Nanotechnology – An Introduction

1. History

Nanoscience is the study of phenomena and manipulation of materials at atomic, molecular and macromolecular scales, where properties differ significantly from those at a larger scale.
Nanotechnologies are the design, characterisation, production and application of structures, devices and systems by controlling shape and size at nanometre scale.

The prefix 'nano' is derived from the Greek word for dwarf. One nanometre (nm) is equal to one-billionth of a metre, 10^{-9} m. A human hair is approximately 80,000 nm wide, and a red blood cell approximately 7000 nm wide. Atoms are below a nanometre in size, whereas many molecules, including some proteins, range from a nanometre upwards.

The conceptual underpinnings of nanotechnologies were first laid out in 1959 by the physicist Richard Feynman, in his lecture 'There's plenty of room at the bottom' (Feynman 1959). Feynman explored the possibility of manipulating material at the scale of individual atoms and molecules, imagining the whole of the Encyclopaedia Britannica written on the head of a pin and foreseeing the increasing ability to examine and control matter at the nanoscale.

The term 'nanotechnology' was not used until 1974, when Norio Taniguchi, a researcher at the University of Tokyo, Japan used it to refer to the ability to engineer materials precisely at the nanometre level (Taniguchi 1974). The primary driving force for miniaturisation at that time came from the electronics industry, which aimed to develop tools to create smaller (and therefore faster and more complex) electronic devices on silicon chips. Indeed, at IBM in the USA a technique called electron beam lithography was used to create nanostructures and devices as small as 40–70 nm in the early 1970s.

The size range that holds so much interest is typically from 100 nm down to the atomic level (approximately 0.2 nm), because it is in this range (particularly at the lower end) that materials can have different or enhanced properties compared with the same materials at a larger size. The two main reasons for this change in behaviour are an increased relative surface area, and the dominance of quantum effects. An increase in surface area will result in a corresponding increase in chemical reactivity, making some nanomaterials useful as catalysts to improve the efficiency of fuel cells and batteries. As the size of matter is reduced to tens of nanometres or less, quantum effects can begin to play a role, and these can significantly change a material's optical, magnetic or electrical properties. In some cases, size-dependent properties have been exploited for centuries. For example, gold and silver nanoparticles (particles of diameter less than 100 nm) have been used as coloured pigments in stained glass and ceramics since the 10th century AD (Erhardt 2003). Depending on their size, gold particles can appear red, blue or gold in colour. The challenge for the ancient chemists was to make all nanoparticles the same size (and hence the same colour), and the production of single-size nanoparticles is still a challenge today.

At the larger end of our size range, other effects such as surface tension or 'stickiness' are important, which also affect physical and chemical properties. For liquid or gaseous environments Brownian motion, which describes the random movement of larger particles or molecules owing to their bombardment by smaller molecules and atoms, is also important. This effect makes control of individual atoms or molecules in these environments extremely difficult.

Nanoscience is concerned with understanding these effects and their influence on the properties of material. Nanotechnologies aim to exploit these effects to create structures, devices and systems with novel properties and functions due to their size.

In some senses, nanoscience and nanotechnologies are not new. Many chemicals and chemical processes have nanoscale features – for example, chemists have been making polymers, large molecules made up of tiny nanoscalar subunits, for many decades. Nanotechnologies have been used to create the tiny features on computer chips for the past 20 years. The natural world also contains many examples of nanoscale structures, from milk (a nanoscale colloid) to sophisticated nanosized and nanostructured proteins that control a range of biological activities, such as flexing muscles, releasing energy and repairing cells. Nanoparticles occur naturally, and have been created for thousands of years as the products of combustion and food cooking.

However, it is only in recent years that sophisticated tools have been developed to investigate and manipulate matter at the nanoscale, which have greatly affected our understanding of the nanoscale world. A major step in this direction was the invention of the scanning tunnelling microscope (STM) in 1982, and the atomic force microscope (AFM) in 1986. These tools use nanoscale probes to image a surface with atomic resolution, and are also capable of picking up, sliding or dragging atoms or molecules around on surfaces to build rudimentary nanostructures. In a now famous experiment in 1990, Don Eigler and Erhard Schweizer at IBM moved xenon atoms around on a nickel surface to write the company logo (Eigler and Schweizer 1990), a laborious process which took a whole day under well-controlled conditions. The use of these tools is not restricted to engineering, but has been adopted across a range of disciplines. AFM, for example, is routinely used to study biological molecules such as proteins.

The technique used by Eigler and Schweizer is only one in the range of ways used to manipulate and produce nanomaterials, commonly categorised as either 'top-down' or 'bottom-up'. 'Top-down' techniques involve starting with a block of material, and etching or milling it down to the desired shape, whereas 'bottom-up' involves the assembly of smaller sub-units (atoms or molecules) to make a larger structure. The main challenge for top-down manufacture is the creation of increasingly small structures with sufficient accuracy, whereas for bottom-up manufacture, it is to make structures large enough, and of sufficient quality, to be of use as materials. These two methods have evolved separately and have now reached the point where the best achievable feature size for each technique is approximately the same, leading to novel hybrid ways of manufacture.

2. Nanoscience and Applications

As nanoscience and nanotechnologies cover such a wide range of fields (from chemistry, physics and biology, to medicine, engineering and electronics), we have considered them in four broad categories: **nanomaterials; nanometrology; nanoelectronics** (electronics, optoelectronics and information and communication technology); and **bio-nanotechnology** and nanomedicine. This division helps to distinguish between developments in different fields, but there is naturally some overlap.

a. Nanomaterials

Introduction

A key driver in the development of new and improved materials, from the steels of the 19th century to the advanced materials of today, has been the ability to control their structure at smaller and smaller scales. The overall properties of materials as diverse as paints and silicon chips are determined by their structure at the micro- and nanoscales. As our understanding of materials at the nanoscale and our ability to control their structure improves, there will be great potential to create a range of materials with novel characteristics, functions and applications.

Although a broad definition, we categorise nanomaterials as those which have structured components with at least one dimension less than 100 nm. Materials that have one dimension in the nanoscale (and are extended in the other two dimensions) are layers, such as a thin films or surface coatings. Some of the features on computer chips come in this category. Materials that are nanoscale in two dimensions (and extended in one dimension) include nanowires and nanotubes. Materials that are nanoscale in three dimensions are particles, for example precipitates, colloids and quantum dots (tiny particles of semiconductor materials). Nanocrystalline materials, made up of nanometre-sized grains, also fall into this category. Some of these materials have been available for some time; others are genuinely new. The aim of this chapter is to give an overview of the properties, and the significant foreseeable applications of some key nanomaterials.

Two principal factors cause the properties of nanomaterials to differ significantly from other materials: increased relative surface area, and quantum effects. These factors can change or enhance properties such as reactivity, strength and electrical characteristics. As a particle decreases in size, a greater proportion of atoms are found at the surface compared to those inside. For example, a particle of size 30 nm has 5% of its atoms on its surface, at 10 nm 20% of its atoms, and at 3 nm 50% of its atoms. Thus nanoparticles have a much greater surface area per unit mass compared with larger particles. As growth and catalytic chemical reactions occur at surfaces, this means that a given mass of material in nanoparticulate form will be much more reactive than the same mass of material made up of larger particles.

In tandem with surface-area effects, quantum effects can begin to dominate the properties of matter as size is reduced to the nanoscale. These can affect the optical, electrical and magnetic behaviour of materials, particularly as the structure or particle size approaches the smaller end of the nanoscale. Materials that exploit these effects include quantum dots, and quantum well lasers for optoelectronics.

For other materials such as crystalline solids, as the size of their structural components decreases, there is much greater interface area within the material; this can greatly affect both mechanical and electrical properties. For example, most metals are made up of small crystalline grains; the boundaries between the grains slow down or arrest the propagation of defects when the material is stressed, thus giving it strength. If these grains can be made very small, or even nanoscale in size, the interface area within the material greatly increases, which enhances its strength. For example, nanocrystalline nickel is as strong as hardened steel. Understanding surfaces and interfaces is a key challenge for those working on nanomaterials, and one where new imaging and analysis instruments are vital.

Examples

Carbon nanotubes

Carbon nanotubes (CNTs) were first observed by Sumio Iijima in 1991 (Iijima 1991). CNTs are extended tubes of rolled graphene sheets. There are two types of CNT: single-walled (one tube) or multi-walled (several concentric tubes). Both of these are typically a few nanometres in diameter and several micrometres (10^{-6}m) to centimetres long. CNTs have assumed an important role in the context of nanomaterials, because of their novel chemical and physical properties. They are mechanically very strong (as rigid as diamond), flexible (about their axis), and can conduct electricity extremely well in one direction. All of these remarkable properties give CNTs a range of potential applications in reinforced composites for sport equipment and car bodies, sensors, nano-electronics and display devices for phones and tablets.

Nanoparticles

Nanoparticles are often defined as particles of less than 100nm in diameter. In line with our definitions of nanoscience and nanotechnologies, we classify nanoparticles to be particles less than 100nm in diameter that exhibit new or enhanced size-dependent properties compared with larger particles of the same material. Nanoparticles exist widely in the natural world: for example as the products of photochemical and volcanic activity, and created by plants and algae. They have also been created for thousands of years as products of combustion and food cooking, and more recently from vehicle exhausts. Deliberately manufactured nanoparticles, such as metal oxides, are by comparison in the minority. In this report we will refer to these as natural, pollutant and manufactured nanoparticles, respectively.

Nanoparticles are of interest because of the new properties (such as chemical reactivity and optical behaviour) that they exhibit compared with larger particles of the same materials. For example, titanium dioxide and zinc oxide become transparent at the nanoscale, however are able to absorb and reflect UV light, and have found application in sunscreens. Nanoparticles have a range of potential applications: in the short-term in new cosmetics, textiles and paints; in the longer term, in methods of targeted drug delivery where they could be to used deliver drugs to a specific site in the body. Nanoparticles can also be arranged into layers on surfaces, providing a large surface area and hence enhanced activity, relevant to a range of potential applications such as catalysts.

Manufactured nanoparticles are typically not products in their own right, but generally serve as raw materials, ingredients or additives in existing products.

Quantum dots
Nanoparticles of semiconductors (quantum dots) were theorized in the 1970s and initially created in the early 1980s. If semiconductor particles are made small enough, quantum effects come into play, which limit the energies at which electrons and holes (the absence of an electron) can exist in the particles. As energy is related to wavelength (or colour), this means that the optical properties of the particle can be finely tuned depending on its size. Thus, particles can be made to emit or absorb specific wavelengths (colours) of light, merely by controlling their size. Recently, quantum dots have found applications in composites, solar cells (Graetzel cells) and fluorescent biological labels (for example to trace a biological molecule) which use both the small particle size and tuneable energy levels. Recent advances in chemistry have resulted in the preparation of monolayer-protected, high-quality, monodispersed, crystalline quantum dots as small as 2nm in diameter, which can be conveniently treated and processed as a typical chemical reagent.

Applications

Current applications

Sunscreens and cosmetics
Nanosized titanium dioxide and zinc oxide are currently used in some sunscreens, as they absorb and reflect ultraviolet (UV) rays and yet are transparent to visible light and so are more appealing to the consumer. Nanosized iron oxide is present in some lipsticks as a pigment but it is not used by the European cosmetics sector. The use of nanoparticles in cosmetics has raised a number of concerns about consumer safety.

Composites
An important use of nanoparticles and nanotubes is in composites, materials that combine one or more separate components and which are designed to exhibit overall the best properties of each component. This multi-functionality applies not only to mechanical properties, but extends to optical, electrical and magnetic ones. Currently, carbon fibres and bundles of multi-walled CNTs are used in polymers to control or enhance conductivity, with applications such as antistatic packaging. The use of individual CNTs in composites is a potential long-term. A particular type of nanocomposite is where nanoparticles act as fillers in a matrix; for example, carbon black used as a filler to reinforce car tyres. However, particles of carbon black can range from tens to hundreds of nanometres in size, so not all carbon black falls within our definition of nanoparticles.

Coatings and surfaces
Coatings with thickness controlled at the nano- or atomic scale have been in routine production for some time, for example in molecular beam epitaxy (MBE) or metal oxide chemical vapour deposition (CVD) for optoelectonic devices, or in catalytically active and chemically functionalized surfaces. Recently developed applications include the self-cleaning window, which is coated in highly activated titanium dioxide, engineered to be highly hydrophobic (water repellent) and antibacterial, and coatings based on nanoparticulate oxides that catalytically destroy chemical agents. Wear and scratch-resistant hard coatings are significantly improved by nanoscale intermediate layers (or multilayers) between the hard outer layer and the substrate material. The intermediate layers give good bonding and graded matching of elastic and thermal properties, thus improving adhesion. A range of enhanced textiles, such as breathable, waterproof and

stainresistant fabrics, have been enabled by the improved control of porosity at the nanoscale and surface roughness in a variety of polymers and inorganics.

Short term applications

Remediation
The potential of nanoparticles to react with pollutants in soil and groundwater and transform them into harmless compounds is being researched. In one pilot study (Zhang 2003) the large surface area and high surface reactivity of iron nanoparticles were exploited to transform chlorinated hydrocarbons (some of which are believed to be carcinogens) into less harmful end products in groundwater. It is also hoped that they could be used to transform heavy metals such as lead and mercury from bioavailable forms into insoluble forms.

Displays
The huge market for large area, high brightness, flat-panel displays, as used in television screens and computer monitors, is driving the development of some nanomaterials. Nanocrystalline zinc selenide, zinc sulphide, cadmium sulphide and lead telluride synthesized by sol–gel techniques (a process for making ceramic and glass materials, involving the transition from a liquid 'sol' phase to a solid 'gel' phase) are candidates for the next generation of light-emitting phosphors. CNTs are being investigated for low voltage field-emission displays; their strength, sharpness, conductivity and inertness make them potentially very efficient and long-lasting emitters.

Batteries
With the growth in portable electronic equipment (mobile phones, navigation devices, laptop computers, remote sensors), there is great demand for lightweight, high-energy density batteries. Nanocrystalline materials synthesized by sol–gel techniques are candidates for separator plates in batteries because of their foam-like (aerogel) structure, which can hold considerably more energy than conventional ones. Nickel–metal hydride batteries made of nanocrystalline nickel and metal hydrides are envisioned to require less frequent recharging and to last longer because of their large grain boundary (surface) area.

Fuel additives
Research is underway into the addition of nanoparticulate ceria (cerium oxide) to diesel fuel to improve fuel economy by reducing the degradation of fuel consumption over time.

Long term applications

Carbon nanotube composites
CNTs have exceptional mechanical properties, particularly high tensile strength and light weight. An obvious area of application would be in nanotube-reinforced composites, with performance beyond current carbon-fibre composites. One current limit to the introduction of CNTs in composites is the problem of structuring the tangle of nanotubes in a well-ordered manner so that use can be made of their strength. Another challenge is generating strong bonding between CNTs and the matrix, to give good overall composite performance and retention during wear or erosion of composites. The surfaces of CNTs are smooth and relatively unreactive, and so tend to slip through the matrix when it is stressed. One approach that is being explored to prevent this slippage is the attachment of chemical side-groups to CNTs, effectively to form 'anchors'. Another limiting factor is the cost of production of CNTs. However, the potential benefits of such light, high strength material in numerous applications for transportation are such that significant further research is likely.

Medical implants
Current medical implants, such as orthopaedic implants and heart valves, are made of titanium and stainless steel alloys, primarily because they are biocompatible. Unfortunately, in some cases these metal alloys may wear out within the lifetime of the patient. Nanocrystalline zirconium oxide (zirconia) is hard, wearresistant, bio-corrosion resistant and bio-compatible. It therefore presents an attractive alternative material for implants. It and other nanoceramics can also be made as strong, light aerogels by sol–gel techniques. Nanocrystalline silicon carbide is a candidate material for artificial heart valves primarily because of its low weight, high strength and inertness.

Water purification
Nano-engineered membranes could potentially lead to more energy-efficient water purification processes, notably in desalination by reverse osmosis. Again, these applications would represent incremental improvements in technologies that are already available. They would use fixed nanoparticles, and are therefore distinct from applications that propose to use free nanoparticles.

b. Nanometrology

The science of measurement at the nanoscale is called nanometrology. Its application underpins all of nanoscience and nanotechnologies. The ability to measure and characterise materials (determine their size, shape and physical properties) at the nanoscale is vital if nanomaterials and devices are to be produced to a high degree of accuracy and reliability and the applications of nanotechnologies are to be realised. Nanometrology includes length or size measurements (where dimensions are typically given in nanometres and the measurement uncertainty is often less than 1 nm) as well as measurement of force, mass, electrical and other properties. As techniques for making these measurements advance, so too does the understanding of nanoscale behaviour and therefore the possibility of improving materials, industrial processes and reliability of manufacture.

As with all measurement, nanometrology is essentially an enabling technology. Nanotechnologies, however defined, cannot progress independently of progress in nanometrology. Apart from their direct influence on scientific research and its application, the solutions developed for nanometrology problems can often be exploited elsewhere. For example, the concept of the atomic force microscopy (AFM), a key nanometrology tool, has had a direct influence on lithographic processes and techniques for molecular manipulation. Conversely, it is likely that continuing research into nanodevices will suggest new measurement methods.

Metrology forms the basis of the semiconductor industry and as such is enormously advanced. Shrinking feature sizes, tighter control of device electrical parameters and new interconnect materials will provide the main challenges for physical metrology methods. To achieve desired device scaling, metrology tools must be capable of measurement of properties at atomic distances. Compounding these is the uncertain nature of the development of device design, making it difficult to predict metrology needs in the long term and in particular the necessary metrology for manufacturing to ensure reliability. A major need is to integrate metrology data into the manufacturing process.

c. Electronics, optoelectronics and information and communication technology (ICT)

Introduction

The past 30 years have seen a revolution in information technology (IT) that has impacted the lives of many people around the world. At the heart of this revolution is the desire to share information, whether the printed word, images or sounds. This requires a technology that can absorb and process information on one side of the planet and deliver it almost instantaneously to the other in a form that is immediately accessible. Such a technology places enormous pressure on advances in processing and storing information, and on transmitting it and converting it from and to a human readable form. It also increasingly requires secure encryption of information so that access to information can ultimately be restricted to particular individuals.

The market size of the IT industry is currently around $1000 billion, the order of $150 for every human being on the planet, with an expectation that it will reach $3000 billion in 2020. In no other industry sector is the trend for miniaturisation so apparent. This is perhaps most obvious by charting the number of transistors, the building blocks of computer chips, over the past 30 years. Remarkably, the physical size of the computer chip has remained virtually unchanged over time; it is the transistor and all the circuitry associated with it that has shrunk dramatically. The increase in the number of transistors on a chip coupled with increased speed have fuelled the economics of the IT industry; in 1971 the fabrication of a single transistor cost about 10 cents; it is currently less than one-thousandth of a cent.

Nanoscience research in ICT shares many of the same goals as other applications of nanotechnologies: an improved understanding of nanoscale properties of materials and devices, advances in fabrication and process technology to satisfy increasingly stringent dimensional tolerances, and exploration of alternative technologies that may offer economic or performance benefit. There is no doubt that the ICT sector has effectively driven a large proportion of nanoscience. Indeed, the first use of the word nanotechnology was in relation to ultra thin layers of relevance to the then up-and-coming semiconductor industry. Since then, the research into all aspects of semiconductor device fabrication, from fundamental physics to process technology, has dominated the nanoscience landscape and will continue so to do. Decreasing device scales will add further impetus to the truly nanoscalar aspects of this global research activity. The ICT sector is, and for historical and economic reasons is likely to remain, heavily silicon-based for the foreseeable future.

Applications

Computer chips

The current 130 nm technology node that produces the Intel Xeon processor defines the size of the DRAM (dynamic random access memory) half-pitch (half the distance between two adjacent metal wires in a memory cell). This is turn places a requirement on the lithography, process technology and metrology required to manufacture a working device to this tolerance. In the broadest sense, computer chips in current manufacture are therefore already using nanotechnologies and have been doing so for over 20 years. Furthermore, it is not simply the DRAM half-pitch that is on the nanometre scale. All the technology that goes into the research, metrology and production of chips has been working, in some cases, at the sub-nanometre atomic level. The variety of tools that support the IT industry includes computer modelling of advanced devices and materials atom by atom, microscopies that can image single atoms, metrologies that can define the absolute position of a single atomic defect over a 30 cm diameter wafer (the substrate used for computer chips), thin-film growth processes that can produce layers of material with atomic precision, and lithographies that can 'write' features, such as the DRAM cell, with an accuracy of sub-10nm.

Information storage

A technology that has necessarily developed in tandem with IT is that of memory for data storage. This can be divided into two quite different types: solid-state memory such as DRAM that a processor chip would use or flash memory for storing images in a digital camera; and disk-based memory such as the magnetic hard drives as found in all computers. The development of the hard disk drive, however, has taken a quite different route in evolution as it is based on reading and writing information magnetically to a spinning disk. It is therefore primarily mechanical, or more strictly electro-mechanical, and presents quite different technical challenges. Once again, however, the importance of length scales is paramount as the ideal disk drive is one that has the minimal physical size with a massive ability to store data. This is reflected in the evolution of the disk drive over the past 50 years.

Although the individual bits of magnetic information that are written onto the disk drive to give it the high-density storage are currently smaller than 100 nm, the constraints related to this nanotechnology on other aspects of the drive require fabrication of components with even greater precision. The importance of this nanotechnology in the related compact disk (CD) and digital versatile disk (DVD) drives that are now commonplace is equally ubiquitous.

Optoelectronics

The other crucial element of the IT revolution, optoelectronics, relates to devices that rely on converting electrical signals to and from light for data transmission, for displays for optical-based sensing and, in the future, for optical-based computing. Technology in this sector is strongly associated with those described above, and relies substantially on the tools developed there. Although some optoelectronic devices do not depend so critically on miniaturisation as computer chips do, there is nevertheless a similar trend towards miniaturisation, with some existing components, such as quantum-well lasers and liquid crystal displays, requiring nanometre precision in their fabrication.

Sensors
Nanotechnologies play several important roles in developing sensor technology. First, the ideal sensor will be minimally invasive and therefore as small as possible. This includes the power supply, the sensing action, whereby the detected property is converted into an electrical signal, and the transmission of the sensing signal to a remote detector. Combining these actions into a device that is smaller than $1mm^2$ will certainly require nanofabrication techniques, similar to those employed by the IT industry. The second role for nanotechnologies will be in designing the sensing element to be as specific and accurate as possible; as the sensor dimension decreases the area of the sensor available to effect detection will also decrease, making increasing demands on sensitivity. In the limit of, say, chemical detection this may require detection at the single molecule level; this is close to the bottom end of the nanotechnology length scale and constitutes a significant technical challenge.

d. Bio-nanotechnology and nanomedicine

Introduction

Without doubt the most complex and highly functional nanoscale machines we know are the naturally occurring molecular assemblies that regulate and control biological systems. Proteins, for example, are molecular structures that possess highly specific functions and participate in virtually all biological sensory, metabolic, information and molecular transport processes. The volume of a single molecule bionanodevice such as a protein is between one-millionth and one-billionth of the volume of an individual cell. In this respect the biological world contains many of the nanoscale devices and machines that nanotechnologists might wish to emulate.

Bio-nanotechnology is concerned with molecular-scale properties and applications of biological nanostructures and as such it sits at the interface between the chemical, biological and the physical sciences. It does not concern the large-scale production of biological material such as proteins or the specific genetic modification of plants, organisms or animals to give enhanced properties. By using nanofabrication techniques and processes of molecular self-assembly, bio-nanotechnology allows the production of materials and devices including tissue and cellular engineering scaffolds, molecular motors, and biomolecules for sensor, drug delivery and mechanical applications. Bio-nanotechnology can be used in medicine to provide a systematic, as well as a preliminary screening, approach to drug discovery, to enhance both diagnostic and therapeutic techniques and to image at the cellular and sub-cellular levels, at a much higher resolution than that of magnetic resonance imaging (MRI).

The primary aim of much current research is to obtain a detailed understanding of basic biochemical and biophysical mechanisms at the level of individual molecules. This knowledge will allow the design rules of naturally occurring molecular machines to be determined, which may lead to new technological applications. Several tools have been developed in recent years, such as scanning probe microscopy (SPM), that allow the direct observation of the behaviour of single molecules within biological systems. Examples range from the relatively large (45 nm) rotary molecular motors that power bacterial flagella 'propellers' to the tiny enzymes such as ATP-synthase (9nm) that catalyse energy conversion in biological processes. The intricate sequence of changes in molecular structure that forms the basis of such biomolecular machines can now be measured directly by using AFM and 'optical tweezers'. The recent development of highspeed AFM has enabled real-time molecular movement within a molecular motor to be observed directly. Future bio-nanotechnology and nanomedicine devices may exploit many classes of functional biological materials.

Applications

Array technologies
The enormously powerful array technologies, which use relatively large biological samples at the micrometre scale, are continuously being enhanced for sensitivity, size and data analysis. The original DNA chip approach, which carries an array of DNA molecules on an inert carrier, is now routinely used in gene and protein analysis. The push towards higher resolution and smaller sample volume makes this an emerging nanotechnology. Lab-on-a-chip technologies, which are used for sensing and supporting disease diagnosis, are also currently in the micrometre range, but progress in nanofluidic systems will potentially lead to integrated nanoscale systems becoming available. These could have a range of applications, for example in improved devices for detection of biological and chemical agents in the field.

Drug delivery
There is enormous potential for nanotechnology to be applied to gene and drug delivery. The vehicle might be a functionalised nanoparticle capable of targeting specific diseased cells, which contains both therapeutic agents that are released into the cell and an on-board sensor that regulates the release. Different stages of this approach have already been demonstrated, but the combined targeting and controlled release have yet to be accomplished. In this event the way will be opened up for initial trials, and the eventual approval of such techniques will be fully regulated as for any new pharmaceutical.

Drug discovery
Nanotechnology techniques offer the possibility of studying drug–receptor interactions at the single molecule level, for example by using optical tweezers and AFM, so that a more direct approach to drug discovery becomes feasible. This approach might also allow, for example, the discovery of disease at the single cell level, long before physical symptoms are manifested. This has been achieved by monitoring changes in atomic forces or ion conductance of a single receptor or ion channel when a drug molecule attaches. However, the industrial process will require the development of large arrays of such instruments working in parallel to create a high-throughput screening capability.

Medical Imaging
Non-invasive imaging techniques have had a major impact in medicine over the past 25 years or so. The current drive in developing techniques such as functional MRI is to enhance spatial resolution and contrast agents. Nanotechnologies already afford the possibility of intracellular imaging through attachment of quantum dots or synthetic chromophores to selected molecules, for example proteins, or by the incorporation of naturally occurring fluorescent proteins which, with optical techniques such as confocal microscopy and correlation imaging, allow intracellular biochemical processes to be investigated directly.

Implants and prosthetics
Some nanomaterials such as nanocrystalline ceramics have certain properties – such as hardness, wear resistance and biocompatibility – that may make them of use as implants in the long term. The development of nanoelectronic systems with high detector densities and data processing capability might allow the development of an artificial retina or cochlea. Important progress is already being made in this area, but many issues must be resolved before they can become viable treatments. Similarly, the introduction of nanoelectronics will allow biological neural processing to be investigated at much enhanced spatial resolution. Neurons of rodents have already been grown on nanofabricated surfaces to form elementary neural networks in which electrical signalling can be measured. By sending and receiving electrical impulses from the network, it might begin to be possible to understand how neurons create memory by their responses to different patterns of stimuli.

e. Nanomanufacturing

Current industrial applications of nanotechnologies are mainly in the characterisation of materials, the production of chemicals and materials, precision manufacturing and ICT. In general, these applications represent incremental rather than truly disruptive advances; however, in the longer term it is likely that many manufacturing processes will be influenced by nanotechnologies, just as they are today by ICT.

There are a wide variety of techniques that are capable of creating nanostructures with various degrees of quality, speed and cost. These manufacturing approaches fall under two categories: 'bottom-up', and 'top-down'. In recent years the limits of each approach, in terms of feature size and quality that can be achieved, have started to converge.

Bottom-up manufacturing

Bottom-up manufacturing involves the building of structures, atom-by-atom or molecule-by-molecule. The wide variety of approaches towards achieving this goal can be split into three categories: chemical synthesis, self-assembly, and positional assembly. As discussed below, positional assembly (with its many practical drawbacks as a manufacturing tool) is the only technique in which single atoms or molecules can be placed deliberately one-by-one. More typically, large numbers of atoms, molecules or particles are used or created by chemical synthesis, and then arranged through naturally occurring processes into a desired structure.

Chemical synthesis
Chemical synthesis is a method of producing raw materials, such as molecules or particles, which can then be used either directly in products in their bulk disordered form, or as the building blocks of more advanced ordered materials.

Self-assembly
Self-assembly is a bottom-up production technique in which atoms or molecules arrange themselves into ordered nanoscale structures by physical or chemical interactions between the units. The formation of salt crystals and snowflakes, with their intricate structure, are examples of self-assembly processes. Although self-assembly has occurred in nature for thousands of years, the use of self-assembly in industry is relatively new. There is an economic and environmental interest in processes through which materials or product components essentially form themselves, creating less waste and using less energy.

Positional assembly
The final bottom-up technique is positional assembly, whereby atoms, molecules or clusters are deliberately manipulated and positioned one-by-one . Techniques such as SPM for work on surfaces, or optical tweezers in free space, are used for this. Positional assembly is extremely laborious and is currently not suitable as an atomic-scale industrial process. The utility and strength of SPM in industry lie in their ability to characterise and measure surfaces with atomic-level precision, rather than in their suitability as fabrication tools.

Top-down manufacturing

Top-down manufacturing involves starting with a larger piece of material and etching, milling or machining a nanostructure from it by removing material (as, for example, in circuits on microchips). This can be done by using techniques such as precision engineering and lithography, and has been developed and refined by the semiconductor industry over the past 30 years. Top-down methods offer reliability and device complexity, although they are generally higher in energy usage, and produce more waste than bottom-up methods. The production of computer chips, for example, is not yet possible through bottom-up methods.

f. Health & Safety of Nanotechnology

Whereas the potential health and environmental benefits of nanotechnologies have been welcomed, concerns have been expressed that the very properties that are being exploited by researchers and industry (such as high surface reactivity and ability to cross cell membranes) might have negative health and environmental impacts and, particularly, that they might result in greater toxicity. The public expresses worries about possible long-term side effects associated with medical applications and whether nanomaterials would be biodegradable. Analogies were made with plastics, which were once hailed as 'the future' but which have proved to have accompanying adverse effects on individuals and the environment.

Some definitions relevant to the Health and Safety discussion:

Hazard is defined as the potential to cause harm: hazard is typically assessed by toxicology, for example testing harmful potential on cultured cells or isolated organs (*in vitro*) or directly on laboratory animals or humans (*in vivo*). Another hazard is the potential for clouds of combustible nanoparticles to explode.

Exposure is the concentration of the substance in the relevant medium (air, food, water) multiplied by the duration of contact.

Dose is defined here as the amount of a substance that will reach a specific biological system, and is a function of the amount to which the individual is exposed, namely the exposure, taking account of the fact that a proportion is eliminated by the body's natural defences and does not reach the target organ.

Risk is a quantification of the likelihood of such harm occurring: risk is assessed from consideration of the likelihood of exposure, the dose and the inherent toxicity of the substance to which humans or other organisms may be exposed. Sometimes, in the case of materials to which exposure has already occurred, risk may be measured directly by the techniques of epidemiology.

Manufactured nanoparticles might be used in products where they are not fixed (such as sunscreens), be used to form composites from which they might later be released, be formed during the self-assembly of nanomaterials (again from which they might later be released), or be created if nanomaterials are damaged or break down. For physical harm to occur, humans or other organisms must come into contact with the materials or be involved in the processes in such a way that the material contacts or enters the body and takes part in reactions with cells, leading to tissue-damaging reactions. Any such damage might be anticipated if the material has toxic properties and reaches the target organ in sufficient dose. If the material is released into the air, it may be inhaled directly. This is the dominant pathway for humans exposed to manufactured nanoparticles released in the workplace, and for all organisms exposed to nanoparticles from sources such as combustion. In addition to inhalation by air-breathing organisms, exposure to nanoparticles could occur from surface contact (for example in cosmetic skin preparations) or from ingestion (if nanoparticles are to be added to food or drink in the future). In the future, medicinal applications may result in particles being injected into the body. Other organisms such as bacteria and protozoa may take in nanoparticles through their cell membranes, and thus allow the particles to enter a biological food chain.

Until research has been undertaken and published in the peer-reviewed literature, it is not possible to evaluate the potential environmental impact of nanoparticles and their behaviour in environmental media. Until more is known about environmental impacts of nanoparticles and nanotubes, it is recommended that the release of manufactured nanoparticles and nanotubes into the environment be avoided as far as possible.

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