



# Nanotechnology: Revolution in Biomedical Sciences to Human Health

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## ABSTRACT

Nanotechnology is at the forefront of a revolution in the biomedical sciences. It has the potential to give both researchers and doctors' abilities they would never have previously dreamt of, including everything from the capability to deliver engineered drugs to specific target tissues to filtering even the smallest harmful particles out of our water supply. With such increased power, however, also comes increased responsibility. Nanotechnologies have as much potential to do harm as they do well. For instance, nanotechnology could be an enormously effective tool in the hands of a bioterrorist. As such, it is critically important for mankind to fully appreciate the technology's awesome potential and the possible harm it may cause before this potential is realized. To this end, this review discusses not only the current and future applications of nanotechnology in the biomedical sciences, but also the incredibly important ethical ramifications of such applications.

## INTRODUCTION

Nanotechnology and nanoengineering stand to produce significant scientific and technological advances in diverse fields including medicine and physiology. In a broad sense, they can be defined as the science and engineering involved in the design, synthesis, characterization, and application of materials and devices whose smallest functional organization in at least one dimension is on the nanometer scale, ranging from a few to several hundred nanometers. A nanometer is one billionth of a meter or three orders of magnitude smaller than a micron, roughly the size scale of a molecule itself [1,2]. The potential impact of nanotechnology stems directly from the spatial and temporal scales being considered: materials and devices engineered at the nanometer scale imply controlled manipulation of individual constituent molecules and atoms in how they are arranged to form the bulk macroscopic substrate. This, in turn, means that nanoengineered substrates can be designed to exhibit very specific and controlled bulk chemical and physical properties as a result of the control over their molecular synthesis and assembly [3].

For applications to medicine and physiology, these materials and devices can be designed to interact with cells and tissues at a molecular level with a high degree of functional specificity, thus allowing a degree of integration between technology and biological systems not previously attainable. It should be appreciated that nanotechnology is not in itself a single emerging scientific discipline but rather a meeting of traditional sciences such as chemistry, physics, materials science, and biology to bring

together the required collective expertise needed to develop these novel technologies. The present review explores the significance of nanoscience and latest nanotechnologies for human health. Addressing the associated opportunities, the review also suggests how to manage far-reaching developments in these areas.

### Scientific and application-oriented research

Living cells are full of complex and highly functional “machines” at nanometer scale. They are composed of macromolecules, including proteins. They are involved in practically every process in the cell, such as information transfer, metabolism, and the transport of substances [4].

Nanotechnologies offer new instruments for observing the operation of these machines at the level of individual molecules, even in the living cell. Using atomic force microscopes, it is possible, for example, to measure the bonding forces between trigger substances, such as hormones, and the associated receptor proteins that act as switches in the cell membrane. Biomolecules can be labelled using quantum dots. The intense light of a specific wavelength that these nanocrystals emit enables the path followed by the biomolecules in the cell to be precisely traced. A great deal of this research is concerned with obtaining information on basic biochemical and biophysical processes in healthy and diseased cells. This knowledge can provide the basis for the development of new prevention strategies and therapies. Beside this primarily knowledge-broadening research, research is also underway into numerous possible applications for nanotechnologies in medicine. Research efforts are particularly intensive in the search for new

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methods and tools for imaging, sensing, targeted drug, and gene delivery systems. More research is also underway into applications in fields such as tissue medical implants and disinfection. Clinical applications are currently scarce partly because of stringent safety requirements. Nevertheless, experts expect a great deal from nanomedicine especially in the longer term [5].

## DIAGNOSTICS

The enormous increase in knowledge of the human genome (genomics) and of expression products, proteins (proteomics), makes it possible in an increasing number of cases to trace diseases to abnormalities at the molecular level. In theory, this gives rise to the possibility of making a diagnosis at a very early stage—and of possibly starting treatment— even before the initial symptoms of the disease appear. Attention in medicine is, therefore, increasingly focusing on prevention. The medical profession has an ever increasing number of technical tools at its disposal for detecting these molecular biomarkers. It is in this field that the impact of nanotechnologies will probably be noticed first. The diagnostic research can be conducted in the laboratory using samples taken from the human body but it can also be carried out directly on the patient. This distinction is important because, in the latter case, the tools/agents have to meet more stringent requirements [6].

Research into patients' genetic material (DNA) can be conducted to measure gene expression— the degree of RNA production—in diseased tissue, or to ascertain which variant of a particular gene a person has. Many human genes exist in several forms, which only differ in a single base pair. These are known as single nucleotide polymorphisms (SNPs). The corresponding protein variants may differ from each other in a single amino acid and then display a considerable difference in functionality. SNPs are the root of all kinds of genetic disorders and also affect a person's sensitivity to chemical substances, including medicines. This refers to their therapeutic effect as well as their side effects. Genetic research offers major possibilities for identifying gene types that predispose a person to certain diseases and for achieving better matches between individual patients and the medicines they are prescribed.

DNA chips used for analyzing DNA have been available for a few years now. They are currently widely used in scientific, biomedical research but they are rarely used in clinical practice. The chips comprise an inert support which carries microarrays of hundreds to thousands of single strand DNA molecules with different base sequences. DNA from a tissue sample that has been labelled with a radioactive or fluorescent material can be identified on the basis of the place on the chip where it binds to the chip DNA. The Dutch Cancer Institute has been using a DNA chip since 2003 to predict the spread of breast tumours on the basis of gene expression profiles. This information makes it much easier than it was in the past to determine which patients would benefit from supplementary chemotherapy after the tumour has been surgically removed. Similar chips are being developed for the diagnosis of leukaemias and mouth and throat tumours. DNA chips and other biochips were originally an achievement of microtechnology but miniaturisation is advancing here too, as with computer chips. Nanotechnologies are also increasingly playing a role in producing the chips and in increasing their detection sensitivity and reliability. A new nanotechnological analytical method uses quantum dots. DNA in a sample is identified on the basis of its bonding to DNA molecules of a known composition embedded in micrometre-sized polymer spheres containing various mixtures of quantum

dots, each of which provides a unique spectral bar code. American researchers have used this method to study SNPs in genes that code for enzymes of the cytochrome P450 family which are involved in the breakdown of substances (including medicines) in the body. The method is very suitable for studying large quantities of samples on many SNPs simultaneously [7].

In theory, the composition of DNA molecules can also be ascertained by pulling them through nanopores in a membrane by means of an electric potential difference. The base sequence can be deduced from the time profile of the electric current through the pores. Researchers have now used this method to identify a mutation in an HIV gene that makes the virus resistant to a particular medicine. If this method, which is still being developed, can be perfected, it will result in a much faster way of determining the base sequence of DNA than has thus far been available. This would involve having to place hundreds of pores on a chip [8].

The aforementioned techniques would, in principle, also be suitable for identifying other biopolymers, such as proteins and carbohydrates. Nevertheless, American researchers have succeeded in developing a chip to detect prostate cancer. The chip contains around one hundred cantilever sensors, which are coated on one side with antibodies to prostate specific antigen (PSA), a biomarker for that disease. Bonding of PSA from a sample placed on the chip bends the cantilevers several nanometres, which can be detected optically [9].

This enables clinically relevant concentrations of PSA to be measured. Antibodies placed on nanowires can be used in a similar way to detect viruses, in a blood sample, for example. The bonding of a single virus particle to an antibody results in a change in the nanowire's electric conductance. The method is extremely sensitive, which means that an infection can be detected at a very early stage. It is also suitable for multiplex analyses. Work is also underway on sensors based on carbon nanotubes, for use in microarrays. Detection methods based on cantilevers, nanowires or nanotubes offer the added advantage that it is not necessary to label the sample. Labs-on-a-chip are pocket-sized laboratories. They can be used for analyzing biopolymers and also for research and for manipulating cells. They are expected to play an important role in the further development of biosensors for the detection of pathogenic bacteria. In due course, there will also be possibilities for point-of-care applications, in which simple analyses can be made in the general practitioner's surgery or in the patients' homes and carried out by the patients themselves. Researchers of the University of Twente are currently working on the development of a lab-on-a-chip for measuring lithium concentrations in the blood. A chip of this kind would enable patients who use psycho pharmaceuticals based on lithium to keep the lithium concentration in their blood at the right level. The ease of use would be comparable with that of current devices that enable diabetic patients to measure glucose levels in their blood. Photonic explorers for bioanalysis with biologically localised embeddings are a final example. These sensors are a few hundreds of nanometers in size and are composed of an inert capsule, made of polymers, for example, containing an indicator colouring agent that emits light as soon as a substance being analysed diffuses through the capsule to the inside and binds with the colouring agent. PEBBLEs were developed for measuring concentrations of small ions and molecules—such as ions of hydrogen, calcium, magnesium and zinc, or glucose—in living cells. Once the nanocapsules have been introduced into a cell, their light emission can be monitored using a microscope. Tools of this

kind are useful when studying certain diseases. For example, an abnormal zinc balance is a characteristic of brain disorders such as Alzheimer's disease and Parkinson's disease [10].

## OTHER APPLICATIONS

The disinfectant effect of silver has long been known but the use of silver in combating pathogenic microorganisms decreased with the emergence of organic antibiotics. The increasing resistance of bacteria to antibiotics has resulted in renewed interest in silver as a disinfectant. The antiseptic effect is based on silver ions. They block the enzymes required for oxygen metabolism, destabilize the cell membrane, and block cell division. Bacteria are not expected to develop resistance to silver, owing to the diversity of the working mechanisms. Especially in the form of nanoparticles, silver is extremely effective thanks to the large contact area with the environment. Moreover, the particles have the advantage that they can be readily integrated with other materials like globular or fibrous proteins and polymers. The nanoparticles then act as depots that continually release new silver ions. When applied to medical instruments or implants, antimicrobial layers of this kind can help reduce the number of infections. Current research is studying uses on catheters, cochlear implants and in bone cement. Antimicrobial wound dressings containing nanocrystalline silver is already on the market. Titanium dioxide nanoparticles also have a bactericidal effect. This is based on a photocatalytic effect. Under the influence of ultraviolet radiation and in the presence of water and oxygen, the particles form extremely reactive molecules (radicals), such as hydroxyl and perhydroxyl radicals, which kill microorganisms. Titanium dioxide can be used to produce antiseptic surfaces that only work in the presence of UV radiation. Fullerenes also have an antimicrobial effect in the presence of light. Various antimicrobial products based on nanoparticles are already on the market.

Radio Frequency Identification labels (RFID labels) consist of a microchip to which a radio antenna is attached. The chip can contain information on a product that contains it or to which it is attached. A scanning device can activate the chip by means of the antenna, which in turn transmits the information stored in the chip. The labels are used for identification and security purposes and for following flows of goods. They have been in use for some time, for locating stolen cars and bicycles, for example, and for identifying domestic pets and cattle. The labels are a product of microtechnology but nanotechnologies offer possibilities for making them smaller and cheaper. This is expected to increase their use considerably. RFID labels are already used in hospitals and care institutions. They are used to prevent newborns from being abducted or confused or demented patients from wandering away unnoticed. They are also increasingly being used for identifying patients or samples taken from patients, alongside or instead of labels with bar codes. This is to enable an early response when the wrong patient is taken to an operating room, for example. They are also expected to reduce the number of wrong blood transfusions. The labels can also simplify the tracing and localisation of expensive hospital equipment, making it easier to trace medicines and to help in combating drug counterfeiting. Implanting RFID labels in victims of disasters can facilitate their subsequent identification.

Meanwhile, RFID labels the size of a grain of rice is available for implantation under the skin. The Food and Drug Administration in the United States approved a label of this kind in 2004. A person's medical record can be stored on the chip. The idea behind this is that faster availability of the right medical information could

save a person's life in an emergency. Apart from health care, these kinds of chips are also finding important role in agriculture and food technologies.

## CONCLUSION

The multidisciplinary field of nanotechnology's application for discovering new molecules and manipulating those available naturally could be dazzling in its potential to improve health care. The spin-offs of nanobiotechnology could be utilised across all the countries of the world. In the future, we could imagine a world where medical nanodevices are routinely implanted or even injected into the bloodstream to monitor health and to automatically participate in the repair of systems that deviate from the normal pattern. The continued advancement in the field of biomedical nanotechnology is the establishment and collaboration of research groups in complementary fields. Such collaborations have to be maintained not only on specialty field level but also internationally. The successful development and implementation of international collaborations fosters a global perspective on research and brings together the benefits to mankind in general. However, nanotechnology in medicine faces enormous technical hurdles in that long delays and numerous failures are inevitable. This is because the effort needed to produce nanoscale biomedical or therapeutic devices is highly interdisciplinary.

As we have seen, it touches on numerous established disciplines, encompassing elements of physiology, biotechnology, chemistry, electrical engineering, and materials science, to name just a few of the fields involved. Obviously, this broad sweep of knowledge is difficult for any one investigator to master fully. The breadth of the effort constitutes just one of the major barriers to entry in the field. Other challenges include inadequate funding, the raw complexity of biology, the fashion in which biologists hold and distribute information, and cultural differences between engineers and biological scientists. Likewise, it should not be taken for granted the dangers and negative consequences of nanobiotechnology when applied in warfare, in the hands of terrorists and disasters associated with its application in energy generation when and wherever it strikes, or the risks associated with nanoparticles in blood circulation. It should be appreciated that nanotechnology is not in itself a single emerging scientific discipline but rather a meeting point of traditional sciences like chemistry, physics, biology, and materials science to bring together the required collective knowledge and expertise required for the development of these novel technologies.

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