

EDITED BY

R. NAVANIETHA KRISHNARAJ • RAJESH K. SANI

# MICROBIAL INTERACTIONS AT NANOBIOTECHNOLOGY INTERFACES

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MOLECULAR MECHANISMS AND APPLICATIONS

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# **Microbial Interactions at Nanobiotechnology Interfaces**

Molecular Mechanisms and Applications

*Edited by*

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## Preface

Nanomaterials have been realized as potential agents for several biological applications including therapy and diagnostics. Realizing the biological activity of nanomaterials and their importance for nanomedicine, the field of nanobiotechnology emerged to emphasize the toxic effects of nanomaterials and biological applications. The field of nanobiotechnology covers concepts on the biological synthesis of nanomaterials, characterization of biologically synthesized nanomaterials, and applications in the biological sector. The unique physicochemical characteristics of the nanomaterials offer interesting activities including antibacterial, antifungal, antiviral, and anticancer. Recent decades have evidenced tremendous advancements in nanobiotechnology research with applications in diagnosis, drug delivery, and therapy.

Considering the importance of the field, the book aims to provide a basic understanding about the interaction of nanomaterials with living cells/proteins/enzymes at a molecular level and factors influencing the interactions. This book covers specialized topics on protein nanoparticle interactions and factors influencing these interactions, shape- and size-dependent activity of the nanomaterials, and surface functionalization of nanoparticles for stability/activity in biological systems. An interesting chapter covering the molecular factors and mechanisms that drives the anticancer activity of the nanomaterials. Understanding the surface factors of nanomaterials influencing the biological activity will help in reverse engineering of nanomaterials with tailored surface characteristics.

Overall this would be an ideal textbook for nanobiotechnology courses for chemical, biochemical, and biomedical engineering students. Glossary and reasoning type questions have also been included at the end of each chapter. This book will also help scientists to understand advanced concepts in nanobiotechnology and nano-biomanufacturing with specific characteristics. This book discusses concepts on factors influencing better microbial interactions and surface

engineering approaches specifically focused on surface engineering of nanomaterials for biomedical applications.

The editors would like to thank all the authors for their valuable contribution and the Wiley editorial team for their support.

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11	Biogeochemical Interactions of Bioreduced Uranium Nanoparticles	S. Sevinç Şengör
12	Characterization and Quantification of Mobile Bioreduced Uranium Phases	S. Sevinç Şengör

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# 1

## Shape- and Size-Dependent Antibacterial Activity of Nanomaterials

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### Objectives

- To understand the importance of studying nanomaterials-bio interface and the factors that dictate it.
- To understand the current situation of antibiotic resistance of microbes and their effect on worldwide healthcare.
- To know the strategies to overcome the antibiotic resistance mechanism and role of nanomaterials in combatting it.
- To understand the mechanism of action of antimicrobial nanomaterials and the factors that influence their antimicrobial properties.
- To understand the key role of size and shape of the nanomaterials on the antimicrobial properties of nanomaterials.

### 1.1 Introduction

Over the past three decades “Nanotechnology” has emerged as a promising strategy to overcome impasses that have accumulated in various fields of science and technology (Albanese, Tang, & Chan, 2012). Nanomaterials (NMs) are defined as minuscule structures having at least one of their dimensions equal to or between 1 and 100 nm. Since there is no single universally accepted definition, so far various organizations have given their own definition to the term “NMs” (Boverhof et al., 2015). US Food and Drug Administration (USFDA) defines nanomaterial as “materials that have at least one dimension in the range of approximately 1–100 nm

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and exhibit dimension dependent phenomena” (Bleeker et al., 2012). As per Environmental Protection Agency (EPA) definition, “NMs can exhibit unique properties dissimilar than the equivalent chemical compound in a larger dimension.” Similarly, the International Organization for Standardization (ISO) defines it as “material with any external nanoscale dimension or having internal nanoscale surface structure.” EU Commission has described it as “a manufactured or natural material that possesses unbound, aggregated or agglomerated particles where external dimensions are between 1–100 nm size range” (Jeevanandam et al., 2018).

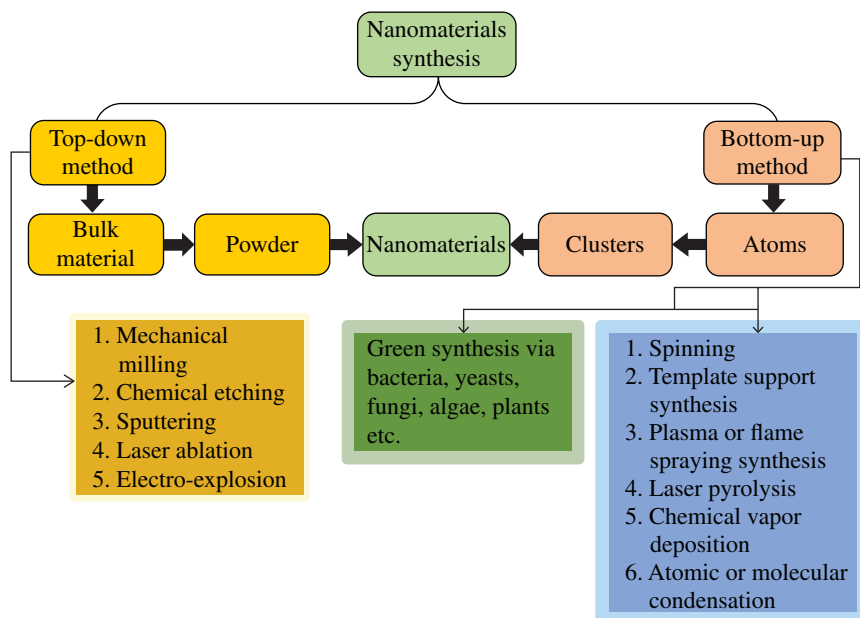
NMs generally exist in the shape of spheres, cubes, rods, tubes, flowers, and platelets (Machado et al., 2015). NMs in the nanoscale dimensions possess a high surface area-to-volume ratio and also a high number of atoms/molecules present on the surface rather than the interior of the materials. These are the properties that majorly contribute to the unique functionality of the nanoscale materials, which vary from the bulk of the same material. Therefore, modulation in their structural properties such as change of size or shape will significantly affect their optical, electrical, magnetic, and biological activity (He et al., 2010; Machado et al., 2015). This is one of the distinct advantages of nanotechnology where by engineering the design or production parameters we can modulate the functionality of the NMs specific to particular application (Machado et al., 2015). Hence, the recent studies in nanotechnology are majorly focused on understanding the effect of physicochemical properties such as size, shape, and surface chemistry of the material on the optical, electrical, magnetic, and biological activities.

Considering the aforementioned advantages, NMs have found enormous applications in various fields and products such as cosmetics, catalysts, fillers, biomedical devices, and semiconductors. As per data report from 2015, approximately more than 1800 products from 622 companies in 32 countries contain engineered NMs. In summary, 762 (i.e. around 42%) of the total products are used in the health and fitness category where silver is the most predominantly used NM, in almost 435 products, which are around 24% of the total. Further, about 528 products (i.e. 29% of total) contain NMs as liquid suspension where dermal contact is highly possible. Hence, the abundant application of these materials is leading towards a long-term co-existence of such NMs with living systems which may result in adverse toxicological effects to the living bodies. In this context, it is necessary to study the effect of these materials on biological entities such as proteins, DNA, RNA, cell membranes, cell organelles, cells, tissues, and organs. The interactions between the biological system and NMs strongly depend upon the environment and the biophysico-chemical property of the nano-bio interface (Nel et al., 2009). As discussed, size, shape, and surface chemistry are the most important factors that govern the physicochemical properties of the NM that in turn throws light at the nano-bio interface. Understanding the effect of these physicochemical factors and extrapolating them toward the interactions at the nano-bio interface would help us

to design or engineer NMs for specific applications with an added advantage of minimal toxicity to living bodies. There are a number of analytical tools to study the interaction of nano-biomolecules/proteins. Among them the most employed are mass spectroscopy, Fourier transform infrared spectroscopy, circular dichroism spectroscopy, Raman spectroscopy, nuclear magnetic resonance, UV-vis spectroscopy, surface plasma resonance, quartz crystal balance, atomic force microscopy, fluorescence correlation spectroscopy, fluorescence spectroscopy, and isothermal calorimetry (Saptarshi, Duschl, & Lopata, 2013). Among the different strategies, mass spectroscopy-based proteomics is the most preferred. Even though the technique is a qualitative measure of proteins bound to NMs, such as nanoparticles (NPs), it can be applied over a wide range of NMs. UV-vis spectroscopy is employed to measure changes observed in the adsorption spectrum caused by NM-protein interaction. Similar to UV-vis spectroscopy, fluorescence spectroscopy is employed to measure changes in the fluorescence spectra caused by the binding of protein on to NMs. Surface plasma resonance is used to study changes in electrons' oscillation on the surface of metal NMs as a result of protein interaction with NM. Isothermal calorimetry analysis is employed to determine the binding constant and other thermodynamic parameters of the nano/bio interface (Saptarshi et al., 2013). Quartz crystal balance is used to measure changes in mass on the surface of oscillating quartz caused by the NM-protein interaction. In a study, adsorption of proteins myoglobin, bovine serum albumin, and cytochrome over the surface of gold NPs was studied using quartz crystal balance (Kaufman et al., 2007). Confocal Raman spectroscopy and confocal spectroscopy can be employed to study and visualize NM-protein interaction and intake of NMs into cells by fluorescent labeling of NPs. In recent times, a combination of these techniques has been strategically employed to study the different aspects of NM-protein/biomolecule interaction. NMs can be synthesized through different routes such as chemical, physical, and green methods. Changes in the synthesis methods, concentration of reactants, and conditions can definitely modulate the morphological parameters (size and shape) of NMs. Taking this into account, the selection of synthesis route also plays an important role in governing NMs' morphological features and their functions. Keeping the aforementioned perspectives in mind, this chapter describes the effects of size and shape of NMs on their biological activity.

## 1.2 Synthesis of Nanomaterials

NMs can be synthesized by a number of methods that are grouped into two different categories: (i) bottom-up and (ii) top-down method. Schematics of typical methods for synthesis of NMs are given in Figure 1.1 as described by Ealias and Saravanakumar (2017).



**Figure 1.1** Schematics of typical methods for synthesis of NMs.

- i) *Bottom-up method*: It is a constructive method wherein the atoms build up clusters that in turn form the NMs. This category includes methods such as sol-gel, spinning, chemical vapor deposition, pyrolysis, and biosynthesis.
- ii) *Top-down method*: On the contrary, the top-down method is a destructive method where the bulk materials are reduced into nanoscale materials. It includes methods such as mechanical milling, nanolithography, laser ablation, sputtering, and thermal decomposition. The typical method of synthesis for various NMs is given in Table 1.1.

### 1.3 Classification of NMs

In nature, NMs are built by nanoscale or submicron-sized blocks that exhibit size-dependent effects. Over the last two decades, a number of NMs or nanostructured materials have been developed and a lot of new developments are underway. The abundant increase in the number of NMs has set forth the need for the classification of these materials. An understanding of the classification would give insight into the interaction of NMs with various surfaces and resultant functionality of the NMs. The first classification of NMs was given by Gleiter (2000) in which the

**Table 1.1** Various approaches for NM synthesis (Ealias & Saravanakumar, 2017).

S. No	Category	Method	NMs
1	Bottom-up	● Sol-gel	● Metal and metal oxide and carbon NMs
		● Spinning	● Organic polymers
		● Chemical vapor deposition	● Carbon and metal NMs
		● Pyrolysis	● Metal oxide and carbon NMs
		● Biosynthesis	● Metal and organic polymer NMs
2	Top-down	● Mechanical milling	● Metal, metal oxide, and polymeric NMs
		● Nanolithography	● Metal NMs
		● Laser ablation	● Carbon and metal oxide NMs
		● Sputtering	● Metal NMs
		● Thermal decomposition	● Metal oxide and carbon NMs

materials were classified on the basis of crystalline forms and chemical compositions. The scheme subdivided the materials into three classes where each class has four kinds of materials (Gleiter, 2000). However, the list of Gleiter was not considered complete as it failed to take account of 0D and 1D NMs such as fullerenes and nanotubes into the classification.

### 1.3.1 Classification Based on Dimensions

Later, Pokropivny and Skorokhod (2007) proposed a new scheme of NM classification where the dimensionality (shape and size or form) of the NMs was considered as a primary criterion. In general, nanostructures are structures with at least one dimension  $d$  equal to or less than 100 nm, which is considered as  $d^*$ . The value  $d^*$  is always dictated by physical phenomena such as path length of phonons and electrons, diffusional length, length of de Broglie wave, penetration length, and correction length. According to the scheme, NMs were classified into four major categories: 0D, 1D, 2D, and 3D (Pokropivny & Skorokhod, 2007).

#### 1.3.1.1 Zero-Dimensional NMs

Zero-dimensional NMs are defined as materials where all the three dimensions are confined to the nanoscale (1–100 nm). The same definition could also be stated on basis of the movement of electrons along the dimensions of the NMs. Zero-dimensional materials are materials where the electrons are merely entrapped in a

dimensionless space without any possible movement (Jeevanandam et al., 2018). The best examples for 0D NMs are NPs and quantum dots. Over the past decades, 0D materials have gained a lot of interest where a number of methods have been designed to fabricate 0D NMs with precise dimensions. 0D NMs can be crystalline or amorphous in nature. They may be mono- or polycrystalline, single- or multi-element, and may exist in various forms (shapes and sizes). These materials have found application in a number of fields such as solar cells (Lee et al., 2009), light-emitting diodes (Stouwdam & Janssen, 2008), single-electron transistors (Mokerov et al., 2001), lasers, therapeutics and diagnosis (Azzazy, Mansour, & Kazmierczak, 2007).

#### **1.3.1.2 One-Dimensional NMs**

One-dimensional NM are the materials where one of the dimensions is in macroscale with other two dimensions confined to the nanoscale ( $<100$  nm) (Xia et al., 2003). Herein, the electrons can move across one axis freely whereas they are entrapped in other two dimensions of the NMs (Jeevanandam et al., 2018). These 1D NMs are ideal choice for studying the dimension-dependent activity of the materials. Similar to 0D NMs they also can be amorphous or crystalline, mono- or polycrystalline, ceramic, polymeric or composite materials of different shapes and sizes. 1D materials such as nanotubes, nanowires, and nanofibers have attracted a lot of interest in the development of hierarchical nanostructures such as nanofilms, nanosheets, and nanoribbons with profound applications in the field of optoelectronics and nanoelectronics (Cui et al., 2001; Kong et al., 2000).

#### **1.3.1.3 Two-Dimensional NMs**

Materials with one of the dimensions in the nanoscale ( $\leq 100$  nm) and the other two dimensions in macroscale are called 2D materials. Here the electrons are confined in one direction whereas they can move across in other two axes freely (Jeevanandam et al., 2018). Similar to 0D and 1D, 2D materials can also be amorphous or crystalline, poly or monocrystalline, single- or multi-element, which also exist in different forms. 2D materials such as nanosheets, nanofilms, and nanoribbons have shown promising applications in the fields of optoelectronics, sensors, and biomedicine (Weaver et al., 2014).

#### **1.3.1.4 Three-Dimensional NMs**

Herein, the materials have all the three dimensions in macroscale but are comprised of uniformly distributed nanometer-sized grains. Hence, the movement of the electrons can be free across all the three dimensions without any confinement (Jeevanandam et al., 2018). 3D NMs also called bulk NMs are widely used in catalysis, electrodes, and magnetic materials. Nano balls, nano coils, and nanoflowers are typical 3D NMs that have high surface area and can provide maximum adsorption sites for all the molecules in a small-area framework (Shen et al., 2008).

### 1.3.2 Classification Based on Chemical Compositions

Similar to dimension, the composition of NMs also plays a vital role in deciding their activities and application. On the basis of composition, NMs are classified into four subcategories, namely: (i) carbon-based NMs, (ii) organic NMs, (iii) inorganic NMs, and (iv) composite NMs.

#### 1.3.2.1 Carbon-Based NMs

The NMs with carbon atoms as their backbone are called carbon-based NMs. They can exist in different forms such as 0D (fullerenes), 1D (carbon nanotubes), 2D (graphene sheets), and 3D (diamond crystal and graphite). General methods to prepare these NM include chemical vapor deposition, arc discharge, and laser ablation. Carbon-based NMs exist in different forms with multiple shapes such as hollow spheres, nanotubes, and ellipsoids (Jeevanandam et al., 2018). Fullerenes are carbon materials with spherical morphology where the carbon atoms are held by  $sp^2$  hybridization. A unique advantage of the fullerenes is their high symmetric property (Astefanei, Núñez, & Galceran, 2015). In general, fullerenes contains 28–980 carbon atoms where the diameter of single layer is up to 8.2 nm and for multilayered fullerenes it is about 4–36 nm (Ealias & Saravanakumar, 2017). Carbon nanotubes are 1D carbon NMs where carbon atoms are wound up to form hollow cylinders, which can also be described as an extension of fullerenes or buckyball. Carbon nanotubes can be single-walled, double- or multi-walled with thickness varying from 0.7 nm for single-walled to 100 nm for multi-walled CNTs. The length of CNTs generally varies from few micrometers to several millimeters (Ealias & Saravanakumar, 2017). CNTs have been exploited in various fields owing to their versatile properties such as elasticity, strength, rigidity, field emission, and electrical conductivity (Saeed & Khan, 2014, 2016). Graphene is one of the 2D carbon-based materials formed by  $sp^2$  hybridized carbon atoms. It is a hexagonal network of carbon atoms with honeycomb atomic structure that is confined to a two-dimensional planar surface. Graphene elucidates commendable physical, chemical, optical, and mechanical properties owing to their unique honeycomb atomic structure. These unique properties altogether make them remarkable materials that are extensively applied in the fields of electronics, optics, storage, thermal applications, photovoltaics, and composite materials (Goenka, Sant, & Sant, 2014; Pumera, 2010).

#### 1.3.2.2 Organic-Based NMs

The NMs formed from proteins, lipids, carbohydrates, and other organic substances are termed as organic-based NMs, which are generally 10 nm to 1  $\mu$ m in size. Commonly exploited organic NMs are dendrimers, liposomes, micelles, and polymeric NPs. The superior advantage of these systems over the other NM

systems is because of their biodegradable and nontoxic nature. Some of these materials like micelles, liposomes, and polymeric NPs have hollow core also called as nanocapsules, which are being exploited for loading and delivery of drug molecules (Biswas et al., 2013; Tiwari, Behari, & Sen, 2008). Apart from that, these materials are sensitive to heat and light, which can be used as platform for responsive and targeted drug delivery system. Similarly, the surface of dendrimers has many chain ends that can also be engineered for specific chemical functions and targeted delivery. Owing to the aforementioned properties coupled with their structural stability, structural integrity, and controlled release profile, organic NMs have emerged as a promising drug delivery system (Wei et al., 2015).

### **1.3.2.3 Inorganic-Based NMs**

The NMs that are based on metal, metal oxide, and ceramic are called inorganic NMs.

#### **1.3.2.3.1 Metal-Based NMs**

Nanometer-sized particles that are synthesized from the metal either by constructive or destructive routes are metal-based NMs. Most of the metals can be synthesized in form of NMs (Salavati-Niasari, Davar, & Mir, 2008); however, the most extensively studied metal-based NMs include cadmium, aluminum, silver (Kim et al., 2007), iron, gold (Sun & Xia, 2002), copper (Ramyadevi et al., 2012; Ruparelia et al., 2008), and lead-based NMs. The size of these materials varies from 10 to 100 nm with high surface area-to-volume ratio, unique surface charge, and pore size. Further, they can be either amorphous or crystalline, which can exist in different sizes and shapes such as spheres, and cylinders.

#### **1.3.2.3.2 Metal Oxide-Based NMs**

Metal-based NMs are sensitive to environmental factors such as heat, sunlight, moisture, and air. In order to overcome the demerits of metal NMs, metal oxide-based NMs were synthesized. One of the most common examples of metal oxide NPs are iron oxide NPs, which are synthesized from the oxidation of iron particles at room temperature. The metal oxide NPs are preferred over metal NPs due to their increased reactivity and efficiency (Tai et al., 2007). Routinely employed metal oxides include: magnetite (Sun & Zeng, 2002), iron oxide, aluminum oxide (Mukherjee et al., 2011), silicon dioxide, titanium dioxide, zinc oxide (Sharma, Jandaik, Kumar, Chitkara, & Sandhu, 2016), cerium oxide, and copper oxide (Ren et al., 2009).

#### **1.3.2.3.3 Composite-Based NMs**

In general, composite materials are described as materials with two or more different materials combined to blend the properties of all the constituent materials. In the same way, the composite-based NM is a multiphase material with at least

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