine or catalysis, which we want to discuss in this section. Therefore, first the functional properties of magnetic and plasmonic NPs are discussed separately, in order to finally better understand why in fact their combination can be advantageous. Applications of magnetic NPs are highlighted in a series of reviews [15,18]. Magnetic NPs such as Fe₃O₄ or Fe₇O₁₄ NPs have a magnetic moment which is oriented in homogeneous magnetic fields, and to which a force is exerted in inhomogeneous magnetic fields. In a simplified way the first effect can be used for employing these NPs as contrast enhancing agent for magnetic resonance imaging (MRI) and for creating heat upon absorption of radio-frequencies (i.e. due to alternating magnetic fields). In a homogeneous magnetic field the magnetic moments of NPs are aligned parallel or antiparallel to the direction of the magnetic field. This influences the relaxation times of the proton spins, what is used for contrasting in MRI. In case alternating (homogeneous) fields are applied to magnetic NPs their magnetic moment can rotate respective to the NP axis (Néel rotation) or the whole NP can rotate (Brown rotation) [15]. In both cases heat is dissipated to the environment, which for example can be used to destroy local tissue [24]. The second effect can be used to direct NPs in a magnetic field gradient. The force hereby is proportional to the field gradient (e.g. the change of magnetic field per distance) and the magnetic moment of the NPs. This can be used to manipulate magnetic NPs with magnetic field gradients to target tissue (magnetic drug targeting) [25], to enhance uptake by cells or permeation in biofilms by locally focussing NPs and guiding them towards their direction (magnetofection) [26–28], and to extract magnetic NPs (and molecules bound to them) from solutions [29]. In addition some magnetic NPs such as Co [30], FePt [31] or FeO [32] NPs also have catalytic properties.

Also plasmonic NPs such as Au, Ag and Pt NPs have a widespread range of applications [19,33]. They can be used for imaging (e.g. photothermal imaging [34]), sensing [35] (e.g. by changes of the surface plasmon resonance frequency [36,37] or by surface enhanced Raman spectroscopy (SERS) [38]), for conversion of light into heat (e.g. for local destruction of tissue [39,40], the breaking of chemical bonds [41], or disintegration of carrier matrices [42,43]), in the case of Au NPs as surface for bioconjugation (–SH groups readily bind to Au surfaces [44]), and in the case of Ag NPs as antibacterial agents [45]. The last two examples show properties which are not directly correlated to the plasmonic properties of Au and Ag. However, noble metals are the classical example of plasmonic NPs and thus we also included these material-specific properties. On the other hand recently also other classes of materials than noble metals have been demonstrated to possess remarkable plasmonic properties, such as for example CuSe NPs [46,47].

Based on the above mentioned properties one can think about several applications for nanoobjects combining magnetic and plasmonic properties, out of which a few will be discussed. Plasmonic materials can be used for overcoating of magnetic NPs. In the case of gold shells or patches surface functionalization of the magnetic NPs is facilitated, as thiol moieties strongly bind to gold [48,49]. In the case of silver shells or patches the magnetic NPs possess antibacterial properties. Via the magnetic NP core these hybrid NPs can be dragged into biofilms, which due to the antibacterial properties of the Ag shell are thus degraded [28]. Plasmonic NPs can be also used for heating. In case magnetic NPs are combined with them to hybrid NPs, the NPs can be guided with magnetic field gradients to the target side, at which upon illumination heat is created, for example for the destruction of local tissue [50,51]. In case of magnetic NPs with catalytic properties heating via adjacent plasmonic NPs could control the reaction kinetics by temperature control via photothermal heating. Thus, the combination of magnetic and plasmonic NPs in fact leads to useful synergy. One also can say that in general the magnetic properties are not altered by the presence of a plasmonic material.
(in case no atoms from the plasmonic domain diffuse in the magnetic domain), but that the presence of magnetic materials may alter the plasmonic properties [52]. In addition to shifts in the surface plasmon resonance carriers trapped at the interface may mainly also alter plasmon dynamics [53–55]. Furthermore the magnetic domain can be used for rotating or oscillating the sample via an applied external alternating magnetic field. In case of anisotropic gold domains also the polarization of the scattering by the plasmonic domain is modulated, which can be used to improve signal-to-noise ratio by removing the unmodulated scattering background [56]. Likewise biomolecules binding to the surface of magnetic–plasmonic NPs can be detected by measuring changes in the relaxation properties (due to increases in hydrodynamic diameter) upon applied magnetic stimuli via the anisotropic scattering of the plasmonic domain [57].

In order to construct hybrid NPs of both types of NPs several approaches are possible [58]. We on purpose will focus on hybrid NPs which possess different domains for their plasmonic and magnetic functionalities, since this approach allows for independently controlling of the plasmonic and magnetic properties, though NP materials exist, such as FeAu, which are as well magnetic as plasmonic [59]. Synthetically most challenging is the growth of one NP domain on top of another NP. This has been achieved for example by the direct growth of Ag and Au NPs on top of Fe3O4/Fe2O3 NPs [60–63], rod-shaped Co NPs [64], and CoPt3 NPs [65,66], respectively, cf. Fig. 1. Here the first NP acts as seed for the growth of the second NP. Besides such colloidal chemistry approaches also other techniques such as flame aerosol technology [67] and templated electrodeposition [68] have been used for combining Ag + Fe3O4 and Au + Fe domains, respectively.

Such types of hybrid NPs often are also termed “Janus”-NPs, as the two different domains are structurally separated. Instead of growing one type of NP on top of another one also core/shell structures are possible. Also here the NP core acts as seed for the formation of the shell of the second material. This has been demonstrated for Fe3O4 [69,70] and Co NPs [71] coated with Au and Au/Ag shells. Vice versa also Au NPs [72] and Ag NPs [73] have been coated with (porous) shells of iron oxide. It is still synthetically very challenging to grow homogeneous and tight, instead of patchy shells. For several applications however also patches instead of homogeneous shells are sufficient. For example also Au islands instead of tight Au shells on top of another NP allow for conveniently attaching molecules via thiols. An interesting alternative approach is trapping of Fe3O4 NPs inside hollow Au NPs [74], which can be achieved by different diffusion rates of gold and oxygen [75]. Instead of growing shells directly onto seed NPs it is synthetically also possible to use organic spacer molecules between the core and the shell. Using polyelectrolyte layers [76], polyethyleneamine (PEI) [77], and carboxylate-dextran/ethanediylbis(isonicotinate) [28] as coating of iron oxide NPs, Au and Ag shells could be grown on top of these spacers. In a similar way silica shells on top of iron oxide NPs have been also used for linkage of Au NPs on their surface [78,79]. Alternatively, several magnetic nanoparticles can be simultaneously incorporated into polymeric nanobeads which change their surface charge upon variation of the pH. Due to electrostatic interactions, positively charged gold nanoparticles can be adsorbed and desorbed by controlling the pH. Hence, the polymer can act as well as spacer as also functional glue for the plasmonic nanodomain [80]. Naturally such objects are typically bigger than for example the Janus NPs as described before, and typically they also comprise several NPs within on hybrid NP. This is even exceeded by other approaches, in which different types of NPs are embedded in one carrier matrix. Typical carrier matrices for forming hybrid NPs out of many smaller NPs are silica or polyelectrolyte capsules [50]. While in Janus NPs a defined spatial control between the different NP domains is guaranteed, the NPs within carrier matrices are statistically distributed. This summary demonstrates that a large variety of synthetic approaches exist for combining magnetic and plasmonic NPs, though this is still a field in its infancy steps. Most publications in this direction originate only from the last years and further impact can be expected in the future.

Fluorescent and magnetic objects

Combining fluorescent and magnetic objects in one system is of special interest for various types of applications where it is necessary to monitor and manipulate at the same time, like for example in biomechinc with the general goal to label and destroy affected tissue (e.g. labeling, magnetic resonance imaging, magnetic particle imaging, hyperthermia and microscopy).

In the case of fluorescent and magnetic nanoobjects, the control of spacing between the emitting species and the magnetic one is of great importance, in order to keep both properties unaltered or at least not strongly reduced in the hybrid system. Especially the fluorescence of the fluorophore can be strongly reduced not only when quenching effects occur, but also simply due to a concurring light absorption process. For the magnetic properties large inducible magnetic moments are of interest, and depending on the type of application, sometimes compromises have to be found between the solutions of both problems. As an example, larger amounts of magnetic material can absorb the light which excites the fluorophore or which is emitted by the fluorophore. Vice versa, smaller amounts of magnetic material would reduce the total magnetic moment and hence the possibility to magnetically manipulate or sense.

As a consequence, a large variety of different approaches for the synthesis of NPs exhibiting magnetic and fluorescent properties exists, which will be discussed in this section. Fluorescent paramagnetic nanoobjects will be only briefly presented due to their relatively small magnetic moment resulting in limited application possibilities (such as for T1 contrast agents in MRI). The main focus of this section will be on fluorescent nanoobjects with superparamagnetic behavior. The variety of applied fluorophores ranging from organic dyes to quantum dots and lanthanide doped NPs showing fluorescence upconversion will be presented and discussed, as well as the different approaches of combining the respective magnetic and fluorescent materials.

In the last decade the field of NPs with combined magnetic and fluorescent properties has more and more become a fast evolving branch of science with an exponentially increasing number of new developments per year. A
number of recent review articles have been published addressing the morphological, chemical and physical properties of multifunctional NPs and their application issues, mainly with the background of biomedical applications [81–85]. As discussed above, the reason for this increasing interest in this kind of multifunctional nanoobjects mainly arises from the possible biomedical applications of multimodal imaging in combination with therapeutic methods, the goal being optimized fluorescence behavior and at the same time high magnetic or superparamagnetic properties.

The approaches of the various groups differ in several ways. Superparamagnetic, like e.g. magnetite NPs, as well as paramagnetic, like e.g. gadolinium or gadolinium containing NPs have been synthesized and combined with several emitting species, such as quantum dots, fluorescent metal NPs, fluorescence dyes or lanthanide doping of either the magnetic NPs themselves or separate insulating NPs. The combination of the magnetic and fluorescent species was achieved either by covalent/coordination chemistry, in combination with assembly methods, by epitaxial growth, or by including both species into a matrix from silica, polymer or oil droplets and liposomes, and numerous publications report about further functionalization of the resulting magnetic and fluorescent NPs, for e.g. biomolecular targeting or with therapeutic agents.

The field of paramagnetic fluorescent NPs includes quantum dots doped with, e.g. transition metals such as manganese [86,87] which are materials of high interest mainly in the field of spintronics, which intends to manipulate electron spins by electric fields. Nanosystems including gadolinium are more of interest for medical imaging applications, since they can be applied as so-called T1 contrast agents in MRI. As a consequence, gadolinium nanosystems have been combined with all kinds of the above mentioned fluorescence species so far [88–101]. To discuss these exciting materials in detail would certainly be a review article itself. However, as mentioned above, orders of magnitude larger magnetic fields can be achieved exploiting superparamagnetic materials in the synthesis of magnetic and fluorescent NPs, allowing a much better manipulation of the resulting hybrid system by external magnetic fields. The manifold materials which in the last years have arisen in this material combination will be discussed more in detail in the following part.

Molecular fluorophores play a significant role in bifunctional magnetic and fluorescent nanoobjects. So far, several routes have been worked out to link molecular dyes to superparamagnetic NPs. An important demonstration on how to surface functionalize magnetite NPs with a fluorescence dye (rhodamine 110) was given by Sahoo et al. [102] in 2005. In a different approach published by Veiseh et al. in the same year, a bifunctional poly(ethylene glycol) was exploited as a linker between the superparamagnetic NPs and a near infrared emitting fluorescence dye (Cy5.5) and a peptide [103]. Bertorelle et al. [104] investigated bifunctional NPs from a magnetic oxide core with covalently bound fluorescence dyes (rhodamine B and fluorescein) and their applications in cell experiments. In further works, dyes like fluorescein isothiocyanate, Cy3, porphyrin, oligothiophenes, or the fluorescent chemotherapeuticum doxorubicin were combined with superparamagnetic nanocrystals [105–110].

Modern coating techniques allow for incorporation of most organic fluorophores inside the organic shell around magnetic NPs [101]. Organic dyes generally have the disadvantage to show blinking and bleaching behavior [111], and to show a much narrower excitation spectrum than quantum dots. On the other hand, an interesting and new functionality can be given by coupling photoswitchable organic dyes to the superparamagnetic NPs, which has been shown by Yeo et al. [112]. This approach resulted in sulfur-oxidized diarylethene encapsulated superparamagnetic iron oxide NPs, whose fluorescence performances could be manipulated optically under UV or visible radiation. Since in this case the resulting fluorescent and magnetic NPs were easily separable from the solution in a magnetic gradient field, this is the first approach in which the solution concentration as well as the fluorescence could (independently) be reversibly switched by external electromagnetic fields.

Apart from direct linking of the magnetic NPs and the fluorescence dye, there is the possibility to embed both species in matrices, such as silica. This generally results in less fluorescence quenching due to better shielding of the dye from the NPs, and results in faster responses to external fields due to the embedding of usually more than one superparamagnetic NP inside one nanoobject [113–123]. Similar effects.
are obtained when a polymer is used as a matrix for the superparamagnetic NPs and the fluorescence dye [124]. The advantages of using a polymer as matrix is that the polymer can be further functionalized easily [125,126], and that due to the nature of the polymer additional functionalities can be added to the nanosystem, such as pH-dependence [80,127], temperature dependence [128], biocompatibility [129] and biodegradability [130]. Also examples for the direct use of fluorescent polymers as matrices for the magnetic NPs are described [131,132].

As already mentioned above, quantum dots (semiconductor nanocrystals in the quantum confined size regime) display interesting optical properties with narrow emission spectra, reduced blinking behavior, strongly reduced bleaching, high luminescence quantum yields and broad absorption and excitation spectra which opens the possibility to excite with a single excitation wavelength NPs of several different emission wavelengths. Hence, they are interesting candidates, for example medical imaging, which explains that a large variety of magnetic fluorescent NPs consists of a combination of superparamagnetic nanocrystals with such quantum dots. One possibility to yield such a combined system is, similarly as described in the previous section, to embed one or both species inside a nano- to microscaled matrix. Generally, a big advantage of such a matrix is that the quantum dots and the superparamagnetic NPs can be synthesized separately in a previous step leading to good control over the building block quality. Additionally, the presence of a matrix can be used for tuning the morphology in terms of fluorophore-magnetic NP distance. Furthermore, these nanoobjects can be further functionalized via functionalization of the matrix, which has the advantage that the NP properties are less altered in the functionalization process than they would be when surface functionalizing the nanocrystals directly.

Approaches for magnetic fluorescent nanoobjects in a matrix have so far been successful with silica [133–138], oil droplets [139] and vesicles [140], as well as polymer matrices, such as dextran [141], polyethyleneimine [142], or liquid crystal micelles [143]. Polystyrene [144,145], poly(tert-butyl acrylate-co-ethyl acrylate-co-methacrylic acid) [146], poly(maleic anhydride alt 1,1 octadecene) [126] were also applied as simultaneous matrices for magnetic and fluorescent NPs. Various techniques, such as co-precipitation methods [126], ultrasonic emulsification [146], miniemulsion/emulsion polymerization [144,147], and co-embedding of both NP types into temporarily swollen poly(styrene/acrylamide) copolymer nanospheres [148] were applied for including the NPs inside the nanoo- objects. An additional method for embedding the fluorescent and magnetic NPs inside polymeric nanoobjects worth mentioning exploits the assembly due to oppositely charged building blocks of polymers, e.g. polyelectrolytes [149,150]. During this so-called layer-by-layer technique magnetic and fluorescent NPs were included between the oppositely charged polyelectrolyte layers forming, e.g. 3 μm diameter microcapsules. With a flow channel system and a local magnetic field gradient the magnetism induced trapping of the magnetic and fluorescent polymer capsules was monitored by fluorescence microscopy [151]. Also Kim et al. exploited electrostatic interactions when synthesizing near-infrared emitting magnetic NPs. Here, the magnetic NPs were included during an ionic gelation process before subsequent assembly of the negatively charged fluorescent nanocrystals [152].

Despite the above described advantages of magnetic fluorescent nanoobjects combined inside matrix nanomaterials, also matrix-free nanoobjects are of great scientific importance. These kinds of objects have the advantage of generally being much smaller due to the absence of a matrix material, which allows monitoring and manipulation on a much smaller length scale.

One matrix-free class of magnetic fluorescent nanomaterials from superparamagnetic NPs and quantum dots results from chemically induced assembly of one of the nanocrystal species onto the other. The exploited techniques mainly involve covalent binding to thiol and carboxyl groups [153,154]. An interesting magnetic and fluorescent nanosystem describes the assembly of quantum dots onto magnetite nanorings [155]. Also in this synthesis route, electrostatic interaction between positively charged poly(ethylene imine) capped highly luminescent CdSe/ZnS quantum dots and citric acid functionalized nanorings was exploited to induce the assembly. Due to the core–shell structure of the quantum dots, the resulting colloid was significantly green fluorescent. The large volume of more than 100 nm diameter and 60 nm height of the magnetic nanorings resulted in quick collective migration to the vial walls upon exposure to external magnetic field gradients (see Fig. 2).

Alternative routes towards matrix free magnetic fluorescent NPs have been developed exploiting in situ chemical synthesis of emitting nanoscale ZnS onto hollow or massive magnetic nano- to microspheres [156–158].

The last class of matrix free magnetic fluorescent NPs are linker free nanoheterostructures in which two inorganic materials are grown directly onto each other. Nanoheterodimers of about 7 nm diameter consisting of an iron platinum compartment and a CdS compartment [159] were a synthetic breakthrough for creating a magnetic and fluorescent colloidal nanoobject consisting of two inorganic materials with direct interface. The materials of the semiconductor compartment of such nanoheterodimers were further extended to ZnS, PbS and CdSe. Although the original idea of this kind of nanoheterodimer synthesis was to obtain small single objects which could be observed and manipulated as an individual particle, however, a significant fluorescence quenching of the semiconductor compartment was reported for all these material constellations when taking the metallic iron platinum as the magnetic compartment [160]. Quenching always has to be considered when bringing fluorophores close to a metal(alloy) surface, which can drastically reduce properties for fluorescence labeling. But also other application possibilities exist. E.g. such dimers from CdS and FePt were proven to be additionally catalytically active and at the same time photocurrent producing materials, which, immobilized onto a gold layer with an appropriate isolation material opens the possibility for light-controlled analysis of hydrogen peroxide concentrations [31].

In 2011 Trinh et al. [161] were able to synthesize a core–shell structure of FePt and CdSe, again showing only weak fluorescence of the colloid. An interesting approach to overcome the problem of fluorescence quenching was reported in by Deka et al. [162]. Here, the magnetic metal...
domain was grown at the end of a dot in rod (core–shell) system, in which the higher bandgap material from the rod acted as a spacer between the magnetic domain and the fluorescent core, so that it was possible to reduce the fluorescence quenching effects. A different route to reduce the problem of fluorescence quenching was described by Gao et al. [163] whose nanoheterodimers consisted of a magnetite (which is an insulating material) and a CdSe compartment (see Fig. 3). The products from this synthetic route were magnetic and fluorescent enough to be able to be manipulated by a small magnet after incorporation inside cells, which could be monitored by fluorescence microscopy. Of course, these nanoobjects would be more helpful for biological applications in which tracking of the magnetic fluorescent NPs is required.

Yet another type of hybrid NPs expressing superparamagnetism and fluorescence was developed in 2011 consisting of silicon and iron oxide [164]. Apart from organic dyes and quantum dots, also lanthanide doped nanocrystals can act as fluorophores in hybrid magnetic and fluorescent systems. A detailed review about lanthanide doped nanocrystals can act as fluorophores in hybrid magnetic and fluorescent systems can be found in [165]. Similarly as for fluorescent magnetic NPs from organic dyes or semiconductor NPs, also lanthanides can be embedded into a matrix together with the superparamagnetic NPs. As a result, silica matrices have been employed to yield NIR emitting [166] or upconversion [167–171] expressing colloidal nanosystems with superparamagnetic behavior. Examples for the exploitation of polymer matrices can be found in [172,173].

As matrix free magnetic luminescent NPs, Nichkova et al. [174] reported the synthesis of magnetic luminescent Co: Nd: Fe3O4/Eu: Gd2O3 core–shell NPs. Groman et al. [175] doped ultrasmall magnetite NPs with 5% europium retaining superparamagnetic behavior and high photostability. Furthermore, superparamagnetic Fe3O4 NPs were doped with Tb leading to a similar bifunctionality [176]. Fe3O4/NaYF4: Yb,Er heteronanoparticles were prepared exploiting a crosslinking molecule for immobilizing the magnetic NPs on the preformed lanthanide doped NPs [177]. The resulting nanoobjects showed fast migration upon the exposure to magnetic gradient fields. Due to the limited influence of the surrounding medium on such lanthanide doped and upconversion showing NPs when compared to dyes and quantum dots, and due to the possibility to excite the fluorophore with near infrared light, these kinds of lanthanide containing materials offer an interesting alternative to the above described dyes and quantum dots. For e.g. biomedical applications the possibility to excite the
fluorescence in the NIR region (here the tissue transparency is usually higher than in the visible regime of the spectrum) can be of great value, as well as the stability of the fluorescence against different surrounding media. Therefore, hybrid nanoobjects from magnetic and lanthanide doped upconversion exhibiting NPs will find their future applications in imaging and manipulation applications.

As an intermediate summary we can conclude that a lot of progress has been achieved already in designing efficient magnetic and fluorescent nanoobjects. While organic dyes can be attached via anchoring groups but easily photobleach, inorganic dyes like quantum dots or upconversion NPs exhibit higher photostability. In most of the cases, quenching effects can be reduced by controlling the spatial distribution of the emitting and the magnetic species and by appropriate choice of the magnetic material. For better magnetic manipulation, synergistic effects of several magnetic NPs within a single nanoobject are of great interest, or alternatively the choice or larger single magnetic NPs. However, when following these two pathways, the products are usually around one order of magnitude larger than dimers, e.g. dimers from one fluorescent and one magnetic compartment, but which again are less luminescent and express smaller magnetic moments.

Many of the discussed systems additionally already deal with further functionalization of the magnetic fluorescent nanoobjects for fabricating multifunctional objects which can be target specific, pH dependent, temperature dependent or diffusion triggered delivery systems being able to manipulate and monitor at the same time. Surely, this trend will develop further in the near future, which will bring new exciting magnetic and fluorescent nanomaterials even closer to real life applications.

**Fluorescent and plasmonic objects**

The combination of plasmonic NPs and fluorescent ones is interesting mainly due to the possible strong interactions between the plasmon in the plasmonic particle and the exciton (electron/hole pair) in the fluorescent NP. The interaction of fluorophores in general with plasmonic surfaces or NPs has been studied exhaustively. Plenty of studies deal with molecular dyes, either in contact or close proximity to a metal NP or a surface coated with plasmonic particles, this topic has been comprehensively reviewed, e.g. by Chen et al. [178] in 2010. Here however, we will focus on interactions between NPs as fluorophores (e.g. quantum dots, QDs) and as plasmonic objects (thus e.g. metal NPs), while molecular fluorophores will be covered only very briefly in this section. Even though all plasmonic/fluorescent hybrid systems known today contain a metallic part as the plasmonic part it should be shortly noted that especially in the recent past other plasmonic materials than just metals, like...
Fluorescent, magnetic and plasmonic—Hybrid multifunctional colloidal nano objects

Fluorescent, magnetic and plasmonic—Hybrid multifunctional colloidal nano objects are of great interest for photothermal therapy [46]. The recent results on this new type of materials were reviewed by Zhao and Burda [47].

Maybe the most crucial factor determining the properties of a hybrid plasmonic and fluorescent colloidal nanoobject is the distance between the plasmonic compartment(s) and the fluorescent compartment(s) and of course the filling of the spacing between the different compartments. Since the plasmonic compartment in all cases of hybrid fluorescent and plasmonic objects investigated till now is metallic in nature, a direct contact or a too close distance of the plasmonic (metallic) part and the fluorescent part of a given system usually results in strong fluorescence quenching effects. This type of fluorescence quenching has been observed in many and diverse systems in which, e.g., a semiconductor compartment of a quantum dot or quantum rod is in close contact with a metal domain (e.g., CdSe rods with gold tips, etc.) [182–185] or when molecular fluorophores are in direct contact with a metal particle [186]. This type of metal induced quenching was also studied with respect to, e.g., quenching based biosensing using CdSe quantum dots as emitters [184].

Thus, in order to observe other types of interactions between fluorescent molecules or quantum dots with plasmonic metal NPs other than just fluorescence quenching, an insulating layer or at least a well-defined distance between the plasmonic particle and the fluorescent quantum dot is necessary. While the quantum dots and the plasmonic NPs are inorganic in nature (apart from the surface ligands which grant solubility/stabilization and functionalization), the spacing material, which shall insulate the quantum dot from the plasmonic metal particle, can either be organic (and then in most of the cases polymeric) or inorganic in nature, resulting in either all inorganic structures or organic inorganic composites.

One fundamental study used the tip of an atomic force microscope to study the distance dependent interactions between fluorescent NPs (CdSe/ZnS core shell particle) and a gold surface. This approach allows of course a very good control over the distance between the gold surface and the quantum dots, yielding a maximum of fluorescence enhancement at a distance of 15 nm in this study and for this system [187]. Also the distance dependent interactions between a single quantum dot and a single gold NP were studied using an AFM for distance manipulation, resulting in drastically reduced fluorescence lifetimes and also drastically reduced fluorescence intermittency (“blinking”) of the quantum dot at close distances to the gold NP [188].

A relatively simple way to sufficiently insulate an ensemble of nanocrystals from the plasmonic NPs was demonstrated by Pompa et al. In this study, CdSe/ZnS core–shell nanocrystals were simply embedded in a polymer (PMMA) and then spin coated on a substrate which contained regularly arranged gold nanotriangles (deposited via electron beam lithography). In the regions of the gold triangles, a fluorescence enhancement up to a factor of 30 was achieved (when compared to areas of the same film which are not close to a gold triangle) [189]. A similar study showed strong fluorescence enhancement of CdSe/ZnS core shell particles embedded in PMMA in close proximity to 100 nm sized Ag islands [190]. Other studies followed with variations of the concept of a polymer film as an insulating layer [191–193].

A rather sophisticated and interesting approach for an organic inorganic hybrid system was demonstrated by Jin and Gao [194]. Here, single hydrophobic quantum dots were first coated with an amphiphilic polymer granting water solubility. Additional polyelectrolyte bilayers could be deposited on top of these particles as additional spacing layers. Then, poly-L-histidine was deposited and finally a gold layer was deposited around this structure. Thus, this report demonstrates the possibility to insulate a single quantum dot from a surrounding hollow gold layer using an organic layer with tunable thickness (see Fig. 4) [194]. The method of using a polyelectrolyte multilayer was however used earlier for tuning the distance between a film of deposited gold NPs and a film of QDs deposited on top of this film, again showing strongest fluorescence enhancement at distances between 10 and 20 nm [195].

Looking at all inorganic systems with an interaction between a quantum dot and a plasmonic metal NP, usually SiO2 is used as spacing and insulating layer between the two. E.g., an ensemble of quantum dots in the vicinity of a SiO2 covered plasmonic gold NP [196] was investigated, while in the recent past, this approach was extended in order to study also the interactions of a single quantum dot with a SiO2 coated gold NP [197]. Of course, the study of individual quantum dots allows for a far easier interpretation of the obtained results, since no heterogeneous ensemble effects are observed.

For correct interpretation of fluorescence enhancement effects and plasmon/exciton interactions in general, it is important to measure not only the steady state fluorescence signal but also the fluorescence dynamics. When, e.g., quenching effects are observed, an unchanged fluorescence lifetime accompanied by a strong change in fluorescence quantum yield is an indicator for an inhomogeneous quenching (some emitters are completely quenched while others

Figure 4 A hydrophobic quantum dot functionalized with a lipid-PEG-COOH conjugate followed by a thickness tunable polyelectrolyte layer and poly-L-histidine for the controlled growth of a surrounding gold shell. Reprinted (adapted) by permission from Macmillan Publishers Ltd.: Nat. Nanotechnol. 4 (2009) 571–576, copyright (2009) [194].
are unperturbed) while a shortening of the fluorescence lifetime proportional to the lowering of the fluorescence quantum yield is an indicator for a homogeneous quenching effect (all emitters are affected in the same way). Of course, several intermediate situations are imaginable between these two extreme situations which in turn lead to multiexponential decay behavior.

Fig. 5 shows the dependence of the fluorescence lifetime on the distance between a single gold NP and a single quantum dot in a colloidal system with silica as spacing layer (namely, a gold NP with a surrounding silica layer and a quantum dot adsorbed to this outer layer) [197]. It is obvious, that the fluorescence decay becomes much faster when the QD is in close proximity (7 nm in this case) to the gold NP, rather than far away from it. Fig. 5 nicely demonstrates how strongly the fluorescence decay rate in such a hybrid system of a single Au NP and a single CdSe QD is affected by the distance between the two (the thickness of the silica layer). While at 7 nm distance, the fluorescence decay of the QD is significantly accelerated, already at a distance of 14 nm, the QD behaves almost as in the absence of a gold particle. This means, that the interactions of a CdSe quantum dot with a gold particle range from complete fluorescence quenching at close contact through a regime of possible fluorescence enhancement at distances around 7 nm (in this case) to a regime of basically no interactions at distances larger than 14 nm. Hence, it is very obvious, that the distance control down to the nanometer level between plasmonic and fluorescent particles is the key parameter when exploiting their interactions. In turn that means that also the interpretation of ensemble measurements, in which several different distances may occur in one sample, can be extremely challenging.

The interpretation of fluorescence decay measurements of QD in the proximity of a plasmonic NP becomes more complicated by the fact that not only the radiative decay rate but also the non-radiative decay rate and furthermore also the excitation rate of the QD are affected by the nearby plasmonic particle [1,198,199]. Recently, also an excitation wavelength dependence of the fluorescence lifetime (and hence of the quantum yield) of a QD in proximity to a silver nanoprism has been reported [200].

While mostly the enhancement of the excitation rate is discussed to be crucial to reach the regime of fluorescence enhancement (since usually the effect of the increase of the radiative recombination rate is overcompensated by an accompanying increase of the non-radiative decay rate), Muneechika et al. [201] reported the possibility to reach a regime of fluorescence enhancement also without an increase of the excitation rate.

As already shortly mentioned, apart from an influence on the excitation and recombination rate, several studies also demonstrate that a nearby plasmonic object can have significant influence also on the fluorescence intermittency (“blinking behavior”) of a quantum dot [188,197,202–205]. This behavior can be clearly seen in Fig. 6, where the blinking behavior of a quantum dot without a plasmonic environment and in the vicinity of an Au NP is seen revealing a strong suppression of “off states” of the QD when the QD is in close proximity to the plasmonic particle. Shown is the emission behavior of an individual CdSe QD in close proximity (7 nm or 14 nm) to SiO2 coated Au NPs traced over 5 min. In all cases a clear “on–off” type of emission is seen while also the emission intensity of the QD in proximity to an Au particle is seemingly stronger.

Statistical analysis in this case reveals an average “on-time” of 37% in the absence of a gold particle and an average “on-time” of 71% in the case of Au particle in 7 nm distance, and hence as mentioned a strong off-state suppression by the nearby Au particle. Generally, this suppression of fluorescence intermittency might be of great interest in future applications, since exactly this type of “blinking” behavior of QD is one big drawback for applications, like e.g. real time labeling applications, etc.

Bharadwaj and Novotny [206] in a recent publication however report that they found indeed the blinking statistics (in terms of power law probability distribution) being not strongly influenced by a close-by plasmonic particle, which thus at least partially contradicts earlier reports, and hence shows that possibly a further in-depth study of blinking behavior of QD in the proximity of plasmonic particles might be necessary.

One possible limiting factor of fluorescence enhancement by plasmon coupling has been investigated by Sadeghi and Nejat [207], revealing that at too high excitation intensities fluorescence enhancement can be inhibited due to heat induced photoionization processes.

It can be seen in the above, that the vast majority of studies QD coupling with plasmonic particles was done with CdSe NPs and more specifically with CdSe/ZnS core shell QD. This choice is obvious, since these particles are the best known QD with high fluorescence quantum yields and with size tunable emission wavelengths in the visible regime of the spectrum. However, also other semiconducting materials have been investigated with respect to their interactions with close-by plasmonic surfaces or particles. Amongst these are CdTe QD [208], CdS QD [209] and InAs QD [210,211].

Apart from fluorescence enhancement of QD, yet another phenomenon which has been investigated in the recent past is the plasmon enhanced energy transfer between quantum dots [212–214]. All these studies suggest that the Förster resonant energy transfer (FRET) between two or more QD is significantly enhanced when metal NPs with a plasmon resonance close to emission wavelength of the QD are present in close proximity of these QD.

The discussion above focused on hybrid NPs with controlled and defined distance between the fluorescent and plasmonic domains, which is required for studying basic photophysical concepts such as quenching, energy- and charge-transfer, and blinking. However, also hybrids of fluorescent and plasmonic NPs without defined interface can be used for a variety of applications. As already mentioned above polyelectrolyte layers can be used for the assembly of NPs. In case of spherical shape so called polyelectrolyte capsules are an interesting carrier system [215]. NPs of different materials can be easily incorporated into the polyelectrolyte walls of these capsules. In case fluorescent and plasmonic NPs are embedded in the walls of the same capsule this capsule can be observed via fluorescence and opened via light mediated heating of the plasmonic NPs [216,217]. As both processes (observation via fluorescent NPs, light-mediated heating via plasmonic NPs) work independently, no defined distance between the different NPs is required. The same is true for another example. Plasmonic NPs are many times
Fluorescent, magnetic and plasmonic—Hybrid multifunctional colloidal nano objects

Figure 5  (a) Fluorescence decay of a single quantum dot at various distances from a single gold NP. (b) Decay rates extracted from the decay measurements [197].
Reprinted (adapted) with permission from [182]. © 2011 American Chemical Society.

Figure 6  Temporal evolution of the fluorescence (left) and the corresponding blinking statistic (right) for a single quantum dot in close proximity to a gold NP at various distances between the two (a and b: no gold particle, c and d: gold particle in 7 nm distance, e and f: gold NP in 14 nm distance).
Reprinted (adapted) with permission from [197]. © 2011 American Chemical Society.

composed out of noble metals, such as Au and Ag, while QDs many times are based on II/VI semiconductors. Both classes of materials have different binding affinities to certain chemical functionalities. While thiols for example bind strongly to Au surfaces, their linkage to CdSe is much weaker. Thus hybrid NPs made out of Au and CdSe domains can be used for spatially selective attachment of molecules. In this way for example thiolated biotin was attached to the Au tips, but not to the CdSe rods of dumbbell shaped CdSe−Au hybrid NPs [12]. The presence of Au spots on fluorescent NPs thus could provide binding islands for thiolated molecules and allow for structures functionalization.

Summarizing, apart from simple fluorescence quenching effects caused by plasmonic (and hence usually metallic) NPs, especially the recent past has demonstrated the possibility to access a regime of strong fluorescence enhancement and also blinking suppression by combining plasmonic NPs and fluorescent NPs in hybrid systems. All results so far point out that the most crucial parameters determining the interactions between fluorescent and plasmonic particles are the interparticle distance as well as the spacing material chosen. Thus, most likely the nanometer precise control of the distance between individual nanoobjects using different spacing materials will be one future focus in nanoscience. Furthermore, the controlled growth of metal/semiconductor hybrid structures allows applications exploiting selective covalent binding to one of these material types.

Fluorescent, magnetic and plasmonic objects

Clearly structurally controlled assembly of 3 different functional domains into one single NP remains a challenge for
the future. For a detailed investigation of the interactions in between the different domains a structurally controlled assembly is required, as for example quenching effects are distance dependent. On the other hand one may again think of applications in which the different properties of the individual functional compounds are used independently. In this direction we want again refer to using polymers as matrix for encapsulation of multiple objects into one singe carrier particle. Via fluorescent NPs such an object could be traced, the integrated magnetic NPs would allow for directing of the particles with magnetic field gradients, and the plasmonic NPs could be used for light-controlled heating at the target site, for example for releasing of cargo [217]. Though such particles would not be well defined concerning their structural properties, i.e. the distance between and the number of the individual integrated NPs would remain statistical, potential applications for such multifunctional objects exists.

Summary and conclusions

The major conclusions of each section were already summarized in the respective sections. Overall, it can be concluded, that especially in the most recent past, the formerly more or less independent research areas of magnetic NPs, plasmonic NPs and semiconductor NPs are more and more often combined in order to produce highly functional hybrid systems with properties and application that can obviously not be granted by one of these types of materials alone. As mentioned in all sections above, the challenges to be overcome rise drastically with the amount of functional compounds used independently. In this direction we want again refer to using polymers as matrix for encapsulation of multiple objects into one singe carrier particle. Via fluorescent NPs such an object could be traced, the integrated magnetic NPs would allow for directing of the particles with magnetic field gradients, and the plasmonic NPs could be used for light-controlled heating at the target site, for example for releasing of cargo [217]. Though such particles would not be well defined concerning their structural properties, i.e. the distance between and the number of the individual integrated NPs would remain statistical, potential applications for such multifunctional objects exists.

Acknowledgement

This work was funded in parts by DFG (contract PA794/11-1).

References

Fluorescent, magnetic and plasmonic—Hybrid multifunctional colloidal nano objects


Y. Ge, Y. Zhang, S. He, F. Nie, G. Teng, N. Gu, Nanoscale Res. 2006 5385—5391.


C. Tu, Y. Yang, M. Gao, Nanotechnology 2008.


Wolfgang J. Parak obtained his PhD in biophysics at the Ludwig Maximilians Universität München, Germany in 1999 in the group of Prof. Dr. Hermann Gaub. After a postdoctoral stay at the University of California, Berkeley, CA, USA in the group of Prof. Dr. Paul Alivisatos he returned 2002 to Munich as Assistant Professor. Since 2007 he is Full Professor at the Physics Department of the Philipps Universität Marburg, Germany. Wolfgang Parak is Associate Editor of ACS Nano.

Dirk Dorfs obtained the PhD in physical chemistry at the Technische Universität Dresden, Germany in 2007 in the work group of Prof. Dr. Alexander Eychmüller. He worked as a postdoc in the work group of Prof. Dr. Uri Banin at the Hebrew University of Jerusalem, Jerusalem, Israel and subsequently in the group of Prof. Dr. Liberato Manna at the Italian Institute of Technology, Genoa, Italy. Currently he is working as a researcher at the Leibniz Universität Hannover, Hanover, Germany.