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REVIEW ARTICLE

NANOBIOTECHNOLOGY: CHANGING HORIZONS OF SCIENCE

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ABSTRACT

Scientists worldwide are continuing to discover unique properties of every day materials at the submicrometer scale. This size domain is better known as nanometer domain and technology concerned with this is known as nanotechnology that involves working with particles at nano level. One of the most important emerging fields of science in this century is Nanotechnology. It deals with designing, construction, investigation and utilization of systems at the nanoscale. The interface between nanotechnology and biotechnology is nanobiotechnology, which exploits nanotechnology and biotechnology to analyse and create nanobiosystems to meet a wide variety of challenges and develops a wide range of applications. Biotechnology gives us a way to understand biological system and to utilize our knowledge for industrial manufacturing. Nanotechnology has great potential and by the help of its application it can enhance the quality of life through in various fields like agriculture and the food system. Around the world, it has become the future of any nation. Important tools used in nanotechnology and application of nanobiotechnology in agriculture sector will be discussed in this review.

Key Words: Nanobiotechnology, submicrometer scale and science.

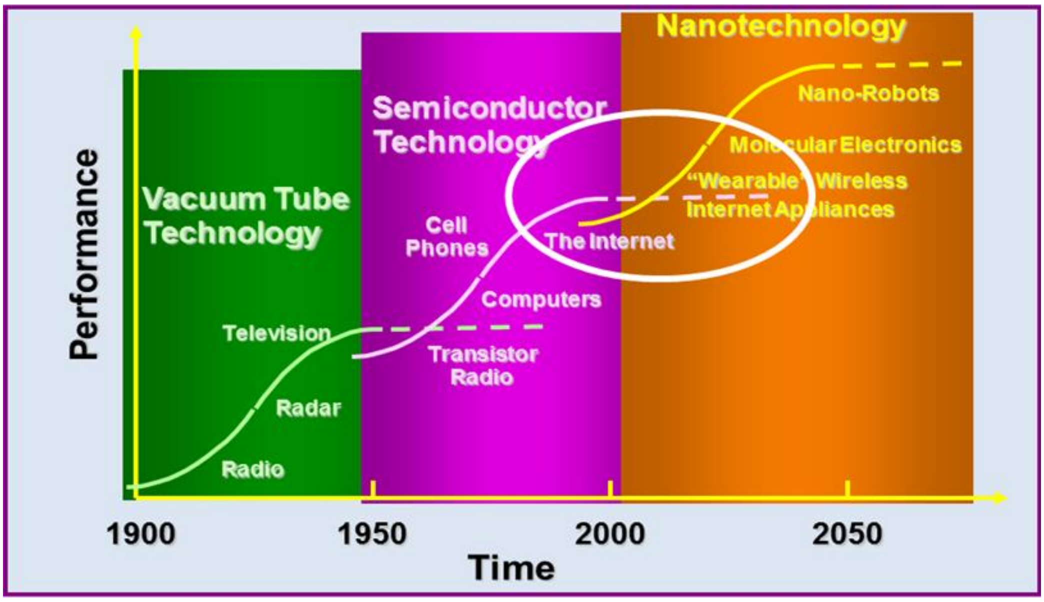
INTRODUCTION

Agriculture Sector has been benefited due to advancement of technologies like development of tractor and other mechanization schemes; the advent of irrigation systems and series of research and technology transfer efforts in the 1960s and 1970s known as the “Green Revolution” that resulted in disease-resistant, high yield crops and agricultural practices that leads to increased output and production yield. The green year is credited with preventing mass famine in India. Norman Borlaug, called “father of Green Revolution”, was awarded the Nobel Peace Prize, the President Medal of Freedom, and the Congressional Gold Medal for his work (Gillen 2011).

Over the course of history, mankind has experienced that whole society has been changed drastically due to numerous revolutions. In recent years, the industrial revolution has brought about—–efficient production and transportation, leading to the creation of larger cities throughout the world. Increasing availability and power of computing and communication devices brought information revolution. Seemingly overnight it possible for connection to be forged across the globe. It has been speculated that we are now entering the nanotechnology revolution (Amin *et al*. 2011).

process of supply chain (e.g. sensors, buy and sell intelligent agents or quality, security and safety control through nano materials in and on food, goods, packaging and freight).

Figure 1. Evolution of technologies (www.purdue.edu/abe)



Nano word has been derived from Greek language meaning "dwarf". In measurement, one-billionth of a meter is nanometer or anything raised to 10^{-9} is nano (Feynman 1959). Another interesting research discipline of current day is biotechnology, which gives us a way to understand the biological system to utilize our knowledge for industrial manufacturing. The credit for the term "nanobiotechnology" goes to Lynn. W. Jelinski, a Biophysicist at Cornell University. Nanobiotechnology joins the breakthroughs in nanotechnology to those in molecular biology. Nanobiotechnology is an interface between nanotechnology and biotechnology. Molecular biologists help nanotechnologists to understand and access the nanosturctures and nanomachines designed in four billion years on natural engineering and evolution-cell machinery and biological molecules. Exploiting the extraordinary properties of biological molecules and cell processes, nanotechnologists can accomplish many goals that are difficult or impossible to achieve by other means (Prasanna 2007). Nanotechnology have a wide application to the

For example nano-sensors can be used in the determination of the ripeness and freshness of packaged produce, and in the detection of pathogens in animal food production systems (e.g. detection of harmful viruses which infect cattle) and in farm, food and environmental samples before they can contaminate the food (Lu and Bowles 2013).

Evolution of Technologies:

The evolution of technologies is shown in Figure 1.

Ancient time of nanotechnology:

In the 4th century, King of Rome, Lycurgus used a cup named Lycurgus cup, which is an example of dichroic glass; colloidal gold and silver in the glass allow it to look opaque green when lit from outside but translucent red when light shines through inside. Luster ceramic glazes are used in the Islamic world, glass window, damascus saber blades and ruby gold contains different types and size of nano particles.

History of Nanobiotechnology:

The first time the idea of nanotechnology introduced was in 1959, when Richard Feynman, a physicist at California Institute of Technology (Caltech), gave a talk called "There's Plenty of Room at the Bottom." Though he never explicitly mentioned "nanotechnology," Feynman suggested that it will eventually be possible to precisely manipulate atoms and molecules. Moreover, in an even more radical proposition, he thought that, in principle, it was possible to create "nano-scale" machines, through a cascade of billions of factories. According to the physicist, these factories would be smaller scaled versions of machine hands and tools. He proposed that these tiny "machine shops" would then eventually be able to create billions of tinier factories. In these speculations, he also suggested that there are various factors, which uniquely affect the nano-scale level. Specifically, he suggested that as the scale got smaller and smaller, gravity would become more negligible, while both Vander Waals attraction and surface tension would become very important. In the end, Feynman's talk has been viewed as the first academic talk that dealt with a main tenet of nanotechnology, the direct manipulation of individual (Feynman 1960).

In 1974, a Japanese professor Norio Taniguchi gives a name to the new field in a scientific paper entitled: "On the Basic Concept of Nano-Technology" (Taniguchi 1974). Basically, he coined the term nanotechnology, after that tiny technology is known as nanotechnology. And in 1981 Kim Eric Drexler published a book named "*Engines of Creation - The Coming Era of Nanotechnology*". In this book, he talked about molecular manufacturing. When the term "nanotechnology" was coined, researchers, starting with Eric Drexler, built up this field from the foundation that Feynman constructed in 1959. He established his own vision of molecular manufacturing as a process of fabricating objects with specific atomic specifications using designed protein molecules. Thus, Drexler stated that molecular manufacturing and the construction of "nano-machines" is a product of an analogous relationship "between features of natural macromolecules and components of existing machines" (Drexler 1981).

Richard Errett Smalley, Gene and Norman Hackerman, Professor of Chemistry and a Professor of Physics and Astronomy at Rice University, Houston, Texas along with Robert Curl, a professor of Chemistry at Rice, and Harold Kroto, a professor at the University of Sussex, were awarded the Nobel Prize in Chemistry in 1996 for the discovery of a new form of carbon, buckminsterfullerene ("buckyballs"), and were a leading advocates of nanotechnology and its many applications, including its use in creating strong, but lightweight materials as well as its potential to fight cancer.

Tools used in Nanobiotechology:

There are three tools basically used in nanotechnology:-

- Transmission Electron Microscope (TEM)
- Scanning Tunneling Microscope (STM)
- Atomic Force Microscope (AFM). These tools are described here briefly.

Transmission electron microscope (TEM):

The first electron microscope was built and publicly demonstrated in 1931 by Max Knoll and Ernst Ruska, working at the High Tension Laboratory of the Technical University, Berlin. TEM is a microscopy technique, whereby a beam of electrons is transmitted through an ultra thin specimen, interacting with the specimen as it passes through. An image is formed from the interaction of the electrons transmitted through the specimen; the image is magnified and focused onto an imaging device, such as a fluorescent screen, on a layer of photographic film, or detected by a sensor such as a CCD camera. TEMs are capable of imaging at a significantly higher resolution than light microscopes, owing to the small de Broglie wavelength of electrons. TEMs find application in cancer research, virology, materials science as well as pollution, nanotechnology and semiconductor research (Martin 1963).

Table 1 : DNA based nanosystems

DNA based nanosystem	Description	References
DNA Cube	Seeman made the first three dimensional (3D) shape out of DNA - the frame for a cube - by making two DNA squares and linking them together. It took a lot of work, and it was difficult to make a lot of cubes at once. It was very hard to make the cube. Cube was one of the first 3 D structures designed. DNA axes can be connected to form a cube. Each edge of the cube has two molecule strands of DNA molecules linked to each other. It contains 6 different cyclic strands	Chen and Seeman 1991
Truncated octahedron shaped DNA	A covalently closed molecular complex whose double-helical edges have the connectivity of a truncated octahedron, and has been assembled from DNA on a solid support. This three-connected Archimedean solid contains six squares and eight hexagons, formed from 36 edges arranged in about 24 vertices. The vertices are the branch points of four-arm DNA junctions, so each vertex has an extra exocyclic arm associated with it.	Zhang and Seeman 1994
DNA Computer	Also known as molecular computing. It is basically a collection of specifically selected DNA strands whose combinations will result in the solution to some problem, depending on the problem at hand.	Adleman 1998
DNA nanotubes	Double crossover arrays can be folded to form DNA nanotubes. It can be made to self-assemble. It can be made at specific diameters. It is more easily connected and modified than carbon nanotubes and it can be made into rings and spirals. It has potential uses in drug delivery, gene therapy and electronic circuit	Borman 2005
DNA origami	Technique to make 2D or even 3D figures out of DNA and help make DNA a useful structural material. Designs are made by folding a single long strand of DNA bound into place by smaller strands of DNA. It is affordable and simple with high yields and hope to use the technology to make faster and smaller computers	Rothemund 2006
DNA tweezers	The highly selective bonding of DNA can be used to grab and release particles. It can be used to grasp and transfer an object to another place. It can go back and forth with almost no lose in efficiency.	Han *et al.* 2008
DNA factories	DNA nanotechnology can be used to make a nano-sized factory. DNA's bonding properties can be used to assembly pieces one by one like a factory and each piece of DNA bonds a certain molecule. These molecules can be added together to create an end product. DNA nanotechnology can be used to create walking bipedal nanorobots.	Singer 2007; Omabegho *et al.* 2009
DNA sensors	Takes advantage of the specific bonding patterns of DNA. It can respond to the pH. Each end is attached with a fluorescent dye. Colour can tell the pH and change is reversible. It can be observed in real time. It can be used inside living organisms and very highly accurate. DNA can be made to detect any metal and it is much faster than traditional test for lead and mercury.	Yuji and Taekjip 2009

Scanning tunneling microscope (STM):

The development of the family of scanning probe microscopes started with the original invention of the STM in 1981. Gerd Binnig and Heinrich Rohrer developed the first working STM while working at IBM Zurich Research Laboratories in Switzerland. This instrument would later win Binnig and Rohrer the Nobel Prize in Physics in 1986.The STM works by scanning a very sharp metal wire tip over a surface. By bringing the tip very close to the surface, and by applying an electrical voltage to the tip or sample, we can image the surface at an extremely small scale – down to resolving individual atoms. The STM is based on several principles. One is the quantum mechanical effect of tunneling. It is this effect that allows us to “see” the surface. Another principle is the piezoelectric effect. It is this effect that allows us to precisely scan the tip with angstrom-level control. Lastly, a feedback loop is required, which monitors the tunneling current and coordinates the current and the positioning of the tip (Binning *et al.* 1982).

Atomic force microscope (AFM):

The atomic force microscope (AFM) or scanning force microscope (SFM) was invented in 1986 by Binnig, Quate and Gerber. Similar to other scanning probe microscopes, the AFM raster scans a sharp probe over the surface of a sample and measures changes in force between the probe tip and the sample. A cantilever with a sharp tip is positioned above a surface. Depending on this separation distance, long range or short range forces will dominate the interaction. This force is measured by the bending of the cantilever by an optical lever technique: a laser beam is focused on the back of a cantilever and reflected into a photodetector. Small forces between the tip and sample by cause less deflection than large forces. By raster-scanning the tip across the surface and by recording the change in force as a function of position, a map of surface topography and other properties can be generated. The AFM is useful for obtaining three-dimensional topographic information of insulating and conducting structures with lateral resolution down to 1.5 nm and vertical resolution down to 0.05 nm. These samples include clusters of atoms and molecules, individual macromolecules, and biological species (Binning *et al.* 1986).

Approaches used in Nanobiotechnology:

There are two types of approaches used in this technique:-

- Top down approach
- Bottom up approach

Top down approach:

Top-down approach is nothing but breaking/etching the bulk materials until its dimensions is reduced to nano-size. The top-down approach is a well matured technology commonly used in the field of micro-electronics. The most important steps involved in this process are lithography, etching (either dry or chemical) and metal deposition (Kelleher *et al.* 1999).

Bottom up approach:

Bottom-up approach is when the structures are built by assembling atom by atom to the required size. Bottom-up approach has become a choice for wide range of materials due to the limitations of the capabilities of the techniques used in top-down approach such as lithography. The most commonly used bottom-up approach methods to fabricate 2D materials, such as thin films are chemical vapour deposition and molecular beam epitxay etc, where epitaxy is a process in which the deposited film adapts the crystal phase and orientation identical to those of the substrate (Kelleher *et al.* 1999).

DNA Nanotechnology:

The conceptual foundation of DNA nanotechnology was first laid out by Nadrian Seeman in the early 1980s and the field began to attract widespread interest in the early to mid 2000s. DNA nanotechnology is a branch of nanotechnology that specializes in the design and manufacture of artificial nucleic acid structures for technological uses. It harnesses the complementary base pairing property of nucleic acid that allows for rational design of base sequences so that a set of strands will assemble to form a desired target structure, leading to a unique ability to form designed, complex structures with precise control over nanoscale features.

DNA nanotechnology is sometimes divided into two overlapping subfields

- Structural DNA nanotechnology
- Dynamic DNA nanotechnology

These subfields of DNA nanotechnology are discussed below briefly.

Structural DNA nanotechnology, sometimes abbreviated as 'SDN', focuses on synthesizing and characterizing nucleic acid complexes and materials which assemble into a static, equilibrium end state. On the other hand, dynamic DNA nanotechnology focuses on complexes with useful non-equilibrium behaviour such as the ability to reconfigure based on a chemical or physical stimulus (Seeman 1999). DNA based nanosystems are listed in Table 1.

Advantages of DNA nanotechnology:

In DNA nanotechnology, it is easy to programme and predict intermolecular interactions. Structure of DNA is well known, making it easy to manipulate. It can hold components in place of molecular electronic devices and its solid support synthesis can be used for DNA based computing. DNA can also be manipulated using different enzymes and is one of the best nanowire in existence because of its properties of self assembley, replication, and adopting various states and conformations. Different DNA can be insulating, semiconducting, or metallic (how?).

Table 2: Applications of Nanobiotechnology

Field	Uses	References
Environmental field	Research carried showed that these CNTs are capable of adsorbing hydrogen and this indicates that CNTs are the ideal building blocks for constructing safe, efficient and high- density adsorbents for hydrogen storage applications like fuel cells and batteries in electronic and automobile applications	Dillion *et al.* 1999; Bruns, 2000;Khan *et al.* 2003
Cosmetics	Nano particles of titan dioxide and zinc oxide are used as UV filter sunscreens. Some special tooth creams for the neck of sensitive teeth contain nanoscale calcium phospohate (apatite) which produces a thin layer similar to natural tooth enamel, which is thus supposed to reduce sensitivity to pain. Tiny particles of nanometer thin pigment can be found in make-up. Nanoparticles from volcanic ash are also in use in mascara, as are ceramic nanoparticles in nail varnish.	Grebler 2010; Li and Robert 2010; Raj *et al* 2012; Sharma *et al* 2012
Space	To making space flight by reducing the amount of rocket fuel.These advances could lower the cost of reaching orbit and traveling in space. In addition, new materials combined with nanosensors and nanorobots could improve the performance of spaceships, spacesuits, and the equipment used to explore planets and moons, making nanotechnology an important part of the 'final frontier.	www.under standingnano. com/space.html
Military	Militaries all around the world is about to embark upon the use of Nano-materials, Nano-bots and Nano-technologies that will make current Weapons of mass Destruction look miniscule. Armies of enormous strengths can be wiped out slowly without even fighting a single battle. The soldiers may never know that they have been nano-poisoned.	Benbow 2004; Wang and Dortmans 2004; Indian daily 2005; Tiwari 2012
Telecommunication	Quantum Photonics Group at DTU Fotonik in collaboration with the Niels Bohr Institute, University of Copenhagen surprise the scientific world with the discovery that light emission from solid-state photon emitters, the so-called quantum dots, is fundamentally different than hitherto believed. Just as walkie-talkies transmit and receive radio waves, carbon nanotubes can transmit and receive light at the nanoscale,	Arora and Padua 2010; Neethirajan and Jayas 2011; Meeto 2011;

Continued ..Table 2: Applications of Nanobiotechnology

Field	Uses	References
Food sector	Nanotechnology is the high-technology, atomically processed antithesis of organic agriculture, which values the natural health-giving properties of fresh, unprocessed whole foods. There are four key focus areas for nanotechnology food research- nano modification of seed and fertilizers/pesticides, food "fortification" and modification, interactive "smart" packaging and food tracking.	Miller and Kinnear 2007; Sharon *et al* 2010; Danielle *et al* 2013
Material Science	From harvesting the cotton to finalizing the fabric it's made into, over 25% of the cotton fiber is lost to scrap or waste. However, Marget Frey scientist from Cornell University developed a technique called electro spinning that makes good use of the scrap material that used to make low value products like cotton balls, yarn and cotton batting and its makes up to 90 percent of cotton material	Frazer 2005
Medical sector	The potential medical applications are predominantly in detection, diagnostics (disease diagnosis and imaging), monitoring, and therapeutics. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. The vision is to improve health by enhancing the efficacy and safety of nanosytems and nanodevices.	Chang 2006; Logothetidis 2006; Surendiran *et al* 2009
Nanobiotechnology in Agriculture	**Analysis of gene expression and regulation** ➢ Nanofabricated gel-free systems and high throughput DNA sequencing ➢ Microarrays and expression profiling ➢ DNA Microarrays ➢ Protein Microarrays **Crop Improvement** ➢ Atomically modified seeds ➢ Silica beak plant cells ➢ Hormones and antibiotic delivery in plants ➢ Particle farming ➢ Seeding iron ➢ Using nanosensors on crops and nanoparticles in fertilizers **Efficient Pesticides and Fertilisers** ➢ Nanocides: Pesticides via encapsulation **Soil Management** ➢ Soil binder-using chemical reactions at the nanoscale to bind soil together ➢ Soil clean-up using iron nanoparticles **Plant disease diagnostics** ➢ Sample Retrieval ➢ Pathogen detection ➢ Smart treatment delivery systems **Monitoring the identity and quality of agriculture product** ➢ Quality maintain **Post-harvest technology** ➢ Nano barcodes and identity preservation	Weigl *et al.* 2003; ETC Group 2004; Prasanna 2007; Chinnamuthu and Boopathi 2009; Jha et al 2011; Cursino *et al* 2011; Martin-Ortigosa *et al.* 2012; Wang et al 2002; Wilson *et al* 2013, ISAAA 2014

Applications of Nanobiotehnology:

There are numerous applications of nanobiotechnology, *viz.*, environmental field, cosmetics, space, military, telecommunication, food sector, medical field and agriculture sector. Applications are listed in Table 2. Nanobiotechnology will leave no field untouched by its ground breaking scientific innovations. The agricultural industry is no exception. Till now, most of the technology is theoretical but it has begun and will continue to have a significant effect in the main areas of the food industry (Biswal et al 2012). Nanobiotechnology can improve understanding of the biology of different crops and thus potentially enhance yields or nutritional values. As for example, particle farming which yield nanoparticles for industrial use by growing plants in defined soils. Research has shown that alfa-alfa plants grown in gold rich soil absorb gold nanoparticles through their roots and accumulate these in their tissues and can be separated by harvesting mechanically (Liz Kalaugher 2002).

Status of Nanobiotechnology in India:

Nano science and technology initiative (NSTI), Delhi, India is an institute involving research and development of Nanotechnology in India. There is no specific institute dealing only with Nanobiotechnology. NSTI spend US $ 5 million to 8 million till date. It has 130 research projects, 20 centers, joint institution-industry projects and one Nano science and Technology Mission program. Status of nanotechnogy is shown in Table 3.

Table 3. Nanotechnology in Agri-Food system- in Developing Country

	LDC*	Developing countries
National activity	-	19
Individual or group interst	1	11
Country interest	3	10

Least developing countries; 44 countries in the game leading China, India, South Africa, Brazil and Trilateral collaborations - Thailand, Phillipines, Malaysia.* *(Source: Sastri K 2006)***

Despite the efforts made by the management scientists, productivity of crops has not realized its potential. This is attributed to low nutrient and water use efficiency by crops and stiff competition by the weeds and crop pests. Breaking this yield barrier through the new scientific approach, nanotechnology may bestow expected result to increase productivity of crops and meet challenges of food security of the country in the coming years. Hence, Indian Government is looking towards nanotechnology as a means of boosting agricultural productivity. Planning Commission of India recommended nanotechnology research and development as one of the six areas of investment (Sreelata, 2008).

Conventionally, remediation for the stress caused by the biotic and abiotic factors on plants starts only after the development of symptoms. By that time the malady may have been widespread and entire fields may have been destroyed. Nanotechnology operates at the same scale as a virus or disease-infecting particle, and thus holds the potential for very early detection and eradication. Smart treatment delivery systems are envisioned for biology and bioactive systems such as drugs, pesticides, nutrients, probiotics, nutraceuticals and implantable cell bioreactors. Experts in agriculture and nanoscience identified some of the important areas in the field of agriculture that have enormous potential for the application of nanotechnology.

Some of the products like nano pesticides have already arrived in the market, while many others are under developing stage and it may take few years before they are commercialized. These applications are largely intended to address some of the limitations and challenges like weed management , slow release fertilizers, conditional release of pesticides and herbicides, precise micro-management of soils, the more efficient and targeted use of inputs and new toxin formulations for pest control as shown in Table 4.

Table 4. Nano agrochemicals under development (http://www.foeeurope.org/astivities/ nanotechnology/Documents/Nano_food_report.pdf)

Type of product	Product name	Nano content	Purpose
Super combined fertilizer and pesticide	Pakistan US Science and Technology Coopraive Progarm	Nano-clay capsule contains growth stimulants and biocontrol agents.	Because it can be designed for slow release of active ingredients, treatment requires only one application over the life of the crop
Herbicide	Tamil Nandu Agricultural University (India) and Technologico de Monterrry (Mexico)	Nano-formulated	Designed to attack the seed coating of weeds, destroy soil seed banks and prevent weed germination
Pesticides, including herbicides	Australian Common wealth Scientific and Industrial Reserach Organizzation	Nano encapsulated active ingredients	Very small size of nanocapusles increase their potency and may enable targeted release of active ingredients

CONCLUSION

Nanobiotechnoogy is one of the main emerging research field in science and engineering. It exists at the interface between nano and biotechnology and deals with the investigation and utilization of the newly conceived nanomaterials as well as the construction of functionalized nanobiosystems. The multidisciplinary field of nanobiotechnology has a great potential in physical, chemical and biological sciences as well as in the development of improved medical engineering. Nanotechnology is the engineering of tiny machine, i.e. ability to build things from the “bottom up”, manufacturing because it aims to start with the smallest possible building materials, ATOMS to create a desired product. By taking advantage of quantum level properties, multiwall nanotubes allow unprecedental control of the material world at the nanoscale, providing the means by which systems and materials can be built with exact specification and characteristics.

In the future, we can visualize a world with medical nanodevices, implanted or even injected into the body. A global perspective and collaboration might be needed in research and development to give such benefits to human kind.

There is Big future waiting for the tiny technology. It has potential to change the course of time. As the size decreases computing speed and computing power will increase, materials will be stronger, and small doses of medicines will cure diseases rapidly and more efficiently then ever. The technology that works at the nanometer scale of molecules and atoms will be a large part of this in the future.

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