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Understanding Nanoparticles and Their Probable Risks

You cannot swim for new horizons until you dare to lose sight of the shore.

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Abstract
This chapter introduces the first part of the book, which focuses on the risks posed by emerging nanotechnology. As industries race to commercialize nanomaterials, safety concerns—especially long-term health and environmental effects—remain underexplored. The chapter outlines the unique properties of nanomaterials and their growing presence in fields like healthcare, electronics, agriculture, and defense. It emphasizes the urgent need for regulation, risk assessment, and research on exposure, dosage, and solubility of nanoparticles, given their ability to enter the body and disrupt cellular processes.

Keywords**:** Nanoparticle-fabrication, magnetic-properties, electrical-properties, thermal-properties, chemical-properties, mechanical-properties, optical-properties, consumer-products

1.1 What is Nanotechnology?

Before understanding the risks associated with nanoparticles, we must know what nanotechnology is.

Nanotechnology—the word alone is enough to make anyone scratch their head. Science of the small? How does that work? Why use nanotechnology? Why is it assumed that smaller is better? These are all questions that arise when talking about nanotechnology. As this field becomes more popular

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Figure 1.1 (Left to right) Propounder of Nanotechnology Nobel Laureate Richrd Feynman; Prof. Norio Taniguchi; and Dr. Kim Eric Drexler.

and useful in science, our understanding of it seems to be getting more and more complex; and every time a solution is found, 20 other questions appear. Let us start with what nanotechnology is.

The idea of nanotechnology was first introduced (Figure 1.1) by Richard Feynman in 1959 [1] in a talk entitled "There's Plenty of Room at the Bottom." Later, further experimentation based on this idea led to the term "Nanotechnology" being coined by Norio Taniguchi in 1974 [2] (he must have taken the word Nano from the Greek word which means extremely small or dwarf). The potential of Feynman's idea was exhibited in the mid-80s by Eric Drexler [3] in his book *Engines of Creation* in which the potential of molecular nanotechnology is explained.

A *nanometer* unit is 10^{-9} m. For nanotechnological purposes, the size of nanoparticles is accepted to be from 100 nm down to the size of atoms, because it is at this scale that the properties of materials can be very different from those at a larger or bulk scale. Nanoparticles are neither visible to the naked eye (which cannot see things smaller than 0.2 mm) nor by the light microscope under which things smaller than 0.2 um cannot be seen.

In a nutshell, nanotechnology involves synthesis design, characterization, production, and application of structures, devices, and systems by controlling shape and size at the nanometer scale as well as application of nanoparticles.

The U.S. National Nanotechnology Initiative defines nanotechnology as "The science, engineering, and technology related to the understanding and control of matter at the length scale of approximately one to hundred nanometers. However, nanotechnology is not merely working with matter at the nanoscale, but also research and development of materials, devices, and systems that have novel properties and functions due to their nanoscale dimensions or components."

Nanoparticles are fundamental units of nanotechnology and are used as raw materials for constructing nanostructures, nanomaterials, nanomachines, and nanodevices. Nanoparticles may be defined as "A particle having one or more dimensions of 100 nm or less."

Every month, thousands of publications appear that cover disciplines, such as chemistry, physics, life sciences, medicine, and engineering, informing the current status of the development of nanotechnology and its applications.

1.2 Unique Properties of Nanoparticles that Differentiate Them from Their Bulk Counterpart

Man has always been intrigued by the behavior of various mechanisms at the sub-atomic level. The properties of physics, chemistry, and biology are altered at this level and many times the laws of physics and chemistry are altered to a great extent, leading to materials having properties that can be exploited for a plethora of commercial and fundamental applications. In this dynamic legacy of atoms and molecules, we step onto a very different platform, where the classical laws of physics used to understand the behavior of material become deceptive. Hence, a very sharp weapon of fundamental physics called quantum mechanics dominates this ever-changing dynasty of material properties. The change in the properties of materials when they combine in many ways became clearer when, due to the invention of instruments, we were able to peek into the world of atoms and molecules. This congregation of molecular arrangements can generate machinery at a very small scale and give birth to one of the most potential subjects of the century, called nanotechnology.

The classical laws of physics and chemistry do not readily apply at this very small scale for two reasons. Firstly, the electronic and optical properties of very small particles can be very different from their larger particle. Secondly, the ratio of surface area to volume becomes much higher, and since the surface atoms are generally most reactive, the properties of a material changes in unexpected ways.

Nanoscience is not just the science of small, but the science in which materials with small dimensions show new physical phenomena, collectively called quantum effects, which are size-dependent and dramatically different from the properties of macro materials.

At the nanoscale, there is a vast increase in the ratio of surface area to volume. Due to this, materials at nanoscale show very different reactive properties as compared to what they exhibit on a microscale; and it is still very difficult to predict the physical and chemical properties of particles of such a very small size. For instance, opaque substances become transparent (copper), inert material becomes catalysts (platinum), stable material turns combustible (aluminum), solids turn into liquids at room temperature (gold), insulators become conductors (silicon). The principal parameters that affect the properties of nanoparticles are their shape (including aspect ratios where appropriate), size, the morphological substructure of the substance, surface characteristics, and inner structure. Nanoparticles can exist as aerosols (solids or liquids in the air), suspensions (solids in liquids), or as emulsions (liquids in liquids).

The composition of a specific nanoparticle can be very complex, depending on what interactions it has had with other chemicals or particles and on its lifetime. The chemical processes taking place on the surfaces of nanoparticles are also very complicated and remain largely unknown. Nanoparticles have different ways of interacting with each other. They can remain free or group together depending on the attractive or repulsive interaction forces between them. These interactions remain difficult to characterize.

Some unique physical and chemical properties of nanoparticles are listed below:

1.2.1 Magnetic Properties

Magnetic properties of nanostructured materials are distinctly different from that of bulk materials. Ferromagnetic particles become unstable when the particle size reduces below a certain size as the increase in surface energy provides sufficient energy for domains to spontaneously switch polarization directions and become paramagnetic. But this transformed paramagnetism behaves differently from the conventional paramagnetism and thus is referred to as superparamagnetism. In other words, ferromagnetism of bulk materials disappears and gets transferred to superpara magnetism in the nanoscale due to the high surface energy.

1.2.2 Electrical Properties

Nanoparticles are good conductors of electricity, which make the electrical devices faster with lower power consumption and with reduced imperfections. Some metals become semiconductors as the size decreases because of quantum confinement, e.g., quantum dots.

1.2.3 Thermal Properties

Metal and semiconductor nanoparticles are found to have a significantly lower melting point or phase transition temperature as compared to their bulk counterparts. The lowering of the melting points is observed when the particle size is >100 nm and is attributed to an increase in surface energy with a reduction of size. The decrease in the phase transition temperature can be ascribed to the changes in the ratio of surface energy to volume energy as a function of size.

1.2.4 Mechanical Properties

At the nanoscale, many of the mechanical properties of the materials are modified such as hardness, fracture toughness, scratch resistance, and fatigue strength. Energy dissipation, mechanical coupling within arrays of components, and mechanical nonlinearities are influenced by structuring components at the nanometer scale. The mechanical properties of nanomaterials increase with the decrease in size. Most of the studies have been focused on the mechanical properties of one-dimensional structures such as nanowires. The enhanced mechanical strength of nanowires or nanorods is ascribed to the high internal perfection of the nanowires. Generally, imperfections such as dislocations, microtwins, and impurities in crystals are highly energetic and should be eliminated from the perfect crystal structures. The smaller the cross section of nanowires, the less is the probability of finding any imperfections in them as the nanoscale dimension makes the elimination of such imperfections possible.

1.2.5 Chemical/Catalytic Properties

The huge surface-to-volume ratio of nanoparticles increases its chemical activities and therefore allows nanomaterials to become an efficient catalyst. Moreover, due to the properties of interacting with biomolecules, nanoparticles exhibit toxicity, reactivity, and also enhanced cellular uptake.

1.2.6 Optical Property

For the last few decades, metallic nanoparticles have fascinated researchers due to their colorful colloidal solutions. Mie was the first to explain the red color of gold nanoparticles in 1908 by solving Maxwell's equation for an electromagnetic light wave interacting with small metallic spheres. The color exhibited by metallic nanoparticles is due to the coherent excitation of all the "free" electrons within the conduction band, leading to an in-phase oscillation, which is known as surface plasmon resonance. Thus, the color of metallic nanoparticles may change with their size due to surface plasmon resonance. The unique optical property of nanomaterials may also be due to the quantum size effect, which arises primarily because of the confinement of electrons within particles of dimension smaller than the bulk electron delocalization length. This effect is more pronounced for semiconductor nanoparticles, where the bandgap increases with decreasing size. The same quantum size effect is also shown by metal nanoparticles when the particle size is >2 nm. Depending on their chemical composition, their optical and electronic properties have generated much attention in studies of properties of particles approaching molecular dimensions.

The properties of nanoparticles, viz., physical, chemical, and biological can be manipulated for the desired objectives. Nanostructures and nanomaterials possess a large fraction of surface atoms per unit volume. The total surface energy increases with the overall surface area, which is in turn strongly dependent on the dimension of the material.

1.3 Fabrication of Nanoparticles

The synthesis of nanomaterials is also called *nanofabrication*. There are two approaches (Figure 1.2 & Table 1.1) involved in the synthesis and fabrication of nanostructures:

(i) *Bottom-up approach* involves assembling single atoms and molecules into larger nanostructures. The bottom-up approach refers to the buildup of material from the bottom, atom-by-atom, molecule-by-molecule, or cluster-by-cluster. This method creates identical structures with atomic precision. Moreover, by arranging molecules to form complex structures, new and useful properties have also been accomplished by this method. The advantage this approach has is that it creates nanostructures with fewer defects while a much more homogeneous chemical composition and better short- and long-range ordering can be obtained. However, it is difficult to make a structure large enough and of desired quality. This approach has the potential of producing less waste and therefore is more economical.

(ii) *Top-down approach* involves breaking down large pieces of material to generate nanostructures or nanoparticles

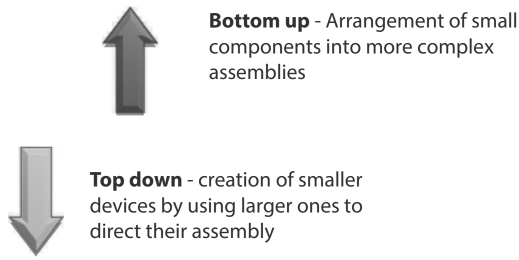

Figure 1.2 Approaches for assembling nanoparticles.

Table 1.1 Examples of various synthesis methods using top-down and bottom-up approaches.

Top-down approach using	Bottom-up approach using
Thermal method	The chemical vapor deposition method
High energy method	Electrodeposition method
Lithographic method	Liquid phase method
Templet method	Seed mediated growth method

of desired size and shape by employing ultrafine grinders, lasers, and vaporizations followed by cooling. The main challenge for the top-down approach is the creation of increasingly small structures with accuracy. Moreover, the top-down approach usually introduces internal stress and surface defects.

These techniques are an extension of those that have been used for producing micron-sized particles. This method is often used for making interconnected and integrated structures, for example, in electronic circuits.

The nanoparticles synthesized by various methods are in the form of colloids, clusters, powders, tubes, rods, wires, and thin films. Apart from various physical and chemical methods of fabricating nanoparticles; there are biological and hybrid techniques available for the synthesis of various nanomaterials. As alternative biological methods or green technology are considered to be safe and sound, the use of biological methods has many advantages over traditional methods. The critical factors in developing a bio-directed self-assembly approach are identifying the appropriate compatibilities and combinations of biological-inorganic material. Biogenic nanoparticles are not supposed to use harmful chemicals.

1.4 Uses of Nanoparticles in Consumer Products

We are living in a time of technological innovation. Nanotechnology, the science of manipulating material at the molecular scale, is a technological development that is moving fast into use and commercialization in many sectors. Over the last few years, nanotechnology has emerged as the science of nanoparticles whose use in many consumer products is very popular. The potential uses and benefits of nanotechnology are enormous. The burgeoning nanoscience field has promised everything from mundane things like better paints, self-cleaning windows, cosmetics to the bizarre tiny submarines that will glide through our veins destroying pathogens and parasites [4].

Today's nanotechnology harnesses current progress in chemistry, physics, materials science, and biotechnology to create novel materials that have unique properties because their structures are determined on the nanometer scale. Nanotechnology has already been embraced by industrial sectors, such as the information and communications sectors, but is also used in food technology, energy technology, as well as in some medical products and medicines.

Already several nanoscale structures are developed and in practical use in areas related to materials science, biology, and medicine, especially in drug designing; targeted drug delivery, tissue engineering, and imaging are also being developed for analytical and instrumental applications. A wide variety of nanoscale materials and coatings are already in use in consumer products such as cosmetics and sunscreens, fibers and textiles, dyes, and paints. Moreover, data storage devices based on nanostructures provide smaller, faster, and lower consumption systems; and new types of microscopes that can produce images of atomic and molecular processes at the surface.

Some of the materials using nanotechnology and nanoparticles that are in the consumer market today are:

- Antimicrobial powders to kill pathogens and contaminants;
- Cosmetics such as sunscreen, nano-liposome-based skin-care products;
- House-cleaning products such as window-washing sprays;
- Lab-on-a-chip devices, biosensors, medical imaging, prostheses and implants, drug delivery devices, etc., for biomedical applications;
- Lighter and stronger ceramics;
- Nanocatalysts;

- Nanoelectronics used in information and communication technology;
- Non-permeable membranes for food packaging;
- Paints, varnishes, and other coatings;
- Remote sensing and tracking devices;
- Sensors, seed improvement, and nano-fertilizer to support agriculture and the environment;
- Solar cells, fuel cells, batteries;
- Various applications in military technology [5].

Apart from the materials that have already found their way into consumer products, others are being intensively researched for solutions to humanity's greatest problems—diseases, clean energy, clean water, etc. Other work is aimed at developing a roadmap for a productive nanosystem, in which a path is sought from today's nanotechnology capabilities to advanced future systems in which molecular tools will build useful materials, devices, and complex systems to atomic precision. The products of advanced nanotechnology that will become available in coming decades promise even more revolutionary applications than the products of current and near-term nanotechnology are providing in the hope of solving critical challenges facing humanity such as:

- Enabling space development;
- Healing and preserving the environment;
- Improving health and longevity;
- Making information technology available to all;
- Maximizing productivity of agriculture;
- Providing renewable clean energy;
- Supplying clean water globally.

1.5 Potential Risks Due to Harmful Effects of Nanoparticles

To know the potentially harmful effects of nanoparticles, we have to know whether and how nanoparticles interact with living organisms, what are the health implications of nanoparticles, do they affect the environment, and above all how to assess the effect of nanoparticles. In this chapter, as well as in this part of the book, we will be addressing this.

Though nanotechnology and nanomaterials offer new opportunities for umpteen applications and even reduction of environmental pollution, we cannot overlook the possible dark side of nanotechnology as it may present new health and environmental risks. Humans have to develop mechanisms of protection against various synthetic nanoparticles of different sizes and their specific characteristics. Chances are that the normal human defense mechanisms, such as immune and inflammatory systems, may not be able to respond adequately to the nanoparticles. Moreover, the dispersal and persistence of nanoparticles in the environment will also have an impact on the environment. For assessing the health risks, two types of nanostructures should be considered: (i) free nanoparticles, and (ii) nanostructure that are an integral part of larger materials such as coatings composed of nanomaterials and other ingredients. Free nanoparticles will pose more interaction with the living system and they pose a greater risk for health or the environment than the nanoparticles fixed to other compounds.

1.5.1 Risk Due to Interaction of Nanoparticles with Living Organisms

Studies dealing with the interaction of nanoparticles leading to toxicity have recently attracted attention. However, they are still scarce. The key factors that affect the interaction of nanoparticles with living structures are:

(i) *Dimensions of Nanoparticles:* Some nanoparticles, have the same dimensions as biological molecules such as proteins. Nanoparticles that are no bigger than a few nm can reach inside biomolecules, which is not possible for larger nanoparticles. Moreover, nanoparticles can cross cell membranes. If inhaled, the nanoparticles can reach through the blood to other sites such as the liver, heart, or blood cells.

(ii) *Surface Characteristics of Nanoparticles:* Nanoparticles may immediately get adsorbed onto the surface of some of the large molecules of living systems they encounter, as they enter the tissues and fluids of the body. Nanoparticles have the unique ability to stick to the molecules of the surface of the living system, due to surface characteristics. This property is useful and relevant for targeted drug delivery using nanoparticles.

(iii) *Dose and Solubility of Nanoparticles:* These are also two of the key factors that help them spread within the body.

Nanoparticles that dissolve easily affect the living organisms in the same way as the effects of the chemical they are made of. But some nanoparticles do not degrade or dissolve readily; hence, they accumulate in biological systems and persist for a long time, which makes such nanoparticles of particular concern.

(iv) *Size of Nanoparticles:* The impact of these factors on the interaction with the living system and the response of living organisms to such nanoparticles are not thoroughly understood. There is a need to understand and categorize the toxicity of nanoparticles. Since nanoparticles of any material are very small in size, they have a much greater surface-to-volume ratio; therefore, relatively more molecules of the chemical are present on the surface. This may be one of the reasons why nanoparticles are generally more toxic than larger particles of the same composition. In addition to being able to cross cell membranes, the nanosized particles reach the blood and various organs easier than larger particles of that same material.

(v) *Shape of Nanoparticles:* Though the effects of nanoparticles on health and the environment have not been evidenced in detail, these are also likely to depend on their shape. For example, CNTs are highly toxic as they produce harmful effects by an entirely new mechanism, different from the normal model of toxic dust.

(vi) *Chemical Composition and Surface Characteristics of Nanoparticles:* These have been found to affect the toxicity of nanoparticles. The composition of any chemicals adsorbed onto the surfaces of nanoparticles also affects the toxicity. However, successful trials have revealed that the modification of surfaces of nanoparticles can make them less harmful to health.

1.5.2 Short- and Long-Term Risks

The first step of chemical safety is hazard assessment, collection, and evaluation of available and relevant information, identifying the presence or absence of intrinsic hazardous properties of the substance. The second step is a comprehensive human hazard assessment that needs information regarding the fate of nanoparticles in the body (e.g., toxico-kinetics of absorption, distribution, metabolism, and excretion; and acute toxicity, irritation and corrosivity, sensitization, repeated dose toxicity, mutagenicity, carcinogenicity, and reproductive toxicity, etc.); and/or a comprehensive environmental hazard assessment, on the impact of nanoparticles on freshwater and marine water (acute and chronic toxicity to aquatic organisms), sediments and soil (toxicity to benthic or sediment-dwelling) organisms, sewage treatment plant and air (toxicity to sewage treatment plant (STP) microorganisms and other relevant environmental properties such as aquatic and terrestrial bioconcentration and bioaccumulation).

This hazardous information will identify the dose descriptor of the substance, which represents a level of exposure above which humans should not be exposed, and the predicted no-effect-concentration (PNEC), i.e., concentration of a chemical, which has unacceptable effects on the ecosystem and its organisms that will not occur during the long-term or short-term exposure. The PNEC is typically given in mg/L or mg/kg.

Guidance on available methods for risk assessment of nanomaterials has been prepared in 2015 by LIFE REACH nano, which has developed a web-based REACH Toolkit to support the chemical safety assessment of nanomaterials.

1.6 Need for Measurement of Exposure to Nanoparticles

In the absence of specific parameters to be considered for measurement of exposure to nanoparticles by an organism, the traditional risk assessment paradigm also holds for nanomaterials [6–9]. The basic components for assessing the risk of chemicals are hazard and exposure, including dose-response estimation, risk characterization, and accounting for uncertainty in the overall assessment. However, many of the tools, test protocols, and guidelines for the assessment of physicochemical properties, fate, exposures, and effects for conventional chemicals, need modifications if they are to be applied to the evaluation of nanomaterials [6]. Because many nanomaterials show particle-specific behavior, they require some specific considerations such as

(i) Different nanoforms can display different behavior both in their fate/toxicokinetics and hazard, and thus in risk. Hence, there is a demand to consider this in those dossiers for regulatory acceptance that comprise more than one nanoform. To consider this regulatory gap, different nanoforms should be addressed, which requires further research and policy considerations. Recently ECHA [10] has given some guidelines on the term "nanoform."

(ii) Life cycle and exposure are another issue raised by many scientists, because the physicochemical properties of nanomaterials may change during their life cycle [11, 12], which may form more hazardous nanomaterials during the life cycle; for example, due to the integration of a coating or photoactivation. It is imperative to consider this in general terms in risk assessment frameworks [13–15]. Other problems that may be encountered are a quantitative measurement of concentrations of nanomaterials such as degree of agglomeration, size distribution, etc., to be measured in complex matrices. This needs the development of computational models for estimating exposures and changes in physicochemical properties during the life cycle.

(iii) Delivered dose of nanomaterial is another criterion that needs attention because it tends to agglomerate, which can have a serious impact on the application of assessment factors [16, 17], especially if the internalized dose is still technically challenging. It requires correlating the *in-vitro* and *in-vivo* data to find ways forward for alternative testing.

(iv) Bioaccumulation and ecotoxicity is an important consideration as their elimination from tissues can be very slow and may take years, especially for hydrophobic non-nano materials. But the basic mechanisms of uptake and elimination differ in nanomaterials and the behavior of nanomaterials cannot be described by chemical equilibrium. Hund-Rinke *et al.* [18] have suggested that for environmental risk assessment of nanomaterials, a pragmatic screening procedure will be needed to determine the nanomaterial concentration in suitable test organisms; whereas for human health risk assessment of nanomaterials, lysosomal fluid may give information on the potential for accumulation.

(v) Assessment factors will vary due to the interspecies and intraspecies differences. The OECD [19, 20] indicates that there are insufficient data to verify if the present standard assessment factors (AFs) of 10 for both interspecies and intraspecies differences apply to nanomaterials.

Indeed, insufficient studies are available that can be directly compared to each other to allow assessment of the variation between studies.

Relevance of exposure, hazard assessment of nanomaterials, such as life cycle, bioaccumulation, and delivered dose, will be discussed in other chapters of this book along with risk assessment frameworks.

1.7 Conclusion

Whenever a commercially applicable branch of science is developed; many industries mushroom to take the early financial advantage. Many nanomaterial-based products are coming on the market. Being a new branch of science, many risks and disadvantages, especially in the long term, have not been assessed. This chapter has given a very basic introduction to nanotechnology and discussed the need to take into consideration the specific regulations, possible hazards, and envisaged risks, which will be discussed further in subsequent chapters.

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