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Nanohybrids in Environmental & Biomedical Applications

Edited by Surender Kumar Sharma Federal University of Maranhao, Sao Luis, Brazil



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Preface

This book will serve as an overview of nanohybrid materials and their prospective applications in the field of biomedical research and development and environmental industry for a wide audience: from beginners and graduate-level students up to advanced specialists. It provides an extensive overview of the synthesis of multifunctional nanomaterials presenting key examples of their safe utilization for biomedical and environmental applications.

This contributed volume shares up-to-date advancements in the area of important nanohybrid materials with in-depth investigation of the cutting-edge developments on this particular subject. The first chapter serves as preparatory material for researchers working in nanotechnology.

It provides a forum for the critical evaluation of multifunctional nanohybrids for benign exploitation in the biomedical and environment sectors that are at the forefront of research in nanoscience and nanotechnology. It also presents highlights from the extensive literature on the topic, including the latest research in this field from the agriculture sector.

> Surender Kumar Sharma Sao Luis, Brazil



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Editor

Surender K. Sharma obtained his Ph.D. degree from H. P. University, Shimla, India. After spending several years in research/teaching positions in Brazil, France, Czech Republic, India, and Mexico working in the area of nanomagnetism and functional nanomaterials, he joined the Federal University of Maranhão, Brazil, as a faculty member in Physics. He is actively involved in research, teaching, and supervising students. He was awarded FAPEMA Senior Researcher grants and has published more than 74 research articles in reputed journals, 5 books as a single author, and 5 book chapters, and has been active in professional organizations.



Contributors

Aman Akash Department of Chemistry Savitribai Phule Pune University Ganeshkhind, India

Kanwal Akhtar Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan

Khuram Ali Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan

Balaprasad Ankamwar Department of Chemistry Savitribai Phule Pune University Ganeshkhind, India

Hafeez Anwar Magnetic Materials Laboratory Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan

Iram Arif Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan

Damayanti BagchiDepartment of Chemical, Biological and Macromolecular SciencesS. N. Bose National Centre for Basic Sciences Kolkata, India

Eduardus Budi Nursanto Department of Chemical Engineering Universitas Pertamina Jakarta Selatan, Indonesia

Allah Ditta Department of Environmental Sciences Shaheed Benazir Bhutto University Pakhtunkhwa, Pakistan and School of Biological Sciences The University of Western Australia Perth, Australia

S. Del Sol Fernández Instituto Politécnico Nacional Centro de Investigación en Ciencia Aplicada y Tecnología Avanzada Ciudad de México, México

Saee Gharpure Department of Chemistry Savitribai Phule Pune University (formerly University of Pune) Ganeshkhind, India

Debanjan Guin Department of Chemistry Institute of Science Banaras Hindu University Varanasi, India

Lienda Handojo Department of Chemical Engineering Institut Teknologi Bandung Bandung, Indonesia

Antonius Indarto Department of Chemical Engineering Institut Teknologi Bandung Bandung, Indonesia

Carlos Jacinto da Silva Grupo de Nano-Fotônica e Imagens Instituto de Física Universidade Federal de Alagoas Maceió-AL, Brazil

Uswa Javeed Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan

Yasir Javed Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan George Z. Kyzas Hephaestus Advanced Laboratory Eastern Macedonia and Thrace Institute of Technology Kavala, Greece

Efstathios V. Liakos Hephaestus Advanced Laboratory Eastern Macedonia and Thrace Institute of Technology Kavala, Greece

Jaise Mariya George School of Chemical Sciences Mahatma Gandhi University Kerala, India

Beena Mathew School of Chemical Sciences Mahatma Gandhi University Kerala, India

Athanasios C. Mitropoulos Hephaestus Advanced Laboratory Eastern Macedonia and Thrace Institute of Technology Kavala, Greece

Oscar F. Odio Instituto Politécnico Nacional Centro de Investigación en Ciencia Aplicada y Tecnología Avanzada Ciudad de México, México

Samir Kumar Pal
Department of Chemical, Biological and Macromolecular Sciences
S. N. Bose National Centre for Basic Sciences Kolkata, India

Ragam N. Priyanka School of Chemical Sciences Mahatma Gandhi University Kerala, India

E. Ramón-Gallegos Instituto Politécnico Nacional Laboratorio de Citopatología Ambiental Ciudad de México, México Edilso Reguera Instituto Politécnico Nacional Centro de Investigación en Ciencia Aplicada y Tecnología Avanzada Ciudad de México, México

Uéslen Rocha Silva Grupo de Nano-Fotônica e Imagens Instituto de Física Universidade Federal de Alagoas Maceió-AL, Brazil

Ilias T. Sarafis Hephaestus Advanced Laboratory Eastern Macedonia and Thrace Institute of Technology Kavala, Greece

Naveed A. Shad Department of Physics Government College University Faisalabad, Pakistan

Syedda Shaher Bano Department of Physics University of Agriculture, Faisalabad Faisalabad, Pakistan

Navadeep Shrivastava Institute of Physics Federal University of Goiás Goiânia, Brazil

Chandra Shekhar Pati Tripathi Department of Chemistry Institute of Science Banaras Hindu University Varanasi, India

Herlys Viltres Instituto Politécnico Nacional Centro de Investigación en Ciencia Aplicada y Tecnología Avanzada Ciudad de México, México

Erving Clayton Ximendes Grupo de Nano-Fotonica e Imagens Instituto de Fisica Universidade Federal de Alagoas Maceio-AL, Brazil

Part I

Biological Applications



1

Controlled Wet Chemical Synthesis of Multifunctional Nanomaterials: Current Status and Future Possibility

Navadeep Shrivastava and Surender Kumar Sharma

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1.1 Introduction

The term "nano" means "dwarf" in Greek. The present scientific and technological achievements in dayto-day human life are continuously being replaced through the use of nanoscience and nanotechnology. The Royal Society of Chemistry defines nanotechnology as "the design, characterization, production and application of structures, devices and systems by controlling shape and size at nanometer scale" (RSRAE, 2004). In fact, nano-based products are being considered as part of the next industrial revolution and are delivering huge impacts on society, the economy and life in general. Nanoscaled materials have the potential to be used in a wide spectrum of areas as in medicine, information technologies, biotechnologies, energy production and storage, material technologies, manufacturing, instrumentation, environmental applications and security. Basically, nanotechnology is not a core industry, but an enabled tool and technology that, combined with other technologies, has the potential to impact most other industries in various ways (Sarveena et al., 2017; Shrivastava et al., 2017). The many promising application areas of nanotechnology have boosted the public funding for research and development rapidly with the support of billions of dollars by several agencies. The basic rationale is that nano-materials, typically of size 1–100 nm in at least one dimension, feature exceptional structural and functional properties, very different to those in bulk materials or discrete molecules. Nanostructured materials have a significant commercial impact due to their unique properties such as finite size and surface effects. Finite size effects are related to the manifestation of so-called quantum size effects, which arises when the size of the system is commensurable with the de-Broglie wavelengths of the electrons, phonons or excitons propagating in them. Surface effects can be related, in the simplest case, to the symmetry breaking of the crystal structure at the boundary of each particle, but can also be due to different chemical and magnetic structures of internal "core" surface "shell" parts of nanoparticles (Liz-Marzán & Kamat, 2003).

The next generations of nanoparticles are about hybridization of two characteristics that mainly come due to individual characteristics of distinct entities. The design and synthesis of materials that simultaneously consists of more than one functional part, called multifunctional or bifunctional material (Shrivastava et al., 2017). Bifunctional nanoparticles have exhibited potentially promising physio-chemical properties, which can revolutionize and transform the landscape of the bio-clinical industry to next-generation advance devices. In particular, colloidal nanoparticles have been extensively investigated as probes in biomedical/devices industries due to their unique size-dependent electronic, optical and magnetic properties among all possible building blocks. Thus, hybrid nanoparticles with combined magnetic and optical properties are much more powerful and can be used in a broad range of applications.

There are also some potential negative environmental and health aspects that may follow the nanotechnology. Engineered nanomaterials can penetrate the skin, lungs and intestinal tract with unknown effects to human health as nanoparticles can travel around in the body and reach, for example, the brain (Oberdörster et al., 2005). The new engineered nanoparticles have novel properties not previously known and it is likely that exactly because of these novel properties they will cause impacts on ecosystems and organisms. Nanoparticles can cause other effects if they react with other substances or even carry other substances into organisms, soil or groundwater. In this chapter, we have focused on the synthesis of nanomaterials with special attention on hybrid nanoparticles and their current status and future possibility in biomedical and environmental applications.

1.2 Classification of Nanomaterials

Nanomaterials are mainly classified into two categories: (a) Organic nanomaterials, and (b) Inorganic nanomaterials. The central focus of this chapter is to present various synthesis methodologies of the modern-day inorganic nanomaterials; hence we are highlighting inorganic nanomaterials in detail in the next subsection.

1.2.1 Organic Nanomaterials

This era of nanoscience has an unbiased growing interest in all kinds of nanomaterial for the ease of day-to-day applications. Organic nanomaterials have shown their positive impacts in the past; hence researchers are highly interested in discovering novelty applications of such materials for biomedicals, sensors, energy storage, catalysis, and environment (Virlan et al., 2016). There is focus on the growing evidence of organic structured based nanomaterials (natural and synthetic) for regeneration of bone, cartilage, wound healing, skin or dental tissue in biomedical applications. Mostly, nanoforms of chitosan, silk fibroin, synthetic polymers, poly acrylic acids (PAAs), Poly (methyl methacrylate) (PMMA) or their combinations are in use but researchers are working on several other organic molecules and composites to reduce to the nano level because of the progress in synthetic chemistry. Novel methods in investigation and manipulation of individual molecules and small ensembles of molecules have produced major advances in the field of organic nanomaterials. The new visuals of optoelectronic characteristics of organic molecules using single-molecule spectroscopy (SMS) and scanning probe microscopy (SPM) have encouraged chemists toward novel molecular and supramolecular designs (Grimsdale & Mullen, 2005). Biodegradable polyesters, such as poly(lactic acid), poly(glycolic acid), their co-polymer PLGA and poly(e-caprolactone), have been of particular interest for drug delivery applications (Soppimath et al., 2001). Several organic films/nanosheets are of interest in the case of radiation detection. As the major focus of this book is on inorganic nanomaterials-based hybrid structures, hence we have confined our discussion on the detailed synthesis procedures and case studies of these nanohybrids for biomedical applications and environmental sciences.

1.2.2 Inorganic Nanomaterials

In this section, we discuss the general synthesis schemes of inorganic nanomaterials. A bottom-up wet chemistry approach has been adopted throughout the book chapter while discussing hybrid nanomaterials. This procedure promotes the preparation of nanoparticles by assembling the individual atoms or molecules in the presence of stabilizer or protecting agents. They prevent the agglomeration of nanoparticles by either steric or electrostatic repulsion among nanoparticles, as agglomeration is a main key issue in the nanoregime. Several chemical methods have been reported for the synthesis of nanomaterials via a bottom-up approach, such as co-precipitation, thermal decomposition, hydrothermal, microemulsion, etc. Wet chemical synthesis permits the manipulation of matter at the molecular level. Additionally, by understanding the relationship between how matter is assembled on an atomic and a molecular level and the material's macroscopic properties, molecular synthetic chemistry can be designed to prepare novel starting components. Better control of particle size, shape and size distribution can be achieved in particle synthesis.

1.3 General Inorganic Synthesis Schemes

There are several standard bottom-up or wet chemical methods to prepare functional nanomaterials. Before discussing the synthesis procedures and protocols to prepare different bifunctional nanomaterials, it is important to understand the general synthesis procedures for hydro (solvo) thermal, microemulsion, co-precipitation, polyol and microwave-assisted approaches, to provide a better idea of the synthesis protocols.

1.3.1 Hydro (Solvo) Thermal Synthesis

The heterogeneous/homogeneous chemical reaction in water (hydro) or non-aqueous medium under constant pressure and temperature is known as hydro (solvo) thermal synthesis (see Figure 1.1a). Usually, the reaction takes place in an autoclave (a sealed thick-walled steel vessel with a Teflon cup) at high temperatures (150–220°C) and high vapor pressure (>1 bar), allowing the subsequent growth of single crystals or crystallization of substances from the solution. Reaction conditions (temperature, pressure, pH, reaction timing, etc.) and solvent (reaction medium) choice are the key issues to tune the size, shape, phase composition, crystallinity, etc. of nanomaterials (Gai et al., 2014). The solvent selection varies from water to different organics, depending upon the need and specification of the reaction, although water still remains the most widely used solvent. In hydro (solvo) thermal synthesis, some organic additives or surfactants with specific functional groups, e.g., oleic acid (OA), polyethylenimine (PEI) or cetyltrimethylammonium bromide (CTAB) are generally added along with the reaction precursors to achieve simultaneous control over the crystalline phases, sizes and morphologies as well as the surface functional groups for the resulting nanoparticles (Ye et al., 2018). The broad range of nanomaterials can be synthesized with the hydro (solvo) thermal method, using optimized reaction conditions such as temperature, pressure and pH.



FIGURE 1.1 Schematic explanation of synthesis mechanism for the formation of nanoparticles by (a) hydrothermal and (b) microemulsion method.

1.3.2 Microemulsion Synthesis

A microemulsion is a thermodynamically stable dispersion of two immiscible liquids (e.g., water and oil) with the aid of a surfactant. Small droplets of one liquid are stabilized in the other liquid by an interfacial film of surfactant molecules. In water-in-oil microemulsions, the aqueous phase forms droplets (~1–50 nm in diameter) in a continuous hydrocarbon phase. Consequently, this system can impose kinetic and thermodynamic constraints on particle formation, such as a nanoreactor. The surfactant-stabilized nanoreactor provides confinement that limits particle nucleation and growth. By mixing two identical water-in-oil emulsions containing the desired reactants, the droplets will collide, coalesce and split, and induce the formation of precipitates (see Figure 1.1b). Adding a solvent like ethanol to the microemulsion allows the extraction of the precipitate by filtering or centrifuging the mixture. The main advantage of the reverse micelle or emulsion method is better control over the nanoparticles' size by varying the nature and amount of surfactant and co-surfactant, the oil phase or the other reacting conditions. The working window for synthesis in microemulsions is usually quite narrow and the yield of nanoparticles is low compared to other methods, such as hydrothermal and co-precipitation methods. Furthermore, because large amounts of solvent are necessary to synthesize appreciable amounts of material, microemulsion is not a very efficient process and is rather difficult to scale-up (Liu et al., 2008; Kharissova et al., 2013).

1.3.3 Co-Precipitation Method

Generally, co-precipitation can be defined as "the simultaneous precipitation of more than one substance from homogeneous solution," which results in the formation of a crystal structure of a single phase (e.g., Fe₃O₄). Co-precipitation is probably the most convenient and efficient chemical pathway to synthesize a broad range of nanomaterials, including magnetic nanoparticles, due to relatively mild reaction conditions, low cost of required equipment, simple protocols and short reaction times (Laurent et al., 2008). Therefore, this method is not only a preferred route to synthesize magnetic iron oxide nanoparticles, but it is also commonly used to prepare a broad range of rare earth ion (RE³⁺)-doped luminescent nanomaterials, such as alkaline-earth tungstates: MWO_4 :RE³⁺ (M²⁺: Ca, Sr and Ba) or rare earth fluorides: NaYF₄:RE³⁺, LaF₃:RE³⁺. The great advantage of the co-precipitation method is the obtainment of a large number of nanoparticles (Mascolo et al., 2013). However, polydispersity and wide particle size distribution are usually obtained with this method due to the kinetic factors that control the growth of the crystal. Generally, two processes are involved in the growth and formation of the particles: rapid nucleation (aggregation of nanometric building blocks such as pre-nucleation clusters), which occurs when the concentration of the species reaches critical supersaturation. The other one is the slow growth of the nuclei by diffusion of the solutes to the surface of the crystal. Therefore, to produce monodisperse nanoparticles, controlling these processes is very important. In a supersaturated solution when the nuclei form at the same time, subsequent growth of these nuclei results in the formation of particles with very narrow size distribution. Co-precipitation methods are popular because these methods allow for the production of large quantities of nanoparticles with a moderate degree of particle uniformity. The major disadvantage of co-precipitation is the lack of fine particle size control as size is primarily determined by kinetic factors. These reactions are typically performed in aqueous environments and utilize a base to initiate the reaction.

1.3.4 Polyol Synthesis

Polyol synthesis (a special kind of sol-gel synthesis) is an excellent method for the synthesis of nanoparticles from metallic salts by using a poly-alcohol, which acts as amphiprotic solvents (Ghosh Chaudhuri & Paria, 2012), as well as complexing, reducing and surfactant agents, depending on the studied system. The poly-alcohols used in this process are ethylene glycol (EG), diethylene glycol (DEG), 1,2-propanediol, tetraethylene glycol and glycerol. Owing to the high boiling point and high dielectric constant of these solvents, they offer a wide range of reaction temperature. Hydrolysis and reduction reactions can be performed in these liquids, allowing the production of a wide variety of size and shape-controlled inorganic nanoparticles from the nano- to the microregime. In this method (Dong et al., 2015a), the precursor compound is suspended in the liquid polyol and heated to the boiling point of the polyol at constant stirring. During this process, the precursor gets dissolved in the polyol leading to the formation of an intermediate followed by reduction to form nanoparticles. This method allows preparation of biocompatible nanoparticles by coating hydrophilic polyol over the nanoparticles, producing particles with higher crystallinity that leads to a better saturation magnetization and narrow particle size distribution as compared to the traditional methods. This process is heralded for its self-seeding mechanism and lack of required "hard" or "soft" templating materials, making it an ideal process for industrial scale-up owing to the low cost of processing.

1.3.5 Microwave-Assisted Method

In recent years, a microwave-assisted synthesis method has been widely used over conventional heating methods to produce nanomaterials with higher yield (Dallinger and Kappe, 2007). A specially designed microwave synthesis reactor allows exquisite control of the reaction temperature, stirring rate and pressure inside the reaction vessel, which is the unique feature of microwave apparatus over conventional heating principles. The heating effect in the microwave arises from the interaction of the electric field component of the microwave with charged particles in the material through both conduction and polarization. The use of microwave heating as a non-classical energy source has been shown to dramatically reduce reaction times, increase product yields and enhance purity or material properties compared to conventionally processed experiments. In conventional methods, the heating of chemical reactions has been achieved using mantles, oil baths, hot plates and reflux set-ups, where the highest reaction temperature achievable is dictated by the boiling point of the solvent used. This traditional form of heating is rather slow and has low efficiency for transferring energy to a reaction mixture as it depends on convective currents and on the thermal conductivity of various compounds or materials that have to be penetrated. This often results in the temperature of the reaction vessel being higher than that of the reaction solution. In contrast, microwave irradiation produces efficient volumetric heating by raising the temperature uniformly throughout the whole liquid volume by direct coupling of the microwave energy to the molecules that are present in the reaction mixture (Gawande et al., 2014).

A single mode microwave reactor closed-vessel microwave synthesis purchased from Synth-wave has been utilized and discussed here: It consists of a single reaction chamber (SRC) which is a large, pressurized stainless steel reaction chamber into which all reactions mixture are placed and prepared simultaneously. The pressurized chamber in SRC serves as the reaction vessel and the microwave cavity and the reaction vessel enables the intensity and distribution of the microwave energy to be optimized with the shape and size of the reaction vessel. There are several benefits of using SRC (Nishioka et al., 2013). Some of them are: (i) it can run multiple parameters or reactions simultaneously; (ii) since all reactions are in the same vessel, nearly any reaction type can be processed simultaneously; (iii) a large range of temperature and pressure; (iv) several stoichiometry combinations and element changes can be modified for inorganic hydrothermal syntheses in a single run, saving weeks of research labor; and (v) control of every reaction is made possible by direct pressure and temperature control.

1.3.6 Thermal Decomposition Synthesis

This is one of the most rated and well-established methods for the synthesis of monodispersed nanoparticles with uniform shape, tailored size and single crystal structure. In this method, organometallic precursors in the presence of organic solvents (such as 1-octadecane [ODE]), and a surfactant (e.g., OA and oleylamine) form organometallic complexes which are rapidly broken down in a hot solvent-containing surfactant at high temperature (usually the boiling points of the solvents). In general, the synthetic process is conducted at elevated temperatures (250–330°C) in an oxygen-free and anhydrous environment, wherein the precursors decompose to form the nucleus for a particle to grow on (Zhang et al., 2005; Unni et al., 2017). The size and shape of the nanoparticles can be controlled by varying the molar ratios of precursor and surfactants and solvents. The most commonly used precursors include lanthanide trifluoroacetate, iron acetoacetonate, iron pentacarbonyl, lanthanide oleates, iron chlorides, lanthanide acetates and lanthanide chlorides. The use of a surfactant can form a protective layer around the nanoparticle, and plays an important role as a dispersant. The surfactants usually contain a functional group to cap the surface of the nanoparticle, for example, up conversion nanoparticles for controlling their growth and a long hydrocarbon chain to assist their dispersion in organic solvents.

1.4 Illustrations of Magnetic and Non-Magnetic Nanomaterials

1.4.1 Synthesis of Magnetic Nanoparticles

The preparation methods of iron oxide nanoparticles are quite simple and easy to handle. They can be obtained by chemical, physical and biological methods (Bhargava et al., 2013; Xu & Sun, 2013). There are several methods and the majority of researchers are interested in exploring the cheap, green and non-toxic protocols and its characteristics for biomedicals, sensors, devices and environmental applications. Among these methods, co-precipitation and thermal decomposition methods are utilized more and these are well understood mechanisms. The initial solution consists of iron sources dissolved in an aqueous solution. Typical iron sources for synthesis are: FeCl₃, FeCl₂, Fe(acac)₃, (acac=acetylacetonate) or Fe(CO)₅. In the co-precipitation synthesis developed by Massart (1981), these precursors (FeCl₃, FeCl₂, Fe(acac)₃) are able to easily dissociate in solution, forming Fe cations leading the reaction in a basic environment to form an iron oxide. Here, the addition of a base to an aqueous solution of ferrous (Fe²⁺) and ferric (Fe³⁺) ions in a 1:2 stoichiometry produced a black precipitate of spherical magnetite (Fe₃O₄) in the absence of oxygen (Massart, 1981). The quality of the final product depends on rapid bursting followed by a particle growth phase, explained by Lamer (Lamer & Dinegar, 1950; Vreeland et al., 2015) (see Figure 1.2). For example, Fe₃O₄ is formed according to the reaction:

$$Fe_2 + 2Fe_3 + 8OH \rightarrow Fe_3O_4 + 4H_2O.$$

In this reaction, nuclear bursting and particle growth phases are overlapping little or there is no overlap. If these phases are not well separated, control of particle size will be severely hindered. The type and properties of the iron oxide nanoparticles produced can be controlled by varying the reaction conditions. One of the most important conditions to control during the synthesis of iron oxides is the oxygen content of the reaction mixture (Laurent et al., 2008). Synthesis of Fe₃O₄ is typically performed in oxygen controlled environments due to the inherent instability of Fe₃O₄ in oxygen. Moreover, Fe²⁺ is oxidized to



FIGURE 1.2 Synthesis of iron oxide nanoparticles.

 Fe^{3+} in aqueous solutions, altering the Fe^{2+}/Fe^{3+} ratio in the reaction mixture, resulting in the potential formation of unwanted species of iron oxides. Thus, nitrogen or argon gas are typically used to purge the reaction mixture. Control over particle size, morphology and uniformity is achieved by altering such factors as the Fe^{2+}/Fe^{3+} ratio, temperature, time and stir speed (Jeong et al., 2004; Zhu et al., 2011).

As stated in Section 1.3.6, the thermal decomposition method is mainly used to obtain precise growth and control over nanoparticles. Recently, Unni and co-workers produced iron oxide nanoparticles with a diminished magnetic dead layer by the controlled and careful addition of molecular oxygen during high temperature synthesis (Unni et al., 2017), which is a step ahead of previous thermal decomposition syntheses (Hufschmid et al., 2015; Lassenberger et al., 2017). The conventional thermal decomposition method of organometallic precursors of iron oxide nanoparticle synthesis with no oxygen and in situ condition, in the past, provided excellent control over shape-size tunability but it was not sufficient to compare with the magnetic characteristics of the bulk data. This conventional method gives a "magnetically dead layer" (Luigjes et al., 2011), crystal defects and mixed iron oxide phases (magnetite/maghemite phases). The dead layer is determined experimentally or through modeling where the magnetic diameter is significantly smaller than the physical diameter. In their novel synthesis, Unni and co-workers (2017) first prepared iron oxide nanoparticles by preparing the iron oleate precursors using Park and co-workers' method (Park et al., 2004) which utilizes iron chloride hexahydrate [Fe(Cl_3)· $6H_2O$], water, sodium oleate, hexane and ethanol at around 60°C (see Figure 1.3). Next, iron oxide was produced by the heating-up thermal decomposition route in the absence of oxygen. This iron oxide includes iron oleate with OA dissolved in trioctylamine as the non-reacting solvent in a three-neck reactor in the presence of a controlled environment of N_2 gas, stirring at 340°C for 1 h at a constant increment of temperature. Further, hexane and acetone were used to wash nanoparticles. In the next crucial step, they prepared magnetic nanoparticles by the extended LaMer thermal decomposition route in the absence of oxygen. The main steps consist of (a) 48.3 mmol of docosane heated to 350°C for 50–60 min at a ramp rate of



FIGURE 1.3 (See color insert.) Controlled growth of both physical and magnetic diameter for iron oxide nanoparticles obtained using the Extended LaMer mechanism based synthesis thermal decomposition synthesis in the presence of molecular oxygen for 2 h. Reused with permission from Unni et al., 2017, American Chemical Society.

7–8°C/min in a 100 mL three-neck reaction flask under controlled inert gas atmosphere and (b) the controlled addition (using a syringe pump) of 30 mL of iron oleate precursor (0.63 M Fe) mixed with 55 mL of 1-ODE at 350°C. The resulting solution was stirred at a constant rate for 5 h. After this, the mixture was cooled to room temperature, and iron oxide nanoparticles obtained at the end of the reaction were purified by suspending 5 mL of the black waxy liquid in 10–20 mL of hexane. The particles were precipitated using 20–40 mL of acetone by centrifuging in an Eppendorf. Postsynthesis oxidation of iron oxide nanoparticles was used in order to improve the magnetic properties. Nanoparticles suspended in organic solvents were thermally treated at 120°C with and without bubbling air for particles synthesized by an Extended LaMer mechanism.

Oxidation by Bubbling in Air: Approximately 15 mg/mL of iron oxide nanoparticles were suspended in 2 mL of OA and placed in a heating block from Fisher for 4 h at 120°C with air being bubbled in the samples. There was significant color change of the sample from dark brown to light brown, and high rates of OA boil off were observed.

Oxidation by Solvent Transfer without Bubbling in Air: Approximately 5 mg of as-synthesized iron oxide nanoparticles were suspended in 2 mL of hexane and sonicated for 10 min. Further, 2 mL of 1-ODE was added to the vial and the particles were left in an oven for 2 h at 120°C. The particles remained well-suspended in 1-ODE, and color change was observed during oxidation.

The difference between Unni and co-workers and other researchers is the use of the oxygen molecule during synthesis (Unni et al., 2017). They also prepared iron oxide nanoparticles using the same general method, but instead of using a perfectly inert atmosphere of argon gas, 20% oxygen gas and 80% argon gas at a constant rate was supplied in a controlled way (see Figure 1.3).

The studies reported here demonstrate the critical role that molecular oxygen plays in determining the magnetic properties of iron oxide nanoparticles obtained through thermal decomposition syntheses. Experiments carried out in "inert" atmospheres using argon and nitrogen as inert blanket and carrier gases demonstrated that the resulting particles possessed magnetic diameter distributions that were smaller and broader than the corresponding physical diameter distributions. Further, experiments with postsynthesis oxidation demonstrated that while an improvement in magnetic diameter distributions can be obtained with such methods, this improvement is difficult to control and limited for larger particles. The results demonstrate that the safe and judicious addition of molecular oxygen as a species in the thermal decomposition synthesis leads to nanoparticles with practically equal physical and magnetic diameter distributions, magnetic properties that resemble those expected for bulk magnetite and improved application-relevant properties such as thermal energy dissipation rate and resolution for magnetic particle imaging (see Figure 1.3).

In another work, magnetic cobalt ferrite (CoFe₂O4) nanoparticles have been successfully synthesized by thermal decomposition of Fe (III) and Co (II) acetylacetonate compounds in organic solvent in the presence of OA/OLA as surfactants and 1,2-hexadecanediol (HDD) or octadecanol (OCD-ol) as accelerating agent (Lu et al., 2015). Lu and co-workers studied the influence of surfactant concentration (dioctyl ether) and reaction time on the morphology of the nanoparticles. In the case of using dioctyl ether, the volume of the solvent was reduced to 20 mL but the concentration of reaction agents was kept constant. Hachani and his colleagues (Hachani et al., 2015) synthesized iron oxide nanoparticles of low polydispersity through a simple polyol synthesis in high pressure and high temperature conditions (see Figure 1.4). The control of the size and morphology of the nanoparticles was studied by varying the solvent used, the amount of iron precursor and the reaction time; this process yields nanoparticles with a narrow particle size distribution in a simple, reproducible and cost-effective manner without the need for an inert atmosphere. They used triethylene glycol (TREG), diethylene glycol (DEG) and tetraethylene glycol (TEG) as solvents. Fe(acac)₃ was used as precursor. A polyol and Fe(acac)₃ was mixed to obtain a red dispersion that was then placed into a 45 ml capacity Teflon liner and the latter was assembled with the autoclave jacket and placed into an oven at 300°C and maximum working pressure of 115 bar for 2 h. The resulting black dispersion was washed with acetone and centrifuged. This procedure yielded iron oxide nanoparticles coated with polyols (see Figure 1.4).

In a work by Mameli and co-workers (Mameli et al., 2016), a thermal decomposition method was utilized to prepare Zn-substituted cobalt ferrite $(Zn_xCo_{1-x}Fe_2O_4)$ nanoparticles (see Figure 1.5). They studied complex magnetic properties' dependence on the properties of the material with the variation of Zn-amount with constraints of the same particle size and distribution, crystallite size and capping agent.



FIGURE 1.4 (See color insert.) (A) Magnetization curves of iron oxide NPs obtained with different polyols (DEG, TREG and TEG). (B) TEM images of iron oxide nanoparticles synthesized using TEG. (C) and (D) TEM images of iron oxide nanoparticles synthesized using different reaction times in tri (EG): (C) 1 h, (D) 2 h. (Reproduced from Hachani et al., 2015. With permission.)

Magnetic properties at 300 K were engaged and correlated to specific absorption rate (SAR) values by combining results originally observed from dc/ac magnetometry and ⁵⁷Fe Mössbauer spectroscopy in different time spans of experimental acquisitions (see Figure 1.5). Synthesis was carried out using acety-lacetonate precursors of Fe, Co and Zn; 1,2-hexadecanediol, oleic acid, oleylamine and dibenzylether in a calculated amount. During syntheses, much attention was given to the control temperature that was elevated from room temperature to 200°C for 2 h and then to 280°C, for 1 h.

1.4.2 Synthesis of Semiconducting or Quantum Dot Nanoparticles

Quantum dots (QDs) have emerged as one of the most exciting fluorescent nanoparticles (in the order of 2–10 nanometers containing approximately 200–10,000 atoms) with a potential for diagnostic and therapeutic application in the field of nanomedicine. In general, QDs are produced using atoms from group II and VI of the periodic table, e.g., cadmium–selenide (CdSe), cadmium tellurium (CdTe), zinc–selenium (ZnSe), group III–V elements, e.g., indium phosphate (InP), indium arsenate (InAs), gallium arsenate (GaAs), gallium nitride (GaN) or group IV–VI elements, e.g., lead–selenium (PbSe). The most commonly used QDs are CdSe or CdTe with a passivation shell made of ZnS which protects the core from oxidation and increases the photoluminescence quantum yield. The surface of the QD is further coated with solubilization ligands, making them water soluble for their use in biology and environmental sciences. QDs have emerged as one of the most exciting nanoparticles with a potential for diagnostic and therapeutic application in the field of nanomedicine (LaRocque et al., 2009). The current fluorophores



FIGURE 1.5 (See color insert.) (a-d) Morphological properties/TEM images of $Zn_xCo_{1-x}Fe_2O_4$ (with x = 0, 0.30, 0.46, 0.53) samples using the JEM-2010 UHR, (e) Magnetization versus magnetic field curves of $Zn_xCo_{1-x}Fe_2O_4$ (with x = 0, 0.30, 0.46, 0.53) samples measured at 300 K. (f) Heating curves of $Zn_xCo_{1-x}Fe_2O_4$ (with x = 0, 0.30, 0.46, 0.53) samples measured at 300 K. (f) Heating curves of $Zn_xCo_{1-x}Fe_2O_4$ (with x = 0, 0.30, 0.46, 0.53) samples measured at 300 K. (f) Heating curves of $Zn_xCo_{1-x}Fe_2O_4$ (with x = 0, 0.30, 0.46, 0.53) samples measured at 300 K. (f) Heating curves of $Zn_xCo_{1-x}Fe_2O_4$ (with x = 0, 0.30, 0.46, 0.53) samples at 25°C, obtained under a magnetic field of 183 kHz and 17 kA m⁻¹. (Reused with permission from open access reference Mameli et al., 2016.)

such as organic dyes, fluorescent proteins and lanthanide chelates suffer the problems of instability, photobleaching and sensitivity to environmental conditions such as pH variations. The unique optical and spectroscopic properties of QDs offer a compelling alternative to traditional fluorophores due to their high quantum yield, high molar extinction coefficient (~600,000 M^{-1} cm⁻¹, roughly an order of magnitude higher than even the strongly absorbing Rhodamine, exceptional resistance to photobleaching as well as to photo and chemical degradation (Huo, 2007; Zrazhevskiy et al., 2010). In addition, the intensity of fluorescence produced by the QDs is 10–20 times brighter than the organic dyes. Conventional dyes suffer from narrow excitation spectra. This requires excitation by light of specific wavelength, which varies between particular dyes. In addition, they have broad emission spectra. This means the spectra of different dyes may overlap to a large extent limiting the number of fluorescent probes that may be used to tag different biological molecules.

An ideal strategy for the synthesis of semiconductor nanoparticle should have the following characteristics: (i) control of the size and shape, (ii) high monodispersity and good crystallinity, (iii) high luminescence quantum yield and (iv) reproducibility. Chemical methods allow the preparation of a broad range of semiconductor nanoparticles and core–shell nanostructures with excellent control over size, shape and dispersity. This method also enables the functionalization of surfaces of semiconductor nanoparticles with various ligands, and the design of higher order nanostructures through self-assembly. Colloidal synthesis offers a versatile route, where nanoparticles are grown using the chemical reaction of their precursors in an appropriate solvent. It follows the usual nucleation and crystal growth mechanism where the latter process is controlled through the use of an appropriate surfactant or capping agent (sometimes the solvent molecule itself serves as capping agent). Control over the size, shape, dispersity and crystallinity can be achieved by adjusting the reaction conditions such as time, temperature, the concentration of the precursor, chemical nature of the capping ligands and surfactants.

A breakthrough in producing monodispersed QDs of cadmium chalcogenide such as CdS, CdSe and CdTe (II–VI semiconductors) was reported by Bawendi and co-workers in 1993 (Murray et al., 1993). They were able to synthesize highly crystalline QDs using organometallic precursors in the presence of a coordinating solvent, trioctylphosphine oxide (TOPO). The reaction was carried out at elevated



FIGURE 1.6 (See color insert.) Figure presents an experimental set-up for QD synthesis by high temperature organometallic method, along with a schematic illustration of CdSe QD capped with TOPO (bound to Cd^{2+}) and TOP (bound to Se^{2+}). (Adapted from Kuno, 2008.)

temperatures (~360°C) under vacuum, using selenium precursor (TOPSe, selenium coordinated to trioctylphosphine) which was injected rapidly into a solution of dimethylcadmium in TOPO (see Figure 1.6). This resulted in burst nucleation followed by crystal growth leading to the formation of crystalline QDs. TOPO served as the main capping agent and the QDs produced possessed narrow size distribution ($\sigma_r < 10\%$), having excellent solubility in nonpolar solvents. Low surface defects, compared to other synthetic methods is another advantage of the high temperature organometallic synthesis. Excellent control over crystal growth was achieved by controlling the precursor concentration, temperature, reaction duration etc. Further, the organic capping agent, which is electrostatically bound to the QD surface, could be replaced by functionalization with a thiol. It is possible to introduce photoactive or electroactive groups on to the surface of a nanoparticle by following this method (place exchange reaction). Numerous attempts have been made to replace dimethyl cadmium with other organometallic precursors due to its extreme toxicity, pyrophoric nature, expensiveness and instability (Hambrock et al., 2001; Peng & Peng, 2001). A marked improvement in the above synthesis strategy was achieved by Peng and co-workers by using a nonpyrophoric and stable cadmium precursor, cadmium oxide, instead of dimethylcadmium (Peng & Peng, 2001).

A significant reduction in reaction temperature (~300°C) as well as in size distribution ($\sigma_r < 5\%$) was observed for the resulting nanocrystals. This was attributed to the thermal stability as well as slow decomposition of the cadmium oxide compared to dimethylcadmium, which led to a slow and homogeneous nucleation and crystal growth (avoiding Ostwald's ripening) (Chen et al., 2008). Several other synthesis protocols were reported by varying the cadmium precursor (e.g. cadmium acetate, cadmium stearate), reaction medium (e. g. 1-ODE, olive oil) and capping agents such as amines, fatty acids, phosphonic acids, etc. (Chen et al., 2008). The design and fabrication of anisotropic semiconductor nanostructures such as nanorods (quantum rods), nanowires (quantum wires), dipods, tripods and tetrapods have drawn attention in recent years. These nanostructures have a lot of potential, particularly for fabricating nanoelectronic, photovoltaic and energy storage devices due to their shape-dependent properties. For example, CdSe nanorods possess polarized emission related to their cylindrical symmetry which makes them a novel photonic material (for, e.g., laser systems) (Alivisatos, 1996).

Recently, Ramasamy et al. (2018), demonstrated a two-step approach to synthesize highly monodisperse InP QDs (<10%) absorbing from 490 to 650 nm (size range of ~1.9 to 4.5 nm). Initially, InP QDs with an average size of 1.9 nm were synthesized and later used as "seeds" to grow larger QDs (see Figure 1.7) by continuously injecting Zn(In)–P complexes as monomers source.

A very nice protocol regarding the synthesis of chiral QDs has been developed by Gun'ko and coworkers (Moloney et al., 2015). They reported the procedure for the synthesis of chiral optically active



FIGURE 1.7 Schematic of "Seed-Mediated" synthesis of larger InP QDs and InP/ZnSe/ZnS QDs. (From Ramasamy et al., 2018. With permission.)

QD nanostructures and their quality control using spectroscopic studies and transmission electron microscopy imaging. They closely examined various synthetic routes for the preparation of chiral CdS, CdSe, CdTe and doped ZnS QDs, as well as of chiral CdS nanotetrapods. Most of these nanoparticles can be produced by a very fast (70 s) microwave-induced heating of the corresponding precursors in the presence of d- or l-chiral stabilizing coating ligands (stabilizers), which are crucial to generating optically active chiral QDs. Alternatively, chiral QDs can also be produced via the conventional hot injection technique, followed by a phase transfer in the presence of an appropriate chiral stabilizer.

Cui's group reported the first example of Ag-doped ZnInSe QDs, which not only have extremely high stability but also have tunable emission in a broad emission scope (Wang et al., 2014a). Due to their extremely high stability, good biocompatibility, low cytotoxicity and tunable emission, as-prepared Ag:ZnInSe QDs are expected to be applicable in optical coding, white light emitting diode (LED) and bioimaging. Nitrates of Zn and Ag were used as precursors in 3-mercaptopropionic acid (MPA). It was observed that pH plays a very important role and can be managed by NaOH solution. NaHSe solution was injected into the mixture after the solution was a controlled atmosphere of N_2 gas for 30 min. Then, the solution was refluxed at 100°C.

1.4.3 Synthesis of Upconverting Rare Earth Nanoparticles

The major focus of biomedical applications is in upconverting nanoparticles where a near infrared (NIR) laser is used to excite the nanoparticles. NIR downconverting nanoparticles are in focus nowadays. A wide variety of synthesis protocols are on trend for nanoparticles such as co-precipitation, thermal decomposition, hydro(solvo)thermal synthesis, microwave-assisted, combustion synthesis and urea homogeneous precipitation with their competitive advantages/disadvantages (Wang & Liu, 2009; Niu et al., 2014; Zhou et al., 2015). Two different protocols can also be combined for preparation. Postsynthesis processes are used as well for the development of upconversion nanoparticles with controlled particle size, chemical composition or surface functionalization. The most convenient and highly cited method from the beginning for producing ultra-small particles is co-precipitation, which has been used by several groups for the synthesis of nanoparticles (5-10 nm) with better size distribution. While having no need for costly equipment and complicated procedures, this method has a fast growth rate and requires post-annealing processes. In a typical process, a solution of lanthanide salts is injected into a solution of the host material. Examples of hosts used are LaF₃, NaYF₄, LuPO₄ and YbPO₄ (Haase & Schäfer, 2011). Particle size and growth rate can be regulated by using capping ligands or chelating agents such as polyvinylpyrrolidone (PVP), polyethylenimine (PEI) or ethylenediaminetetraacetic acid (EDTA) (Dong et al., 2015b). In particular, PEI provides a good platform for direct surface functionalization of nanoparticles with bioligands. However, a heat treatment step is required for post processing, which is one of the disadvantages of this method.

Thermal decomposition is another synthetic method that produces highly monodispersed particles with no need for post-annealing processes. In a typical procedure, metal precursors, mostly triuoroacetate, are thermolyzed together with OA and ODE (Wang et al., 2014b). OA acts as the primary solvent that prevents agglomeration of particles and ODE acts as the high boiling solvent (350° C). The advantages of oleate-based synthesis include narrow particle size distribution, high luminescence efficiency and high phase purity of the particles. Although this method produces high quality particles, it requires expensive air sensitive precursors, results in mostly hydrophobic particles and has toxic by-products (Wang et al., 2010; Wang et al., 2011a,b). Examples of the reported hosts for this method are LaF₃, NaYF₄ and GdOF (Eliseeva & Bunzli, 2009; Park et al., 2009).

The hydro (solvo) thermal method is a good method for preparation of highly crystalline materials at a much lower temperature and with no need for post annealing. The process is performed in an autoclave reaction vessel that maintains the required temperature and pressure for a desired period of time. By keeping solvents in temperatures and pressure above their critical point, the autoclave enhances the solubility of solid and increases the reaction rate between solids. Since the reaction happens in a closed cylinder, growth monitoring is virtually impossible. Particle size and morphology can be manipulated in this method by using polyol- or micelle-mediation. Some of the popular hosts reported for this method include LaF₃, NaYF₄, La₂(MoO₄)₃ and YVO₄ (Liu et al., 2009; Chen et al., 2017; Shrivastava et al., 2018). In contrast to time-consuming solvo(hydro)thermal methods, microwave-assisted synthesis is fast and provides good control over size and shape tunability. The particle sizes and shapes depend on the reaction temperature, which is governed by the ratio of the metal ions to solutions involved (Shrivastava et al., 2017, 2018).

Recently, You and co-workers prepared uniform lanthanide (Ln+)-doped NaREF₄ (RE=rare earth) nanocrystals (You et al., 2018). They reported this synthesis via a facile solid–liquid thermal decomposition (SLTD) method by directly employing NaHF₂ powder as a fluoride and sodium precursor. The proposed SLTD strategy is easy to perform, time-saving and cost-effective, making it ideal for scale-up syntheses. Particularly, over 63 g of β -NaGdF₄:Yb,Er@NaYF₄ core–shell NCs with narrow size variation (<7%) were synthesized via a one-pot reaction. This sodium precursor, which decomposes to NaF and HF at an elevated temperature and may react with RE compounds in the liquid phase (OA and ODE) for the nucleation and growth of Ln³⁺-doped NaREF₄ nanoparticles. The crystalline structure, particle size and morphology can be well tuned by adjusting the reaction temperature or the added amounts of sodium acetate (NaAc). The synthesis scheme and quality of the product have been presented in Figure 1.8.

1.4.4 Synthesis of Plasmonic Nanoparticles

Plasmonic nanoparticles are metal particles whose electron density can couple with electromagnetic waves (in most cases, infrared or visible light) of wavelengths far larger than the size of the particles; unlike in the usual case where there is a limit of the wavelength that can be coupled to a piece of metal depending on its size (Eustis and El-Sayed, 2006). This is due to the properties of the metal-dielectric interface between the particles and the surrounding medium. The plasmonic effect can occur only when the light frequency is lower than or equal to the plasma frequency of the nanoparticles. For the light of a higher frequency than the resonance frequency, the destructive interference of electron oscillation will occur inside the particle and there will be no plasmonic effect. The reason why plasmonic nanoparticles are important in biomedicals or environmental applications is that they have a very strong optical absorption at the resonance wavelength. Some other characteristics of plasmonic nanoparticles (Au, Ag, Pt) can be stated as: they are chemically inert and therefore samples labeled with Au nanoparticles are very stable and have a very long self life and lifetime; they have a very strong plasmonic resonance and, hence strong absorption, making them ideal labels for detection and the third is that they can be easily functionalized so that they can specifically bind to the target biomarkers (Merkel et al., 2009). The most straightforward approach for the synthesis of plasmonic nanoparticles is the direct one-pot-one-step synthesis. Depending on the reaction conditions (e.g., temperature, solvent, additives), certain morphologies can be obtained as spheres, stars, rods, plates and prisms. Usually poly vinyl pyrrolidone (PVP) is utilized as a reducing and a capping agent for plasmonic nanoparticles, playing an important role in the nucleation, the growth and the final shape of nanoparticles due to its interaction with metal ions and surfaces as well as the preferable attachment to distinct crystal facets of certain metals (e.g., silver) (Pastoriza-Santos & Liz-Marzán, 2002; Behera & Ram, 2013). The most common strategy to synthesize



FIGURE 1.8 (See color insert.) (a) Schematic procedure for the synthesis of Ln^{3+} -doped NaREF₄ NPs. (b) XRD of NaGdF₄:Yb,Er NPs synthesized at different temperature. The black and red vertical lines in (b) represent the standard pattern of β -NaGdF₄ (JCPDS No. 027-0699) and α -NaGdF₄ (JCPDS No. 027-0697), respectively. (c) TEM image of α -NaGdF₄:Yb,Er NPs synthesized at 250°C. (d–f) TEM images of NaGdF₄:Yb,Er NCs synthesized at 290, 300, and 310°C, respectively. (g–k) TEM images of the as-prepared β -NaSmF₄, β -NaEuF₄, β -NaGdF₄, β -NaTbF₄ and β -NaYF₄ NOs, respectively. (Reproduced with permission from You et al., 2018.)

metal nanoparticles is to dissolve and reduce metal salt in the presence of molecules that can prevent the nanoparticles from aggregating. The concentration ratio of reduction agent to metal salt affects the growth kinetics of the nanoparticles, and thus affects their size. Often the reduction agent also stabilizes the nanoparticles, thus filling a dual role. As an illustration, gold nanoparticles of sizes at the nanoscale (10–200 nm) can show the surface plasmon, particularly, localized surface plasmon resonances (LSPRs) upon illumination (Figure 1.9). These are usually coherent (particular range of light illumination) with free conduction band electrons. (Abadeer & Murphy, 2016).

Synthesis of Au Nanoparticles: One example is the method first described by Turkevich et al. in 1951 where gold chloride (HAuCl₄) was reduced by sodium citrate generating fairly monodispersed gold nanoparticles suspended in an aqueous solution. This method was later improved by Frens who produced gold nanoparticles with a diameter of ~10–150 nm (Frens, 1973). In this procedure, citrate acts both as a reducing agent and electrostatic stabilizer where the size of the particles can be controlled by varying the ratio between the gold salt and the citrate. The reaction temperature is also important for the formation of the metal nanoparticles since both the reaction kinetics and oxidation potential are dependent upon the temperature. The excess of citrate anions forms a complex multilayer around the particles which prevent aggregation and gives the particles a net negative surface (Martinsson, 2014).

A more efficient method to control the size and shape of gold nanospheres was proposed in 2000 by Natal and co-workers using a seed growth process (Brown et al., 2000). Small seed nanoparticles are first synthesized and further grown via the reduction of the metal salt in the presence of surfactants to stabilize the nanoparticles. Seeds are generated using a first reducing agent (sodium borohydride or sodium citrate) whereas the growth is done with a second milder reducing agent (often ascorbic acid). The ascorbic acid reduces the metal salt in an intermediate state which becomes metallic gold (Au⁰) only after a catalyzed reduction occurs at the surface of the seeds. Even if the work of Natan et al. gave good spherical gold nanoparticles, gold nanorods were also obtained during the synthesis, affecting strongly



FIGURE 1.9 Schematic of the localized surface plasmon resonance on gold nanospheres. Upon illumination at resonant wavelengths, conduction band electrons on the gold nanoparticle surface are delocalized and undergo collective oscillation. (From Abadeer & Murphy, 2016. With permission.)

the resulting batch monodispersity. In 2011, Bastús and colleagues successfully synthesized citrate-stabilized monodisperse gold nanospheres via seed growth (Bastús, et al., 2011). The factors influencing the size distributions of nanoparticles are the initial seeds concentration, the number of growth steps and of secondary nucleation. CTAB (hexadecyl-trimethyl-ammonium bromide) was used as a surfactant during the seed growth and enables better control of the final morphology of the gold nanoparticles. This new process gave gold nanoparticles a more spherical appearance while forming fewer gold nanorods. However, this method leads to the nanoparticles that are not easily functionalizable a posteriori, which can be disadvantageous. Indeed, the CTAB is strongly anchored and attached onto the surface of gold nanoparticles and ligand exchange with another molecule having an affinity for the gold surface is not straightforward, requiring multiple steps and specific synthesis conditions. In 2016, Malassis et al. demonstrated that it is possible to obtain rather spherical monodisperse gold nanoparticles of different sizes through the reduction of gold salt using ascorbic acid by tuning the pH of the mixture (Malassis et al., 2016). The real advantage of this synthesis was its easy implementation. Indeed, the synthesis method only involves one step as compared to the multiple synthesis steps necessary in the seed growth process. Moreover, ascorbic acid is very easily exchanged by other stabilizing agents allowing multiple postfunctionalizations of the obtained gold nanoparticles.

Recently, Xiahou et al. have reported high quality gold nanoparticles with size ranging from 5.5 to 17.8 nm in high yield via a simple, one-step seeded growth method (see Figure 1.10) with the assistance of Tris-base (TB) (Xiahou et al., 2018). The sizes of these small Au nanoparticles can be finely controlled by varying the gold precursors (HuCl₄) and/or seed amount according to an established relationship between the nanoparticles' diameter and the particle number of the seeds (or the mass of gold precursor in some cases).

A controlled preparation of Au nanoparticles in the size range of 6 to 22 nm (see Figure 1.11) was explored by Suchomel et al. (2018). The Au nanoparticles were prepared through the reduction of



FIGURE 1.10 Representation of the detailed test principle of the $2-ME/S_2O_3^{2-}$ -TB-Au_{5.5} NP sensor for the detection of Pb²⁺ ions. (From Xiahou et al., 2018. With permission.)



FIGURE 1.11 TEM images and particle size distribution histograms of gold nanoparticles prepared via reduction of tetrachloroauric acid by maltose at alkali pH at various concentrations of Tween 80: 10 mmol/L (a), 1 mmol/L (b), 0.1 mmol/L (c), 0.01 mmol/L (d). (From Suchomel et al., 2018. With permission.)

tetrachloroauric acid using maltose in the presence of nonionic surfactant Tween 80 at various concentrations to control the size of the resulting Au nanoparticles. With increasing concentration of Tween 80, a decrease in the size of produced Au nanoparticles was observed, along with a significant decrease in their size distribution.

Synthesis of Ag and/or Pt Nanoparticles: The most fundamental reactions to prepare silver nanoparticles can be divided into two groups where AgNO₃ is reduced into products at a high temperature in (i) oleylamine (OAm), that is, cis-1-amino-9-octadecene and (ii) ethylene glycol (EG). These two solvents (reaction media) are helpful in understanding the nucleation and growth of Ag nanoparticles (Sun, 2013). Surfactants can be added to OAm and EG. When AgNO₃ is dissolved into OAm/EG (solvents), it releases Ag⁺ ions which further associates with solvent or surfactant molecules (Deng et al., 2009). The solvent's capability for reducing silver precursors depends on the reaction temperature; hence, nucleation of Ag nanoparticles can be tuned finally by tuning temperature; there is obviously not only a single factor in preparing Ag nanoparticles. Liz-Marzán and co-workers have successfully synthesized silver nanoplates in boiled N,N-dimethylformamide (DMF) containing AgNO₃ and poly vinyl pyrrolidone (PVP) (Pastoriza-Santos & Liz-Marzán, 2002). They could demonstrate that tuning reaction precursor (AgNO₃), hence Ag⁺ ions with respect to PVP has an impact on the morphology of nanoparticles as particles were showing changes from isotropic spheres to anisotropic nanowires and nanoplates on increasing Ag⁺ ions. The aqueous-based colloidal synthesis using C_n TABr, a cationic surfactant, has attracted much attention as a simple and facile method (see Figure 1.12) that fabricates size- and shape-tunable metal nanoparticles (Zheng et al., 2014; Seo et al., 2018). Unlike other surfactants including carbonyl groups, CnTABr binds weakly to metal surfaces making it easy to regulate particle shape and preserve catalytically active sites (Zheng et al., 2014). Recently, a study was published showing a correlation between the surfactant concentration and particle size of synthesized Pt nanoparticles using cationic surfactants $(C_n TABr)$, a K₂PtCl₄ precursor and a NaBH₄ reducing agent (Seo et al., 2018). A solution mixture of C_nTABr and K_2PtCl_4 heated to 50°C in an oil heat bath under stirring was formed cloudy to transparent. This cloudy compound is known as the real precursor formed by coulombic interaction between



FIGURE 1.12 (See color insert.) Schematic flowchart of the synthetic procedure for the Pt nanoparticles (NPs). (From Seo et al., 2018. With permission.)

 $[C_nTA]^-$ and $[PtBr_4]^{2-}$ forming $[C_nTA]_2[PtBr_4]$ (Sau & Murphy, 2004). Subsequently, an ice-cooled aqueous solution of NaBH₄ was added as a reducing agent (Zhuang et al., 2008). The aqueous solution was kept at 50°C during the reaction for 24 h while releasing hydrogen gas in a controlled way.

Direct synthesis of Pt nanoparticles can be obtained by reducing a hexachloroplatinic complex in EG at room temperature, but elemental platinum is obtained at 110°C. The product can be obtained after a few hours of reaction and was found to be composed of colloidal particles with a size smaller than 10 nm. The PVP can be used to avoid sintering in colloidal platinum dispersions.

1.5 Preparations and Illustrations of Hybrid Nanomaterials

Currently, the major research area regarding preparation of hybrid nanomaterials can be categorized into three different sections: (i) inorganic–organic, (ii) inorganic–inorganic, and (iii) organic frameworks. Hybrid nanoparticles stand for their structure, characteristics, and unusual joining of nanoentities. Some major classes of functional nanoplatforms, such as (i) magnetic nanoparticles, (ii) nanophotonic materials and (iii) plasmonic nanoparticles have been extensively studied and widely used in a variety of fields. The next generation of nanoparticles is about hybridization of two characteristics that mainly come due to individual characteristics of distinct entities. Bifunctional nanoparticles have exhibited potentially promising physio-chemical properties, which can revolutionize and transform the landscape from bio-clinical industry to next-generation advance devices. In particular, colloidal nanoparticles have been extensively investigated as probes in biomedical/devices industries due to their unique size-dependent electronic, optical and magnetic properties among all possible building blocks. Thus, hybrid nanoparticles with combined magnetic and optical properties are much more powerful and can be used in a broad range of applications. Moreover, they offer new modalities that neither luminescence nor magnetic nanoparticles exhibit. For example, the demonstration of real field dependent luminescence phenomenon called magneto-luminescence, and magnetomotive-photoacoustic phenomenon. This novel phenomenon shows remarkable potential in several other important applications, such as high accuracy and secure communication, aircraft guidance and radiation field detection and modulation of the magnetic and optical fields. Furthermore, these nanocomposites can be used as nanoblocks to build various nanoelectronic and photonic devices by applying an external magnetic field to manipulate or arrange the magnetic nanoparticles and optical signals.

There are several kinds of strategies to prepare nanoparticles and a few of the key terms that can be mentioned here are core-shell engineering, composites, multi-shell nanoparticles, yolk-shell nanoparticles, porous silica-based hybrid nanoparticles, polymeric hybrid nanoparticles, doped nanohybrids, dumbles, tetrapods, Janus, and core-satellite. The core-shell structure is the most common type of bifunctional nanosystem. In this type of nanoarchitecture, generally, a core (e.g. magnetic) is combined with (fluorescent) molecules, metal nanoparticles or semiconductor nanocrystals, etc. and therefore exhibits unique optical, magnetic and electrical properties. However, different components in these kinds of bifunctional nanoparticles interact with each other, which generally weaken or reduce the functionality of each unit. Recent advances in the synthesis of various functional superparamagnetic iron oxide nanoparticles with heterostructures offer promising solutions to this problem by creating anisotropic nanoparticles. They consist of functional units with different chemistry, polarity or other physico-chemical properties on asymmetric sides without sacrificing their own properties. The superior properties of these heterostructures rely on synergistically enhanced magnetism and synthesis strategies for precise control of particle size, morphology and chemical composition along with functionalization with fluorescent material (e.g., dumbbell nanoparticles). The desire to design more sophisticated nanoarchitecture with unusual properties is definitely needed. This kind of integration offers exciting opportunities for discovering new materials, processes and phenomena. At the nanoscale, these kinds of bifunctional materials have their own advantage: (i) tuned and controlled size depending on application, (ii) nanoparticles manipulated by external force (magnetic field) "action at a distance," and (iii) multimode applications, e.g., MRI contrast agents and multimodal imaging sensors.

1.5.1 Magnetic-Luminescent Nanoparticles

Since magnetic-luminescent bifunctional nanoparticles may provide new and promising two-in-one characteristics, there are also some challenges to overcome in their fabrication: (i) the complexity in the preparation, which frequently involves multi-step synthesis and many purification stages leading their production which are quite technical and time-consuming; (ii) the risk of quenching of the luminophore on the surface of the particle by the magnetic core and (iii) the risk of quenching each other by the incorrect number of fluorescent molecules attached to the surface of the particle. To resolve these challenges, several techniques have been proposed to integrate the luminescence and magnetic nanomaterials. The fabrications of these are commonly achieved as hybrid conjugates of magnetic and luminescent entities, core–shell or composite structures using coating, layer-by-layer deposition and optical materials (QDs) on magnetic nanoparticles or vice-versa. Another method is the functionalization of magnetic iron oxide with fluorescent dyes and luminescent complexes, called the cross-linking attachment of molecules (Khan et al., 2014; Shrivastava, 2017). Moreover, the use of SiO₂, ZnS or C as spacers between iron oxide and luminescent materials is of great importance to the performance of nanohybrids.

Magnetic-luminescent multifunctional molecularly imprinted polymer (MIP) nanospheres containing luminescent LaVO₄:Eu³⁺ nanocrystals (NCs), magnetic Fe₃O₄ nanoparticles, and the recognition sites of template organophosphate pesticides were successfully prepared via a facile and versatile bottom-up self-assembly strategy (Ma et al., 2012). Interestingly, both the favorable photoluminescent LaVO₄:Eu³⁺ nanoparticles and magnetic Fe₃O₄ nanoparticles are incorporated within the final composite nanospheres, thus rendering them susceptible to both magnetic guidance and photoluminescent detection. The whole synthesis process has been summarized in Figure 1.13.



FIGURE 1.13 (See color insert.) Scheme for the fabrication of multifunctional MIP composite nanospheres and the luminescence response via the removal and rebinding of template analytes. (From Ma et al., 2012. With permission.)



 $\label{eq:FIGURE 1.14} The formation process of multifunctional Fe_3O_4@nSiO_2@nSiO_2@NaYF_4:Yb^{3+}, Er^{3+} nanocomposites.$

Acar's group prepared nanohybrids composed of luminescent QDs and SPIO iron oxides by the ligand exchange mechanism in a simple and versatile extraction method (Kas et al., 2010). In this method, aqueous QDs (CdS or CdTe) coated with carboxylated ligands exchange the fatty acid (lauric acid) coating of SPIOs in a water–chloroform extraction process. QDs form a coating around SPIOs and transfer them into the aqueous phase in high efficiency.

The synthesis (using a facile two-step sol-gel process), characterization and application in controlled drug release are reported for monodisperse core-shell-structured $Fe_3O_4@nSiO_2@mSiO_2@$ NaYF₄:Yb³⁺,Er³⁺/Tm³⁺ nanocomposites with mesoporous, upconversion luminescent and magnetic properties (Gai et al., 2010). The synthesis protocol can be understood from Figure 1.14. Authors have proposed a novel and facile strategy for the fabrication of multifunctional nanocomposites using silicacoated Fe_3O_4 spheres as the core, ordered mesoporous silica as the shell, and are further functionalized by the deposition of NaYF₄: Yb³⁺, Er³⁺/Tm³⁺ upconversion phosphors.

1.5.2 Magnetic-Plasmonic Nanoparticles

As we discussed in previous sections, multifunctional nanohybrid designs have been proven to be an important way to fulfill the several biomedical requirements and environmental applications. In this section, we discuss two efficient nanoheaters combined into a multifunctional single nanohybrid (Espinosa et al., 2015). This nanohybrid consists of a multi-core iron oxide nanoparticle optimized for magnetic hyperthermia, and a gold branched shell with tunable plasmonic properties in the NIR region, for photothermal therapy which impressively enhanced heat generation, in suspension or in vivo in tumors, opening up exciting new therapeutic perspectives, at low excitation doses (Espinosa et al., 2015). Gold nanoparticles such as gold nanoshells, nanostars and nanorods are often preferred due to their strong absorption cross-sections. We are all aware of the application of iron oxide nanoparticles. This combination of systems is called a magneto-plasmonic nanoparticle, which is subjected to external magnetic and laser stimulations. Indeed, gold-based nanoparticles exhibit strong LSPRs in visible and NIR spectral regions; this property has been explored in a plethora of exciting applications ranging from molecular dark-field, reflectance and photoacoustic imaging to photothermal therapy and drug release (Sun, 2013). Similarly, superparamagnetic nanoparticles are of great interest because of their applications in various cell and molecular separation assays, magneto-motive optical and ultrasound imaging, MRI and hyperthermia cancer treatment.



FIGURE 1.15 (See color insert.) (a) The seeding-growth process used for the synthesis of the magneto-plasmonic NPs (MagPlasNP) of different ratio Au/Fe. (b) Elemental analysis of different MagPlasNP-1. HAADF image, EELS Fe map (green), EELS O map (blue), EELS Au map (red) and overlaid maps. Superparamagnetic behavior of the nanohybrid: (c) Attraction of MagPlasNP-2 by a permanent magnet and (d) Magnetization curves of MagNP and MagPlasNP-1,2 and 3. (From Espinosa et al., 2015. With permission.)

Espinosa et al. prepared this kind of nanoparticle using a two-step polyol synthesis process (see Figure 1.15). First, maghemite multi-core nanoparticle (MagNP) synthesis was performed using $FeCl_3.6H_2O$ and $FeCl_2.4H_2O$ precursors in a liquid mixture of NMDEA and DEG with 1:1 (v/v) ratio. NaOH was dissolved in polyols (Hugounenq et al., 2012), which was later mixed in the first solution and stirred. Then, the temperature was elevated to 220°C slowly and the solution was stirred for 12 h at this temperature. After cooling, it was cleaned and washed to get magnetic nanoparticles. Fe-nitrate, dissolved in water, was mixed with these nanoparticles. Then, this mixture was heated to 80°C and stirred. Again, they were cleaned with appropriate agents. In this way, multi-core magnetic nanoparticles were created.

In the second step of the preparation of materials, first seeding the surface of MagNPs with gold (as MagNP-seeds) was allowed, and further growth of gold nanoparticles over MagNPs was performed. In order to deposit seeds on the surface of the MagNPs, their surface was functionalized with citrate anions at 80°C. Under vigorous stirring, in 100 ml of Millipore water alkalinized with ammonia, citrate treated MagNPs and 680 μ l of a 35 mM HAuCl₄ aqueous solution were mixed. The mixture was heated at 40°C, followed by magnetic separation and redispersion of the NPs in 100 ml of water. 1 ml of a freshly prepared 0.1 M NaBH₄ solution was added to the previous suspension under vigorous stirring. Nanoparticles were magnetically separated and washed. Finally the nanoparticles were redispersed in a solution of PVP in ethanol. The schematic scheme, quality of materials, magnetic separation and evidence of superparamagnetic nanoparticles are highlighted in Figure 1.15. Recent advances in nanoparticle research allow the synthesis of various composite nanoparticles with core/shell and dumbbell structures that offer a promising solution to this problem encountered with single-component magnetic nanoparticles. For example, Au–Fe₃O₄ dumbbell nanoparticles were applied by conjugating anticancer drug cisplatin