Chapter 5
Application of Nanoparticles

Abstract In this chapter we discuss the applications of bionanoparticles (BNP) in biomedical and environmental fields. In the biomedical field, these nanoparticles have been investigated for antimicrobial applications, biosensing, imaging, and drug delivery. In the environmental field, nanoparticles have been investigated for applications in bioremediation of diverse contaminants, water treatment, and production of clean energy. Overall, the BNP have attracted the attention of diverse researchers because their syntheses are more environmentally friendly, produces more homogeneously distributed nanoparticles and some of them can be easily biodegradable. Although there are several studies investigating the application of BNP, these nanomaterials are still way less studied than synthetic nanoparticles, since researchers are still identifying the microbiological synthetic pathways of these BNP. It is expected that with the advancement of the understanding of BNP synthesis pathways, the application of BNP will expand to many more fields than biomedical and environmental and will be potentially applied in diverse nanotechnological industries.

5.1 Introduction

The application of nanostructures and nanoparticles of biological nature is an emerging field. These nanoparticles of biological nature or produced by biological systems are typically classified as bionanoparticles (BNP) (Thakkar et al. 2010). Several researchers also classify hybrid nanomaterials composed of both bionanoparticles and synthetic nanoparticles as bionanoparticles (van Rijn and Böker 2011; Yang et al. 2011). In the latter, these bionanoparticles are used together with non-biological nanoparticles to enhance their properties. The interest for BNPs has increased in the past years because they present very different properties and functions than synthetic nanoparticles and they tend to be more biocompatible than their inorganic non-biological counterparts. There are, however, advantages and disadvantages about using BNP instead of synthetic nanoparticles in different fields.

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The most obvious disadvantages of BNP are that they frequently do not withstand high or low temperatures, extreme pH values, presence of harsh chemicals and potential environmental conditions that could lead to their hydrolysis (van Rijn and Böker 2011). It is possible, however, that BNPs from extremophiles might overcome these issues. Research to address these disadvantages is still in its infancy. In the meanwhile, the synthetic inorganic nanomaterial counterparts are preferred, whenever these conditions are present in a given system, since they have higher stability under these conditions than BNPs. Despite these disadvantages, these BNPs have advantages that are essential to produce new exciting materials.

The more obvious advantage of BNPs is that nature has perfected the synthesis and reproducibility of these nanostructures over the last billions of years (van Rijn and Böker 2011). Although the reproducible synthesis of synthetic monodispersed nanoparticles have improved tremendously over the years, it is far from being as perfect as the BNP synthesized by biological systems (Hussain et al. 2016). For instance, in the case of a protein-based nanoparticle, the size and shape are directly dependent on the sequence, composition, and number of amino acids in the protein chain. Typically, any variation in amino acid sequence and length will affect the structure, folding and overall function of the protein. In the case of synthetic nanoparticles, although they can possess catalytic activities, they are not as efficient and operate as well as proteins under physiological conditions.

Other great advantages of BNPs are their very diverse sizes and shapes, as well as their capability to form very complex structures (van Rijn and Böker 2011). For instance, BNPs can have spherical, ring, rod, and even banana shapes. In addition to the shapes, BNPs can form different structures, such as solid, hollow, present pores, or not, within the range of nano- to several micrometers. They can also be formed by one single structure or by self-assembled structures. Some of the BNPs are formed by several non-covalently connected subunits, hence they can easily disassemble and reassemble. This dynamic property is unique to BNPs and can be very useful for different applications, especially in drug delivery.

BNPs are also advantageous over synthetic nanoparticles since they are typically biodegradable (van Rijn and Böker 2011). In many cases, the biodegradability property of BNPs is an advantage over inorganic nanoparticles since synthetic nanoparticles are more difficult to remove without using physical or chemical processes that can be very costly and not very environmentally friendly. This advantage also applies to the biodegradation of BNPs when they are used in vivo and need to be released or disposed in a natural fashion (Lin and Dufresne 2014).

These advantages and unique properties of BNPs make them very attractive for different applications. The field of technological application of nanoparticles is called nanotechnology. Nanotechnology involves not only nanometer sized materials, but also devices and systems at the nano-size level. Recently, these nanoparticles have entered a commercial exploration period. The application of BNPs is still underdeveloped, but several studies have suggested that they can be effectively used in biomedical and environmental applications. In the biomedical applications, nanoparticles are used for example for antimicrobial applications, biosensing, imaging, and drug delivery and; while for environmental applications,

nanoparticles are used for bioremediation of diverse contaminants, water treatment, and production of clean energy. More details on some of these applications are described below.

5.2 Biomedical Applications of BNPs

5.2.1 Bionanoparticles as Anti-microbial Agents

In the U.S. alone, the fourth leading cause of death are hospital acquired infections (i.e. nosocomial infections) with more than 2 million cases reported annually leading to more than $5 billion in added medical costs per year (Wenzel 2007). The majority of these nosocomial infections, about 60–70 %, are associated with bacterial contamination of implanted medical devices (Donlan 2001; Bryers 2008). This number has remained high over the years, especially because of the emergence of antibiotic-resistant pathogenic strains and pathogens displaying multiple drug resistance. Hence, the need of new anti-microbial agents has increased tremendously. Nanoparticles (NPs) are currently being viewed as a powerful nanotechnology to control hazardous microorganisms due to their intrinsic antimicrobial properties. A large number of synthetic NPs have been explored for their antimicrobial properties. These include NPs of silica/iron oxide, graphene, graphene oxide, bifunctional Fe_3O_4-Ag NPs, titanium, copper, zinc, silver and gold, just to name a few (Kang et al. 2008; Rodrigues and Elimelech 2010; Narayanan and Sakthivel 2011; Santos et al. 2012; Mejias Carpio et al. 2014; Musico et al. 2014; Rodrigues et al. 2015).

More recently, BNPs have emerged as an alternative to the NP synthetic process (Narayanan and Sakthivel 2011; Hussain et al. 2016). The synthesis of NPs using biological systems is more attractive, since it is less labor-intensive and does not require expensive toxic chemicals for their production. Hence, the synthesis of BNPs is considered to be a greener process than the current physical and chemical methods of NP synthesis (Gericke and Pinches 2006). Although, researchers have investigated the biological synthesis of BNPs, very few investigations have explored their antimicrobial properties. The most common BNPs investigated as anti-microbial agents are silver, gold, zinc, TiO_2 and biocellulose (Thakkar et al. 2010; Narayanan and Sakthivel 2011; Sharma et al. 2012). These nanoparticles are typically synthesized by either bacteria, fungi, algae, and plants. In this review, we will focus on the BNPs synthesized mainly by bacteria and fungi.

5.2.1.1 Silver BNPs

Today, silver nanoparticles are already being commercially used as antimicrobial agents. For example, silver NPs are currently found in surgically implanted catheters in order to reduce the infections caused during surgery, in toys, personal

care products, and silverware. The reason for using silver for anti-microbial applications is because silver possess antifungal, anti-bacterial, anti-inflammatory, and anticancer effects (Kalishwaralal et al. 2009; Sheikpranbabu et al. 2009). Silver NPs have been described to be synthesized by both Gram+ and Gram− bacteria (Nanda and Saravanan 2009; Thakkar et al. 2010). Microbial synthesis of silver nanoparticles, however, is restricted to certain groups of microorganisms since most microbes tend to be sensitive to silver ions. Similarly, reduction of silver ions by microorganisms involve specific biomolecules, such as enzymes, vitamins, and polysaccharides through complex pathways involving electron transfer and conversion of NADPH/NADH to NADP$^+$/NAD$^+$ (Matsumura et al. 2003; Gholami-Shabani et al. 2014).

In most studies, the silver BNPs were shown to have antimicrobial properties against different microorganisms. For instance, the silver nanoparticles produced by Gram-negative bacteria, e.g. *Klebsiella pneumoniae* and *Shewanella oniedensis* MR-1, were shown to have antimicrobial properties against both Gram+ and Gram− bacteria, such as *Escherichia coli*, *Bacillus subtilis* and *Staphylococcus aureus* (Shahverdi et al. 2007; Suresh et al. 2010). In another study, *Pseudomonas aeruginosa* strain BS-161R produced monodispersed spherical particles with a size range of 13 nm (Kumar and Mamidyala 2011). These NPs exerted antimicrobial activity against a large array of microorganisms in a concentration as low as 8 µg/ml. The microorganisms inhibited by the presence of these NPs were *S. aureus*, *Micrococcus luteus*, *Candida albicans*, and *Candida krusei*.

In the case of Gram-positive bacteria, AgNPs were described to be produced by *Streptomyces hygroscopicus* and *Bacillus licheniformis* (Zinjarde 2012). Typically, the extracellular components of these microorganisms led to the production of AgNPs. In the case of *S. hygroscopicus*, AgNPs in the size of 20–30 nm were produced (Sadhasivam et al. 2010). These BNPS significantly inhibited the growth of medically relevant Gram-negative bacteria (*E. coli* and *Salmonella typhimurium*), Gram-positive bacteria (*B. subtilis* and *Enterococcus faecalis*), and the yeast *C. albicans*. In the case of *B. licheniformis*, the BNPs were able to inhibit biofilm formation of *P. aeruginosa* and *Staphylococcus epidermidis* in a study aiming to prevent growth inhibition of contact lenses (Kalishwaralal et al. 2010).

Fungi is another group of microorganisms also able to produce silver NPs. In most fungus genera, the production of AgNPs has been described to involve the enzyme nitrate reductase, which reduces the metal ions (Duran et al. 2005; Kumar et al. 2007). Studies of production of AgNPs with different fungi species, such as *Cladosporium cladosporioides*, *Fusarium semitectum*, *Fusarium solani*, *Fusarium acuminatum*, and *Trichoderma asperellum*, showed that these microorganisms are able to produce extracellularly AgNPs of 4–100 nm in solutions containing silver salts. These nanoparticles were shown to inactivate not only Gram-negative, but also Gram-positive bacteria and some species of fungi. The AgNPs produced by *Amylomyces rouxii* showed antimicrobial activity against *Shigella dysenteriae* type I, *E. coli*, *S. aureus*, *P. aeruginosa*, *Citrobacter* sp., *B. subtilis*, *C. albicans* and *Fusarium oxysporum* (Sharma et al. 2009). These results suggest that the AgNPs produced by microorganisms has a broad microbial spectrum.

5.2.1.2 Gold BNPs

A few microorganisms from the group of fungi, yeasts, and bacteria have been described to synthesize antimicrobial gold nanoparticles (AuNPs) (Das et al. 2009). Some of them were also investigated for anti-microbial properties. For instance, *Rhizopus oryzae* was able to produce AuNPs with an average diameter of 10 nm through an in situ reduction of $HAuCl_4$ (Das et al. 2009). These AuNPs showed strong antimicrobial property against several Gram-negative and Gram-positive bacteria, as well as against yeasts (*Saccharomyces cerevisiae* and *C. albicans*). *Shewanella oneidensis* could reduce tetrachloroaurate (III) ions to produce homogenous extracellular gold spheres with an average size of 12 ± 5 nm (Suresh et al. 2011a, b). The antimicrobial activity of these AuNPs were shown to be negligible towards *E. coli*, *S. oneidensis,* and *B. subtilis*. This finding was interesting, since it showed that not all gold BNPs have antimicrobial properties. In addition to bacteria, the yeast *Candida guilliermondii* was also shown to produce extracellular AuNPs in the size range of 50–70 nm (Mishra et al. 2011). The AuNPs displayed antimicrobial activity against five pathogenic bacterial strains. These particles were most toxic to *S. aureus*. The comparison of these studies showed that the size and the toxicity levels of the AuNPs to different microorganisms were dependent on the type of microorganisms synthesizing them. It is possible that different capping proteins would be responsible for affecting the antimicrobial properties of AuNPs.

5.2.1.3 Metal Oxides BNPs

Among the metal oxides produced by microorganisms, zinc oxides and titanium dioxide are the most described in the literature (Jones et al. 2008; Jha and Kulkarni 2009). Like silver, zinc oxide BNPs (ZnO NPs) have also received a tremendous amount of attention since the synthesis of synthetic ZnO NPs requires the use of toxic organic solvents, expensive and labor intensive reaction conditions, such as high temperature and pressure, and long refluxing time for its synthesis. The interest for ZnO has grown over the years since it has been shown to have unique antibacterial, antifungal, superior catalytic, UV filtering properties and photochemical activity (Jones et al. 2008). More importantly, ZnO nanoparticles presents antibacterial and antifungal activities at lower concentrations and can be easily used for coating surfaces to serve as antimicrobial surfaces. Additionally, the antimicrobial property of ZnO has been described to be very specific to pathogenic microorganisms. A study in soil, showed that the addition of ZnO nanoparticles acted as antifungal and did not affect the soil fertility like some other antifungal agents (Jayaseelan et al. 2012).

The mechanisms of toxicity of these ZnO NPs towards microorganisms was determined to be related to the disruption of the membrane lipid bilayer followed by release of cytoplasmic contents. Further studies showed that exposure time to the NPs would enhance the cell membrane contact with the nanoparticles and lead to cell

disruption (Sharma et al. 2010). Most studies aiming at producing ZnO BNPs were investigated with plants, a few studies, however, investigated the role of microbes in ZnO BNP production. A study with *Aeromonas hydrophila* demonstrated that this microorganisms could synthesize ZnO NPs (57.7 nm, spherical) that exhibited antimicrobial activity against *E. coli*, *P. aeruginosa*, *S. aureus*, *E. faecalis, Streptococcus pyogenes*, *C. albicans, Aspergillus flavus*, and *Aspergillus niger* (Jayaseelan et al. 2012). Another study with *Pichia fermentans* JA2, showed that the ZnO NPs produced an effective zone of inhibition in the presence of *Enterococcus* sp., *S. aureus*, and *Proteus mirabilis* (Chauhan et al. 2015). To date, only two studies investigated the production of ZnO NPs by microorganisms. Hence, the production of ZnO NPs by microorganisms is still in its infancy, however, these preliminary results with *A. hydrophila* suggests that ZnO NPs produced by microorganisms can be of great potential for antimicrobial applications.

In the case of TiO_2 NPs, the biological synthesis of TiO_2 NPs tends to be preferred over synthetic methods because the biosynthesis provides synthesis rates faster or comparable to the chemical processes. More importantly, the biosynthesis of TiO_2 can be potentially used in various fields that requires human contact with these particles, such as foods, cosmetics, foods and sunscreens (Quadros and Marr 2010). Contrary to ZnO NPs that has just one biosynthesis report, the TiO_2 NPs can be synthesized by different species of bacteria and fungi. For instance, the bacteria *Lactobacillus* sp, *A. hydrophila*, *B. subtilis* and the fungi *F. oxysporum*, *Sachharomyces cerevisae* and *Aspergillus tubingensis* were described to be able to synthesize TiO_2 NPs (Bansal et al. 2005; Jha and Kulkarni 2009; Kirthi et al. 2011; Jayaseelan et al. 2013). Typically, TiO_2 presents antimicrobial activity only when activated with UV light. Very few studies describe the ability of TiO_2 to present antimicrobial activity under visible light (Cheng et al. 2009). However, a more recent study with *A. flavus*, showed that it is possible to synthesize TiO_2 that is active under visible light (Rajakumar et al. 2012). The authors showed that both Gram-positive and Gram-negative microorganisms could be inactivated by these nanoparticles. Inactivation experiments performed by the authors showed that *S. aureus*, *Shigella flexneri* and *Acinetobacter baumannii* were inactivated by the new visible-light-activated TiO_2 BNPs (Cheng et al. 2009). The authors attributed the antimicrobial effect to production of reactive oxygen species, such as hydroxyl radicals, which led to phospholipid peroxidation, followed by cell death. Although, TiO_2 can be used as antimicrobials, researchers tend to prefer to use these nanoparticles for other applications, such as photocatalysts or electrical insulators, as discussed later in this chapter.

5.2.1.4   Nanocellulose BNPs

Bionanocellulose is not considered to have antimicrobial microbial properties by itself, however, this nanomaterial can serve as a scaffold for antimicrobials due to its unique properties. For instance, nanocellulose can provide a porous network structure, which is essential for the transfer of antibiotics or other antimicrobial

agents into a wound, and at the same time can serve as an efficient physical barrier against external infectious agents (Andresen et al. 2007). Another advantage of nanocellulose is that this nanomaterial is compatible with biological tissues and presents significant bioavailability and biodegradability (Maneerung et al. 2008; Luan et al. 2012). In order to obtain an antimicrobial nanocellulose material, researchers have investigated many physical or chemical process to couple antimicrobial agents with nanocellulose. Typically, nanocellulose-based antimicrobial biomaterials can be produced in two different ways. The first, involves incorporation of other anti-microbial nanoparticles, such as silver, titanium, gold, etc. The second, involves the incorporation of organic antimicrobial agents, such as antibiotics or enzymes (e.g. lysozymes) to confer antimicrobial properties to nanocellulose.

The most common anti-microbial nanoparticle used to impregnate nanocellulose is silver. Silver has been the most extensively studied and used anti-microbial nanoparticle since ancient times to fight infections and prevent spoilage. The silver nanoparticles have effective antibacterial, antifungal, as discussed earlier on this chapter. Simple impregnation of silver nanoparticles is a common approach to introduce a silver antimicrobial agent into nanocellulose-based nanomaterials. This impregnation confers to the nanocellulase similar antimicrobial property to silver nanoparticles. In this case, the unique property of nanocellulose, as a porous network structure, facilitates the transfer of the antimicrobial silver ions into the wound, meanwhile serving as an efficient physical barrier against any external infection (Andresen et al. 2007). In addition to silver nanoparticles, recent studies reported that zinc-oxide nanoparticles could also be used for impregnation on nanocellulase. These composite were able to yield antibacterial properties to the nanocellulose composite (Azizi et al. 2013; Martins et al. 2013).

Besides nanoparticles, other antimicrobial agents were also easily incorporated in nanocellulose. Examples of such compounds are: porphyrin, octadecyldimethyl (3-trimethoxysilylpropyl) ammonium chloride (Andresen et al. 2007), allicin and lysozyme (Jebali et al. 2013). The incorporation of such compounds led to a nanocellulose material with excellent antimicrobial properties against diverse microorganisms. Overall these antimicrobial nanomaterials from nanocellulose exhibited compatibility with biological tissues as well as significant bioavailability and biodegradability (Luan et al. 2012). There were, however, issues raised in these studies about the balance among the improvements of antimicrobial activity, cytotoxicity to human cells, and duration effect of antimicrobial properties, which still needs to be investigated for all these nanocellulose impregnated materials before real biomedical applications.

5.3 BNPs for Biosensing Applications

The sensors described in the literature that are BNP-based are typically composed by gold NPs or magnetic NPs. These biosensors BNP-based are frequently described for biomedical diagnosis or forensic analysis to detect biological agents,

as well as toxic compounds or diseases (Diamond 1998). Sensors are composed typically of two main components: a recognition element (i.e. bioreceptor) and a signal transduction element (i.e. transducer). The recognition element typically binds to a specific compound, called analyte. In the case of gold nanoparticles, these NPs can be used as biosensors since they exhibit unique electronic and optical properties. These properties are directly related to the size and shape of these nanoparticles. For instance, AuNPs possess an intense absorption peak in the 500–550 nm range (Jain et al. 2006), due to surface plasmon resonance (SPR) (Eustis and El-Sayed 2006).

Surface plasmon resonance occurs when a photon from an incident light hits the gold NP surface (Fig. 5.1). The incident photons lead to resonant excitation of the conductive electrons of the gold nanoparticles. This movement of the electrons are called plasmon and they can generate an electric field and generate changes in the refractive index in the vicinity of the surface (Homola et al. 1999). Detection of the sample analyte can be obtained by measuring the changes in the reflected light after immobilization of the analytes on the nanoparticle surface. Typically, the amount of surface concentration can be quantified by monitoring the reflected light intensity or tracking the resonance angle shifts. A SPR biosensor has a detection limit in the order of 10 pg/mL and has been described to be one of the most powerful biosensing technologies. Typically, the interparticle plasmon coupling can lead to a red-shift (650 nm) and broadening of the plasmon band, which can be detected colorimetrically.
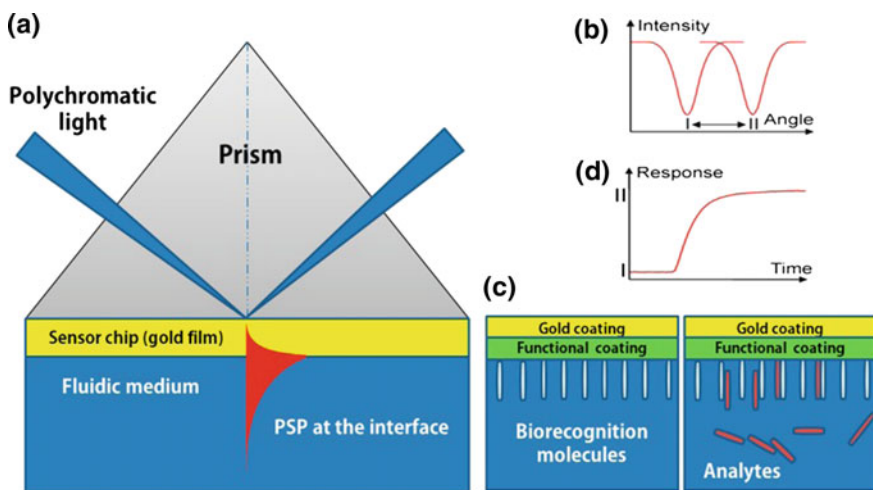

Fig. 5.1 Concept of a surface plasmon resonance (SPR) biosensor: **a** Kretschmann geometry of the ATR method; **b** spectrum of reflected light before and after refractive index change; **c** analyte-biorecognition elements binding on SPR sensor surface and **d** refractive index changes caused by the molecular interactions in the reaction medium. *Source* Nguyen et al. (2015). Copyright © 2015, MDPI. Reproduced with permission

Besides the plasmon property of gold nanoparticles, these particles possess conductivity properties that can be applied to electroanalytical biosensing (Yu et al. 2003). In the literature, there are several systems describing the use of nanoparticle-enzyme hybrids that can be used as electrochemical sensors of diverse health related molecules, proteins and even DNA. For instance, a bioelectrocatalytic sensor for glucose measurements (for diabetes) was developed by binding the AuNPs to the glucose oxidase enzyme (apo-GOx). After binding the enzyme-AuNP hybrid system to an electrode, the sensor could effectively detect the electrical changes in the presence of different concentrations of glucose under real physiological conditions (Xiao et al. 2003). An analogous electron transfer sensor was developed to monitor hydrogen evolution from a zinc-substituted cytochrome c immobilized on TiO_2 NPs (Astuti et al. 2005).

In the case of protein sensors, Velev and Kaler developed an antigen–antibody based protein sensor that was designed to detect human IgG at 0.2 pM (Velev and Kaler 1999). The antibody was immobilized in AuNPs. Besides antibodies, DNA is another biomolecule relevant for biomedical fields that can be detected with AuNP-based sensors. Mirkin et al. developed a selective DNA sequence based on olignucleotide-functionalized Au-NPs (Cao et al. 2002; Park et al. 2002). In this sensor, short-chain oligonucleotides were deposited onto the electrode surfaces containing gold nanoparticles. In the presence of the target DNA sequence, the DNA could hybridize to the oligonucleotides. To enhance the sensitivity of the sensor down to 50 fM and to increase the mutation selectivity factor to about 1:100,000, the authors deposited silver on the surface of the gold nanoparticles. The coating of the AuNP with silver enhanced significantly the conductivity, and therefore, the sensitivity of the sensor.

Another biosensor method using AuNP is the Surface enhanced Raman scattering (SERS) method (Fig. 5.2) (Aroca et al. 2005; Doering et al. 2007). These AuNP sensors were developed by labelling AuNP with Raman-active dyes and oligonucleotides. These biosensors are able to detect simultaneously different target DNA molecules (Cao et al. 2002). This SERS method is also described to be able to detect the interactions of protein-small molecules and protein-protein, as long as the NPs are coupled with specific proteins and Raman dyes to detect these interactions (Cao et al. 2003). In addition to biosensors using AuNPs, researchers have also used magnetic nanoparticles, with or without coupling with AuNPs.

For instance, Mirkin's group developed a "bio-barcode" type of biosensor for nucleic acids or proteins involving both AuNPs and magnetic NPs. In the case of nucleic acid detection, magnetic nanoparticles carrying a partial complementary sequence to the target DNA is hybridized to a "bio-barcoded" AuNPs in the presence of the target DNA. After magnetic separation of the hybridized nucleic acids and denaturation of the double stranded DNA, the bio-barcode is released for analysis through PCR. This method is comparable to many PCR-based approaches (Nam et al. 2004). In the case of protein detection, the magnetic NPs contain specific antibodies to the target protein. After interaction of the target protein with
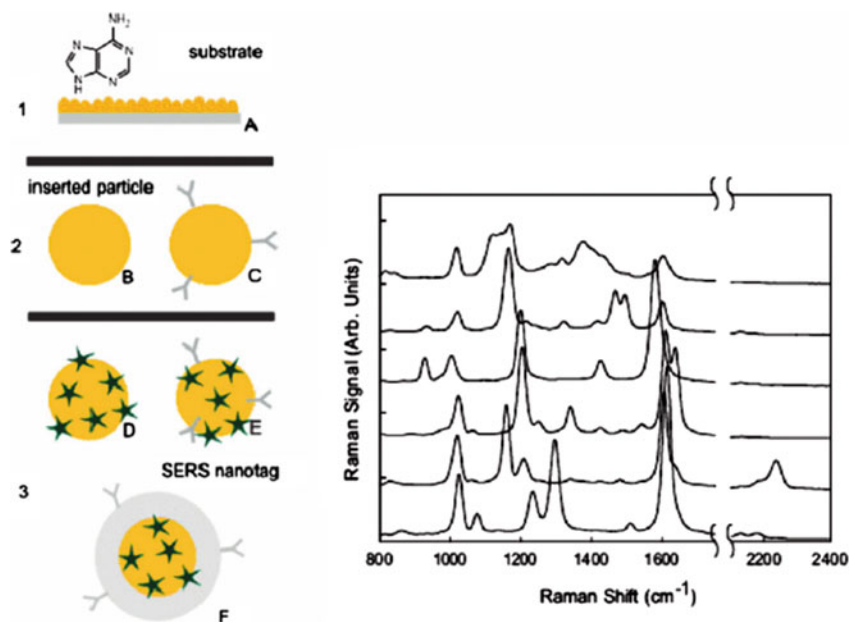
Fig. 5.2 Architectures used in SERS experiments. *A* 2D substrate with adenine on the surface. *B* Bare particle. *C* Antibody-targeted particle. *D* Reporter labeled particle. *E* Targeted and labeled particle. *F* Targeted particle with encapsulated Raman label. *A* Represents the substrate approach, *B* and *C* are examples of the inserted particle approach while *D*, *E*, and *F* can all be thought of as SERS nanotags/Raman spectra of six different Nanoplex biotags. From *top* to *bottom*, the label molecules used were 4-[4-hydroxyphenylazo]pyridine, 4,4′-azopyridine, d8-4,4′-dipyridyl, bis(4-pyridyl)ethylene, bis(4-pyridyl)acetylene, 4,4′-dipyridyl. *Source* Doering et al. (2007). Copyright © 2007, Wiley. Reproduced with permission

the antibody, the AuNPs is exposed to obtain and antigen-antibody interaction. This approach was described for detection of mixtures of DNA and proteins by using a mixture of different bio-barcoded AuNPs probes (Stoeva et al. 2006).

Another biosensor using magnetic nanoparticles was developed by Peng et al. In this study, a multi-functional core–shell glucose oxidase–Au–polydopamine–Fe_3O_4 magnetic bionanoparticle (GOx–Au–PDA–Fe_3O_4 MBNPs) was fabricated to detect glucose (Peng et al. 2013). In another study with magnetic bionanoparticles only, the authors developed a high-performance amperometric fructosyl valine (FV) biosensor (Chawla and Pundir 2011). This study aimed to immobilize the enzyme fructosyl amino-acid oxidase (FAO), as a model enzyme, on a core–shell magnetic bionanoparticles modified gold electrode. Chitosan was used to introduce amino groups onto the surface of the magnetic BNPs. The sensor showed outstanding sensitivity, response time, and long term shelf-life. These studies show that BNPs, especially AuNPs and Magnetite NPs can be used to develop biosensors for different medical applications.

5.4   Bionanoparticles for Imaging

As of today, there are several imaging tools available for the medical field. The most common ones are magnetic resonance imaging (MRI), optical (OI) and ultrasound (USI) imaging (Sharma et al. 2006). Among these imaging tools, magnetic and luminescent/fluorescent NPs have contributed significantly to the advancement of bioimaging tools (De et al. 2008). Fluorescent NPs, such as AuNPs, are frequently used for OI, while magnetic NPs are typically used for MRI. In addition to inorganic nanoparticles, such as Au and iron oxides, virus particles have also been described to serve for imaging purposes (Manchester and Singh 2006). In this section we will discuss how these NPs can be applied for MRI or OI and present a few examples of inorganic and organic NPs used in MRI and OI applications.

MRI is one of the most powerful and noninvasive imaging technology possessing exceptional soft tissue contrast and resolution. MRI relies on magnetic fields and radio frequencies. The signal intensity of MRI is related to the relaxation times of protons from free molecules, such as lipids, water, and proteins that are present in organs (Lam et al. 2013). Because of the development of highly specialized and efficient contrast agents, MRI has become one of the most powerful noninvasive imaging tools in medicine. In MRI, to increase contrast, various inorganic nanoparticles and contrast agents are administered prior to the scanning. The contrast agents used can be composed by either ferrites, magnetite, or iron oxide NPs. These contrast agents are responsible for providing negative contrast in the image.

The main BNP currently investigated for MRI application, as contrast agent, is ferritin. This protein stores a ferrihydrite/magnetite core/shell structure and is synthesized by microorganisms. When the ferritin iron content is removed, magnetite predominates. Furthermore, the exterior shell of ferritin can be easily functionalized, which facilitates incorporation of specialized binding sites or other dyes (Uchida et al. 2007). There are descriptions in the literature, where ferritin can be conjugated with different Alexa Fluor dyes. This conjugation leads to fluorescence resonance energy transfer (FRET) in a single nanoparticle (Fernandez et al. 2008). The incorporation of optical functionality in magnetic NPs is of growing interest since it would allow simultaneous target labeling, optical and magnetic imaging. This simultaneous imaging would facilitate cell sorting and even cell separation for diagnostics and treatment (Wang et al. 2005; Wetz et al. 2007).

In addition to using magnetic NPs to enhance MRI signals, researchers have also embedded iron oxide in AuNP shells. In this case, the iron oxide provides magnetism, whereas the Au shell incorporates the optical properties of AuNPs (as described later in this section) (Lim et al. 2007; Boisselier and Astruc 2009). The application of AuNPs for the development of new MRI contrast agents has also been investigated. In these studies, AuNPs were used as templating carriers of gadolinium chelates, which is currently used in MRI imaging. The results showed that the sensitivity of magnetic resonance imaging improved significantly with this composite. Besides using AuNPs for MRI, these NPS can also be used for OI.

The OI involves fluorescent labelling of a target macromolecule, organelle, cells or even tissues for their location and diagnosis. This tool relies on specific binding of the fluorescent nanoparticle to a target to reveal its location under a fluorescence microscope. The most used BNP for OI is AuNP, which includes AuNPs with nanorods and nanospheres shapes. AuNPs can be used for OI by producing antibody-conjugated AuNPs. These conjugated nanoparticles are able to bind to antigens either in cells or tissues. The main characteristic of AuNPs that makes this NP attractive over other labeling dyes is because they are extremely stable under continuous illumination and do not bleach. Furthermore, the AuNPs fluorescence spans over an entire spectrum of light; these NPs exhibit plasmonic effects and fluorescence in both one-photon (Eustis and El-Sayed 2005; Li et al. 2005) and two-photon (Imura et al. 2005) modes with high efficiencies in contrast to other organic fluorophores. These unique properties of AuNPs make them perfectly suited for OI.

In addition to inorganic BNPs, more recently, virus NPs were recognized as part of nanotechnological applications involving BNPs. Viruses have been considered as BNPs since they are of biological nature and are typically found in the nanosize range like most NPs (Steinmetz 2010). Plant and certain animal viruses are particularly of interest since they typically do not cause diseases in humans. More importantly, viral NPs can be engineered to target a specific cell or tissue type and to contain fluorescent or contrast agents necessary for imaging. The proteinaceous composition of viral NPs allows the incorporation of specific ligands and imaging agents, on a single platform (Young et al. 2008), which may lead to potential applications in targeted imaging and therapy. One example of application of viral NPs for MRI is the study performed with the Cowpea chlorotic mottle virus (CCMV). This BNPs was engineered and expressed in the yeast Pichia pastoris. The authors in this study successfully produced and purified the CCMV coat protein, which possess a metal binding domain. The resulting modification of CCMV with Gd^{3+} was able to generate a paramagnetic NPs for MRI application (Allen et al. 2005). This report is just one of many reports using viral NPs from different origins for the development of image-contrast agents. Other studies have also investigated the viral NPs for OI applications.

The reason viruses are also attractive BNPs for optical imaging is because most viruses have multivalent capacities that allow incorporation of fluorochromes compatible with different microscopes for imaging and diagnosis. As a rule of thumb, the application of viral BNPs in the imaging and diagnosis of alterations in cells or tissues, which are related to diseases, depends on the use of fluorochromes that are compatible with the imaging technology. In the case of fluorochromes, imaging has been achieved with the development of two-photon laser scanning microscopy (TPLSM) (Denk et al. 1990) and development of fluorophores optimized for two-photon absorption (TPA) (Massin et al. 2013). The TPLSM has been very promising since it produces background-free images with reduced photobleaching and photodamage (Niehl et al. 2015). This system was investigated with the Tobacco mosaic virus (TMV). In a recent study, researchers synthesized TMV particles carrying a two-photon fluorophore to obtain images of mouse brain
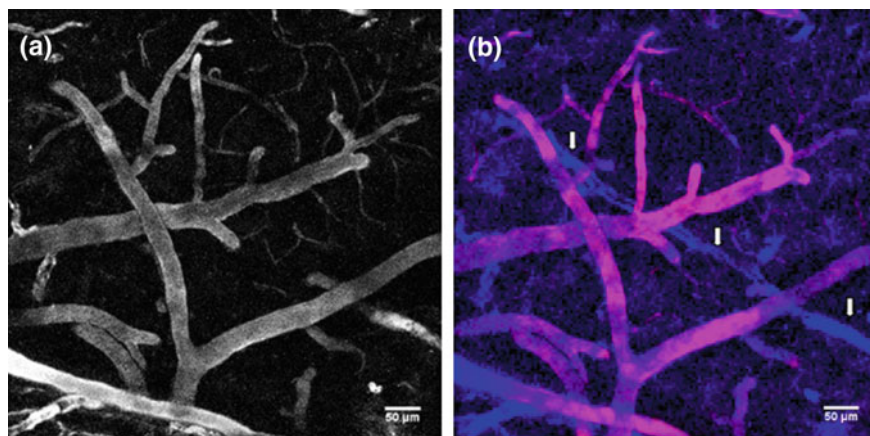
Fig. 5.3 Intravital imaging of the mouse brain vasculature with TMV-BF3 particles. **a** Mouse brain vessels labeled with TMV-BF3 at 1 h after intravenous injection into the tail vein. **b** Same observation window as shown in **a** but after a second injection, this time with sulforhodamine B; *blue*, fluorescence emitted from TMV-BF3; *red*, fluorescence emitted from sulforhodamine B. The 3D projections were performed with Fiji software using the standard deviation projection method. *Source* Niehl et al. (2015). Copyright © 2015, Frontiers. Reproduced with permission

vasculatures (Fig. 5.3). In this study, the authors demonstrated that the fluorescent signal emitted from the BNP was stable and did not leak into surrounding tissues. This study suggested that viral NPs have the potential for visualization of pathological alterations in the brain vasculature in a noninvasive manner. Caution, however, needs to be taken with viral NPs, since it is still not clear whether they present any in vivo toxicity and immunogenicity. However, these studies open the doors for potential future application of theses viral NPs for imaging.

5.5 Bionanoparticles for Drug Delivery

In the past decades, researchers investigating pharmaceuticals realized that drug delivery is a fundamental part of drug development. An ideal drug delivery system should maintain therapeutic concentration and drug stability over time, and permit reproducible and long-term release of the drug at the target site (Kubik et al. 2005). Nanotechnology has emerged as a new approach for drug delivery; and most of the studies to date with nanotechnology focus in cancer research. These studies demonstrated that both inorganic and organic nanoparticles can be employed successfully for drug delivery. Among the BNPs that have been investigated for drug delivery there are magnetic, cellulose and viral nanoparticles.

The most investigated nanoparticles for drug delivery are magnetic nanoparticles. These nanoparticles are either functionalized with anticancer drugs or encapsulated with biocompatible polymers that contain the drug to be delivered.

For instance, one study convalently functionalized the magnetic nanoparticles with doxorubicin (DOX), an anticancer drug (Kattan et al. 1992). The authors showed that the drug delivery system released the drug in mild acidic conditions. Another study, showed that an antibody-conjugated magnetic Poly-(D,L-lactide-co-glycolide) (PLGA) nanoparticles with doxorubicin could be used for simultaneous anticancer drug release and imaging system, because of the magnetite NPs. A similar study, used the antibody Herceptin1 for targeting breast cancer (Yang et al. 2007). These studies indicated that the system is very efficient for delivery of drugs to different cancerous cells.

Although most of the magnetic-targeted drug carriers uses synthetic Fe_3O_4 or Fe_2O_3 as cores coated with biocompatible polymers for drug delivery, this system presents several issues. The major issues for using these nanoparticles are that they have the propensity to aggregate in aqueous solutions and during their synthesis, it is difficult to control their shape and size, as well as their drug loading, which tends to be low (Sarikaya 1994). More recently, researchers have investigated bacterial magnetosomes, synthesized by certain bacteria, as replacements for synthetic magnetic-targeted drug carriers (Schuler and Frankel 1999; Hopkin 2004). These BNPs have unique features, such as narrow and nano-scale size distribution, paramagnetism and are typically membrane bounded (Bazylinski et al. 1994; Sun et al. 2007). These BNPs have also been previously used as carriers for antibodies, enzymes, and nucleic acids (Sun et al. 2007). More recently, these BNPs were demonstrated to also effectively serve as a drug delivery system for doxorubicin. The results showed superior drug delivery with this BNP.

Another well study drug-delivery system is viral capsid. These particles are typically monodispersed, possess nanometer sizes, can reversibly disassemble and reassemble upon certain stimuli and therefore provides an easy route for loading and release of drugs. In addition to drugs, viral particles have been used to store artificial DNA (Mukherjee et al. 2006), single enzymes (Comellas-Aragones et al. 2007), and DNA micelles with hydrophobic components inside the hydrophobic domain of the micelle (Minten et al. 2009). These properties of viruses offers unique possibilities to introduce DNA as a gene therapy system, as well as specific drugs or bio-catalysts delivery systems into the body.

Biocellulose is another BNPs that has a long history in drug delivery applications. Cellulose matrices are frequently used for oral drug delivery through tablets since it has an exceptional compaction property. Cellulose also can be easily modified to bind different drugs. For instance, Burt and collaborators used this property of cellulose to bind water soluble antibiotics and anticancer agents (Jackson et al. 2011). Nanocellulose-based drug carriers can be typically divided into three forms: microspheres (or microparticles), hydrogels (or gels), and membranes (or films) (Table 5.1).

Lin and collaborators developed a pH-sensitive cellulose-alginate microsphere drug delivery system. This system presented higher encapsulation efficiency, reproducible swelling patterns and more importantly, continuous and sustainable release of the drug (Lin et al. 2011a). Hydrogels have also been produced with nanocellulose. In one investigation, the nanocellulose was grafted with cyclodextrin

Table 5.1 Types of drug carrier systems based on nanocellulose

Carrier form	Material component		Model drug	Release time and medium	Ref
	Nanocellulose	Matrix			
Microsphere or bead	Cellulose nanocrystals (CNC)	EA; MMA; BMA	Propanolol hydrochloride	12 h in pH 6.8 PBS	Jackson et al. (2011)
		Sodium	Theophylline	16 h in pH 7.4, pH 6.8, pH 1.0 PBS	Lin et al. (2011b)
	Cellulose nanofibrils (CNF)	–	Indomethacin; nadolol; atenolol; metropolol tartrate; verapamil; ibuprofen	10–14 d in pH 7.4 PBS	Kolakovic et al. (2012)
		Hydrophobin	Itraconazole	90 min in pH 1.2 NaCl/HCl solution	Valo et al. (2011)
Hydrogel or gel	CNC	Cyclodextrin/Pluronic	DOX	6.5 d in water	Lin and Dufresne (2013)
		Cyclodextrin/Pluronic	Bovine serum albumin	20 h in pH 7.4 PBS	Zhang et al. (2010)
		Regenerated cellulose	Bovine serum albumin	48 h in simulated body fluid	Wang and Chen (2011)
	Bacterial Cellulose (BC)	–	Bovine serum albumin	48 h in pH 7.4 PBS	Muller et al. (2013)
		–	Collagen; hyaluronan; growth factors	36–96 h in PBS	Lin et al. (2011a)
		Acrylic acid	Bovine serum albumin	8 h in simulated intestinal fluid	Amin et al. (2012a)
		Polyacrylamide	Theophylline	24 h in pH 7.4 PBS	Pandey et al. (2013)

(continued)

Table 5.1 (continued)

Carrier form	Material component		Model drug	Release time and medium	Ref
	Nanocellulose	Matrix			
Membrane or coating for tablet	CNF	–	Paracetamol	5–10 min in water	Kolakovic et al. (2011)
		–	Lysozyme	10 h in pure water or water/ethanol solution	Cozzolino et al. (2013)
		–	Caffeine	9 h in water	Lavoine et al. (2014)
		–	Indomethacin	30 d in pH 5.0 phosphate buffer	Kolakovic et al. (2012)
		–	Itraconazole	90 d in pH 1.2 NaCl/HCl solution	
		–	Beclomethasone dipropionate	90 d in water	
	BC	–	Paracetamol	2 h in pH 5.8 PBS	Amin et al. (2012b)
		–	Lidocaine	7 h in pH 7.4 PBS	Trovatti et al. (2011)
		–	Lidocaine; ibuprofen	8 h in pH 7.4 PBS	Trovatti et al. (2012)
		–	Caffeine	15 h in pH 7.4 PBS	Silva et al. (2014)
		–	Berberine hydrochloride, berberine sulfate	24 h in pH 2.1 HCl or H_2SO_4 solution; pH 6.8 PBS; pH 12.0 NaOH solution	Huang et al. (2013)
		–	Glycerin	24 h in vivo evaluation (skin)	Almeida et al. (2014)
		Poly(vinyl alcohol)	Vanillin	1 h in water	Stroescu et al. (2013)
Aerogel	CNF	–	Beclomethasone dipropionate	700 min in pH 8.0 SDS solution	Valo et al. (2013)

for the encapsulation of the drug doxorubicin. The drug release study revealed that the hydrogels exhibited prolonged release of the drug (Lin and Dufresne 2013). Kolakovic and collaborator demonstrated the formation of nanocellulose films that had long-lasting sustained drug delivery properties (Kolakovic et al. 2011). The study demonstrated that the film allowed sustainable release of certain model drugs over a period of three months. The authors also showed that certain drugs had limited release due to poor diffusion. The authors explained that the difference in the release for the different drugs was due to the drug solubility in the solution medium (Kolakovic et al. 2012). In another study regarding biocellulose membranes, Huang and collaborators investigated the delivery of berberine hydrochloride and berberine sulfate in comparison to commercial tablets. The results showed that the membranes significantly extended the duration of the release of the drugs (Huang et al. 2013).

In addition to the traditional drug trapping strategies, some researchers have also explored the direct attachment of drug molecules to nanocellulose. This process was done through covalent coupling of the drug to the nanocellulose. Researchers employed in this process a series of oxidation, reductive-amination, and esterification reactions (Dash and Ragauskas 2012). Overall, the use of natural nanocellulose as a drug delivery system is a very attractive concept, however the physiological influence in the release of drug release, interactions between the drug molecules and the NPs are still of concern and needs to be further investigated.

5.6 Environmental Applications of BNPs

5.6.1 BNPs for Environmental Remediation

Besides the medical applications of BNPs, researchers have also investigated their application for environmental remediation (Njagi et al. 2011; Hussain et al. 2016). In these studies, microorganisms or BNPs have been shown to clean hazardous waste sites (Elango and Roopan 2015; Kalaiselvi et al. 2015). Current studies show two main ways of cleaning contaminated sites using BNPs, the first one involves adsorption of the pollutant and the other involves degradation or dehalogenation of the contaminant.

Adsorption is a very attractive method to remove contaminants, since is typically highly efficient, minimizes chemical sludge and does not require strong technological knowledge (Aksu 2005). The main drawback of this technique is that it can be mainly used in surface water and groundwater. Removal by adsorption using BNPs were investigated mainly for heavy metals and textile dyes (Dotto et al. 2012a, b). In the case of heavy metals, researchers were able to remove heavy metals using cellulose BNPs and nanoparticles made of microbial biomass.

In the case of bacterial cellulose nanofibers (BCF), researchers have become interested in this BNP because of the unique structure and properties of this bionanomaterial (Carpenter et al. 2015). This BNP possess a nanofibrillar structure,

high mechanical strength, high surface area-to-volume ratio, inherent environmental inertness, and can be easily functionalized by incorporating chemical moieties that will increase the binding efficiency of pollutants. These properties are essential for adsorbents used in the remediation of environmental contaminants (Shah and Brown 2005; Wan et al. 2006).

The more commonly used method to increase adsorption capacity of cellulose is carboxylation. Yu and collaborators investigated the incorporation of succinic acid groups onto cellulose. They demonstrated that this modification significantly increases the binding efficiency of this NP to lead and cadmium (Yu et al. 2013). The removal of these heavy metals was further enhanced by the conversion of the carboxylic acid groups to sodiated carboxylates. Another example of successful carboxylation that led to improved heavy metal removal was demonstrated by Srivastava and collaborators. The incorporation of carboxylic groups into cellulose increased by 3–10 % the removal of Ni^{2+}, Cr^{3+}, Cd^{2+} and Pb^{2+} than unmodified NPs (Srivastava et al. 2012). Besides heavy metals, Ma and collaborators demonstrated that cellulose could remove radioactive uranyl ions (UO_2^{2+}) from an aqueous solution (Ma et al. 2012). The presence of carboxylate groups in the cellulose produced a material able to achieve 2–3 times greater removal of UO_2^{2+} than traditional adsorbents (i.e. silica particles, hydrogels, polymer particles, and montmorillonite). Alternatively, researchers also demonstrated that the incorporation of cysteine, which possess thiol groups, was effective in the removal of Cr(VI) and Pb(II) (Yang et al. 2014).

Studies have also demonstrated that biosorption using non-active (dead) microbial mass, allows the removal of pollutants from aqueous solutions (Gupta and Suhas 2009; Ngah et al. 2011). The advent of nanotechnology and the unique properties of nano-based materials have led researchers to investigate the application of dead microbial biomass conversion to nanoparticles. Dotto's research group has investigated extensively the production of Spirulina platensis bionanoparticles (Dotto et al. 2012a, b; Dotto et al. 2013) from dead microbial biomass for the removal of diverse pollutants, such as textile dyes, heavy metals and phenol. The reason for the good removal of these BNPs was because of the high surface area-to-volume ratio, which led to a faster mass transfer, and a variety of functional groups (carboxyl, hydroxyl, sulfate, phosphate and others) in the nanoparticles that have high affinity for these pollutants.

Besides adsorption, researchers have also investigate the application of BNPs for the catalytic removal of contaminants in water sources, soils and sediments. Bacterial cellulose nanofibers (BCF)-modified with other nanoparticles have been shown to exhibit excellent catalytic hydrogenation performance (Patel and Suresh 2008). For instance, a study demonstrated that it is possible to modify BCF with palladium (Pd) and copper (Cu) to prepare a BCF composite material for the application in catalytic denitrification (Sun et al. 2010). In this study, modified BCF nanocomposite was prepared by immersing BCF in a solution containing $PdCl_2$ and $CuCl_2$, followed by reduction of the absorbed metals into the BCF with potassium borohydride. The Pd-Cu/BCF showed high catalytic activity when used for water denitrification.

In addition to BCF, researches have also extensively investigated the application of BNPs for dehalogenation of organic contaminants. BNPs of Pd have attracted extensive interest for remediation purposes because Pd is one of the most widely applied catalysts in chemistry for dehalogenation, reduction (Mabbett et al. 2004; De Windt et al. 2006), hydrogenation (Creamer et al. 2008; Wood et al. 2010) and C–C bond forming reactions (Sobjerg et al. 2009) under ambient conditions, and currently synthetic production methods of Pd nanoparticles are not very environmentally friendly or sustainable for large scale production. Most research, however, for commercialization of bio-Pb focused on dehalogenation of contaminants in wastewater, groundwater and in soil remediation.

Extensive studies have been done for PCB degradation using bio-Pd-catalyzed dehalogenation (Baxter-Plant et al. 2003; De Windt et al. 2005). These studies showed that PCBs have a fast dehalogenation rate in the presence of bio-Pd (De Windt et al. 2006). Another study, however, pointed out that release of Pd in aquatic environment would be troublesome, hence, the magnetical characteristics of some bio-Pd nanoparticles (Creamer et al. 2011) or the combination of Pd with biogenic magnetite NPs (Coker et al. 2011) have been investigated. This approach would facilitate the recovery of the catalyst after reaction and prevent its release to the environment. The treatment of groundwater contaminated with a mixture of chlorocyclohexanes (HCH) and chlorobenzenes using bio-Pb in a fluidized bed reactor has also been investigated by Hennebel and collaborators (Hennebel et al. 2010). Results showed superior treatment than existing activated carbon filters. In soil, Cr(VI) remediation using bio-Pd produced by C. pasteurianum was shown to be effective (Chidambaram et al. 2010). However, the injection of Pd into soils can be concerning, since leaching of Pd(II) or nanoparticulate Pd(0) into the soil and the groundwater could potentially happen. Hence, strong attachment of Pd to the cells is essential, or alternatively, ex situ treatment should be preferred since Pd can be extracted from the soil after treatment. Although BNPs have been investigated for site remediation, they are still not being commercialized due to potential hazardous effects to the environment. More research needs to be done to investigate their impact to the environment.

5.6.2 Application of BNPs in Water Treatment

Another environmental application of nanoparticles is in water treatment. Some BNPs, such as cellulose nano- and microfibers have been investigated for the fabrication of membranes for water treatment due to the dimensions and strength of this material. Studies have investigated the fabrication of membranes with pristine cellulose, but also the incorporation of this nanomaterial into different polymer matrices. Among the polymers investigated with BCF, there are poly(vinylidene fluoride) (PVDF), poly(ethylene oxide) (PEO), poly(acrylonitrile) (PAN), cellulose triacetate, poly(vinyl alcohol) (PVA), poly(3-hydroxybutyrate) (PHB), poly(ether sulfone) (PES), and polypyrrole (PPy) (Wang et al. 2013; Kong et al. 2014; Lalia

et al. 2014; Carpenter et al. 2015). These different membranes were investigated for nanofiltration, microfiltration, ultrafiltration, membrane distillation, and hemodialysis. Researchers demonstrated that additions of different amounts of biocellulose within the polymer matrices generated membranes with different properties, such as membranes with different tensile strength, surface hydrophilicity, selectivity, permeability and even resistance to biofouling. Typically an improvement on the performance of the membranes was observed with incorporation of small amounts of BCF.

Most of these bacterial cellulose nanofibers (BCF) membranes have also been modified with other nanoparticles to generate hybrid nanocomposite materials (Cho et al. 2005). For instance, BCF membranes produced by *Acetobacter xylinum* have been modified with titanium dioxide (TiO_2) nanoparticles dopped with nitrogen and fluorine to improve catalytic activity of TiO_2 under visible light (Brauer and Szulczewski 2014; Wei et al. 2014). This nanohybrid membrane was able to inactivate both Gram-negative and Gram-positive bacteria under fluorescent light. The authors also demonstrated that the photocatalytic activity of these membranes against microorganisms was dependent on the type of bacteria, and degree of N–F-co-doped TiO_2. Silver nanoparticles are also very attractive nanomaterials for coating BCF membranes. Silver have been used for centuries to treat potable water, due to the antibacterial properties at trace levels of these metals. Silver nanoparticles, however, possess greater surface area than bulk silver, hence it is more bioactive against microorganisms (Mpenyana-Monyatsi et al. 2012). Silver nanoparticles have been used extensively used in water filtration applications to prevent fouling of membranes (Dankovich and Gray 2011; Carpenter et al. 2015).

Organic and biological fouling reduces the water flux during treatment. Self-cleaning membrane mechanisms is very attractive since it can eliminate many cleaning chemicals used for membrane cleaning. Hence, AgNPs have been used extensively as membrane coatings to prevent biofouling of membranes and other types of filters. For instance, an ultrafiltration membrane made of poly (vinylidene fluoride) (PVDF) was modified with AgNPs to prevent both organic and microbial antifouling (Li et al. 2013). The modification of the membrane with AgNPs improved the hydrophilicity of the membrane surface, which led to a reduced contact angle (81–68°) and increased permeate flux (36.4–108.6 L/m^2 h). The organic antifouling and biofouling performance of the membranes were investigated with bovine serum albumin and *E. coli* as model foulants, respectively. The results confirmed the superior antifouling property of the AgNP coated PVDF membranes.

Besides membranes, silver nanoparticles have also been used to coat beads, paper filters and ceramic filters. In the study with AgNPs with coated resin beads, these beads were used to develop a column filtration system for microbial inactivation (Mthombeni et al. 2012). The authors evaluated the performance of the coated resin beads as a function of bed mass, initial bacterial concentration and flow rate using *E. coli* as model contaminant in water. The *E. coli* survival rate were plotted as breakthrough curves (BTCs). The results were modeled using sigmoidal regression equations to obtain relevant rate parameters. The performance of the

column was determined using the capacity of the bed and the number of bed volumes processed at breakthrough point. Results show that performance increases with a decrease in initial bacterial concentration, an increase in flow rate and an increase in bed mass.

Paper filters were also coated with AgNPs to inactivate microorganisms percolating through the filter instead of by sieving mechanisms during filtration. In this study, the AgNPs were deposited on cellulose fibers of a blotting paper sheet. The authors investigated the leaching of silver ions and their antimicrobial capabilities. The results showed that the nanoparticles released about 0.1 ppm of silver ions that could inactivate 6 and 3 logs of *E. coli* and *E. faecalis*, respectively (Dankovich and Gray 2011). This amount of silver ions, even though it was antimicrobial, was below the current USEPA and WHO limits for silver in drinking water. These results show that the presence of AgNPs could be effective against hazardous microorganisms in drinking water.

Other studies related to point-of-use drinking water purification using ceramic porous media with AgNPs were also investigated (Ren and Smith 2013). The authors investigated several methods to incorporate AgNPs in the ceramic filters, such as paint-on, dipping, and fire-in method. The authors investigated a water sample with complex chemistry, which was moderately hard and contained monovalent and divalent inorganic ions. The ceramic porous medium fabricated with Ag-NPs by the paint-on and dipping methods, presented significant release of AgNPs into the water effluent as opposed to the fire-in method (where the AgNPs were added to the ceramic components during the ceramic porous medium fabrication). These results demonstrated that the fire-in method produces a better quality filter with longer antimicrobial properties than the others method.

The application of silver nanoparticles have been extensively investigated and are now commercially available for home-water purification systems. Among the current water treatment systems already available on the market, there are Aquapure and QSI-Nano (Dhandapani et al. 2012).

5.6.3   Renewable Energy Source

Nanomaterials have also been extensively explored in supercapacitors, batteries and fuel cells to assist in sustainable energy generation. For instance, Ni_3S_2 nanoparticles have been successfully incorporated on bacterial cellulose nanofibers (BCN) to be used in a supercapacitor (Yu et al. 2014). Supercapacitors are considered a new-type of energy store device with higher power density than traditional dielectric capacitors and batteries (El-Kady et al. 2012). They can be used as a power back-up for portable electronic devices as well as in electrical vehicles (Miller and Simon 2008; Simon and Gogotsi 2008). The new nanocomposite of Ni_3S_2/BCN presented high specific capacitance and good cycle stability. The authors used in the setup of the supercapacitor a positive electrode with Ni_3S_2/BCN and just BCN as a negative electrode in 2 M KOH electrolyte. This asymmetric

supercapacitor showed excellent cycling stability with 97 % specific capacitance retained after 2500 cycles.

In addition of supercapacitors, researchers have also explored BCNs in batteries. This bionanomaterial has attracted a lot of attention since it can be fabricated on a large scale via a simple and cost effective method (Wan et al. 2015). More importantly, BCN is environmentally friendly, can be abundantly synthesized by diverse bacterial species, and is highly conductive and flexible. These properties make this bionanomaterial suitable for the fabrication of flexible electrodes. In order to improve electrochemical performance researchers have commonly incorporated metal oxides, i.e. SnO_2, MnO_2, Fe_2O_3 and Fe_3O_4 to these BCNs. Among these oxides, Fe_3O_4 has been considered to be one of the most promising electrode materials since it has high theoretical capacity, low processing costs, abundance and environmental friendliness (Wu et al. 2010; Wan et al. 2015). This nanoparticle, however, aggregates very easily, possess poor electronic conductivity and large volume variation, which limit its performance. Alternatively, the construction of hybrid Fe_3O_4/BCNs have shown to solve these issues and produce working electrodes in lithium-ion batteries without metal current collectors, conducting additives, or binders. Another biomaterial investigated for battery applications as ion insertion materials was siliceous material produced by bacteria and diatoms (Joerger et al. 1999). These studies clearly show that different BNPs can be used for applications in batteries.

Another growing research field applying BNPs for energy generation is proton exchange membranes for fuel cells. These membranes have attracted a lot of attention because of their high power density, high energy conversion efficiency, tensile strength, environmental friendliness, and the hydroxyl groups on its backbone which provide high hydrophilicity. These features are crucial for the operation of polymer electrolyte membrane fuel cells (Wang 2004; Yang et al. 2009). The main material used for these membranes are bacterial cellulose, typically from *A. xylinum.* These membranes are typically modified with other nanoparticles, such as palladium and platinum, to increase the electron current and better catalyze the generation of hydrogen oxidation reaction in microbial fuel cells. More importantly, these biomembranes with other nanoparticles have shown higher thermal stability and lower gas crossover when compared to other synthetic polyelectrolyte membranes. These results indicate that renewable bacterial cellulose membranes are promising prospects for membranes used in the fuel cell field.

5.7   Final Conclusions and Remarks

The production of nanoparticles by microorganisms has been showing to be very promising for different applications in biomedical and environmental fields. These bionanoparticles can be used by themselves in these applications or combined with other bionanoparticles or synthetic nanoparticles. Despite the fact that several researchers have investigated the synthesis of these BNPs and their potential

application, it is still essential to understand what would be the health and environmental impacts of these nanoparticles compared to their synthetic counterparts. Several researchers believe that BNPs are more environmentally friendly, which is true for their synthesis, but it is still not clear whether these particles are really safer for Nanotechnological applications than the synthetic ones.

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