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Nanotechnology: The Beginning of New Era

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ABSTRACT

Nanotechnology is the engineering of functional systems at the molecular level. It is the study of the control of matter on an atomic and molecular scale. Nanotechnology is providing completely new concepts and new approaches in medicine and dentistry which will enable us in making better, earlier and sure diagnosis as well as treating patients with least possible interventions and without any adverse effects. Still we are in the emerging era of nanotechnology and there are a lot of fields to be explored for nanotechnology and nanotools use. In the coming future, Nanotechnology will enable us in better understanding of various aspects of human Physiology. Nanotechnology will be boon for betterment of Pharmacology in the form of new drug development, better and accurate drug delivery and decreasing adverse effects of drugs. In 2015-20, Nanotools will be our daily companians not only in hospitals but also in homes but miles to go for newer discoveries in Nanotechnology.

Keywords: Nanodentistry, Nanodiagnostics, Nanomedicine, Nanorobots, Nanotechnology.

INTRODUCTION

Nanotechnology, shortened to "nanotech", is the study of the control of matter on an atomic and molecular scale. Generally nanotechnology deals with structures of the size 100 nanometers or smaller in at least one dimension, and involves developing materials or devices within that size. Nanotechnology is very diverse, ranging from extensions of conventional device physics to completely new approaches in medicine and dentistry in the form of nanodiagnostics, cancer chemotherapy, nanolithography, photothermal antimicrobial nanotherapy, nanodiamonds, newer drug delivery systems, nanorobots, cell repair, nanonephrology and many more to be explored.

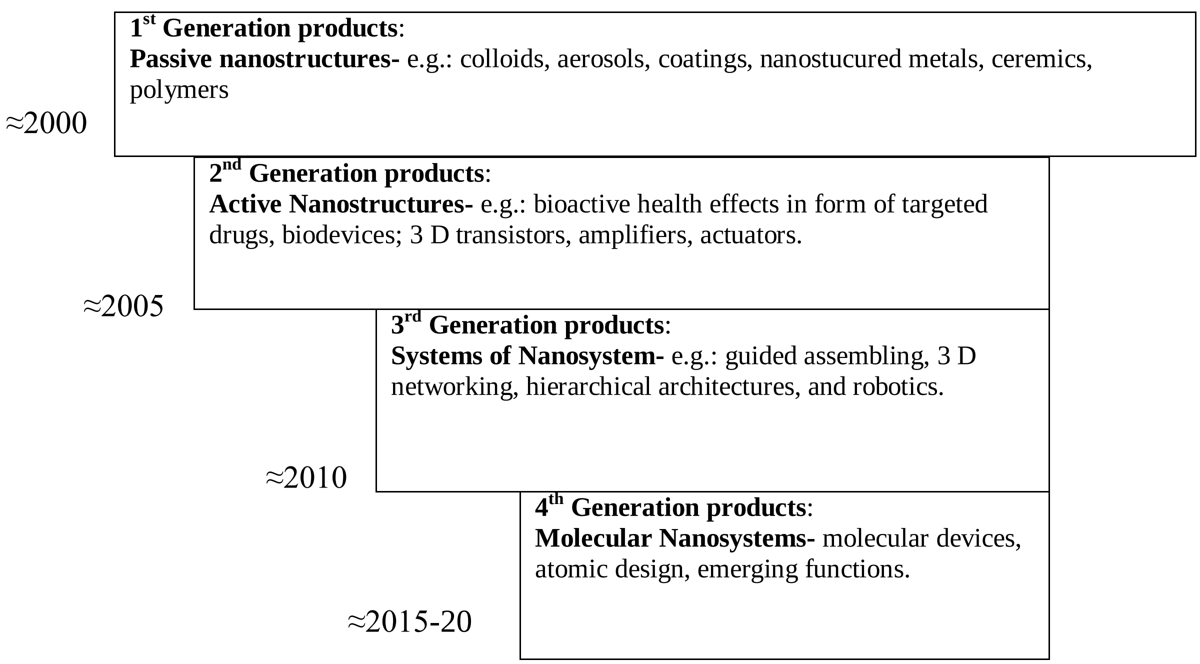
Nanomedicine is a large industry, with nanomedicine sales reaching 6.8 billion dollars in 2004, and with over 200 companies and 38 products worldwide, a minimum of 3.8 billion dollars in nanotechnology R&D is being invested every year[1]. As the nanomedicine industry continues to grow, it is expected to have a significant impact on the economy.

Nanotechnology is sometimes referred to as a general-purpose technology because in its advanced form it will have significant impact on almost all industries and all areas of society. It will offer better built, longer lasting, cleaner, safer, and smarter products for the home, for communications, for medicine, for transportation, for agriculture, and for industry[2].

History: on 29th December 1959, the late Nobel Prize–winning physicist Richard P. Feynman presented a talk at Caltech entitled “There’s Plenty of Room at the Bottom” [3] at the annual meeting of the American Physical Society. He suggested that such nanomachines, nanorobots and nanodevices ultimately could be used to develop a wide range of atomically precise microscopic instrumentation and manufacturing tools. The vision of nanotechnology was born. Forty years ago, this talk was greeted with astonishment and skepticism. However, since then, we have made remarkable progress towards realizing Feynman’s vision. Even Feynman had notions of how nanotechnology could be applied to medicine.

The term "nanotechnology" was defined by Tokyo Science University Professor Norio Taniguchi in 1974 paper[4] as follows: "'Nano-technology' mainly consists of the processing of, separation, consolidation, and deformation of materials by one atom or by one molecule." Engines of Creation: The Coming Era of Nanotechnology by Dr. K. Eric Drexler,is considered the first book on the topic of nanotechnology. In 2000, the United States National Nanotechnology Initiative was founded to coordinate Federal nanotechnology research and development.

Four Generations: Mihail (Mike) Roco of the U.S. National Nanotechnology Initiative has described four generations of nanotechnology development (figure). The current era, as Roco depicts it, is that of passive nanostructures, materials designed to perform one task. The second phase, which we are just entering, introduces active nanostructures for multitasking; for example, actuators, drug delivery devices, and sensors. The third generation is expected to begin emerging around 2010 and will feature nanosystems with thousands of interacting components. A few years after that, the first integrated nanosystems, functioning much like a mammalian cell with hierarchical systems within systems, are expected to be developed.[2]



Figure

Defining Nanometer: Nano is derived from $\nu\alpha\nu o\zeta$, the Greek word for dwarf. A nanometer is 10^{-9} meter, or one-billionth of a meter.
Nanotechnology will change medicine, dentistry, health care and human life more profoundly than many developments of the past.

Fields of Nanotechnology: various fields related to nanotechnology are:

Nanobiotechnology is the branch of nanotechnology with biological and biochemical applications or uses. Nanobiotechnology often studies existing elements of nature in order to fabricate new devices[5].

Nanodiagnostics: this is the branch related with the advancement in diagnostics using nanotools such as Quantum Dots (QDs), gold particles and cantilevers, for more sensitive and cost-effective diagnostic applications as well as intracellular imaging.

Nanoelectronics refer to the use of nanotechnology on electronic components, especially transistors.

NanoMedicine is the medical application of nanotechnology.[6] This is the science and technology of diagnosing, treating and preventing disease and traumatic injury; of relieving pain; and of preserving and improving human health, through the use of nanoscale-structured materials, biotechnology and genetic engineering, and eventually complex molecular machine systems and nanorobots. Nanomedicine research is receiving funding from the US National Institute of Health. Of note is the funding in 2005 of a five-year plan to set up four nanomedicine centers. It includes many new commercial applications in the pharmaceutical industry such as advanced drug delivery systems, new therapies, and in vivo imaging.[7]

NanoDentistry is the application of nanotechnology in dentistry. There will be enormous advancement in the field of dentistry by the use of various nano tools. New treatment opportunities may include dentition renaturalization, permanent hypersensitivity cure, complete orthodontic realignments during a single office visit, covalently bonded diamondized enamel and continuous oral health maintenance through the use of mechanical dentifrobots.

Nanonephrology is a branch of nanomedicine and nanotechnology that deals with 1) the study of kidney protein structures at the atomic level; 2) nano-imaging approaches to study cellular processes in kidney cells; and 3) nano medical treatments that utilize nanoparticles and to treat various kidney diseases. The ability to direct events in a controlled fashion at the cellular nano-level has the potential of significantly improving the lives of patients with kidney diseases. **Nanometrology** is a subfield of metrology, concerned with the science of measurement at the nanoscale level. Nanometrology has a crucial role in order to produce nanomaterials and devices with a high degree of accuracy and reliability in nanomanufacturing.

Green nanotechnology is the development of clean technologies, "to minimize potential environmental and human health risks associated with the manufacture and use of nanotechnology products, and to encourage replacement of existing products with new nano-products that are more environmentally friendly throughout their lifecycle."[8] One major project that is being worked on is the development of nanotechnology in solar cells.

Nanolithography is that branch of nanotechnology, which deals with the study and application of fabrication of nanoscale structures like semiconductor circuits. Nanolithography is a very active area of research in academia and in industry.

IMPLICATIONS OF NANOTECHNOLOGY

Nanotechnology is being applied in various fields related to human well being and research is going on for various implications. Soon, we'll be able to find Nano researches as the onset of new era in medicine. Starting from general infections to seroius mutations, from anaesthesia to surgery, from diagnosis of cacers to their treatment, soon, we'll get Nanotools everywhere. Following are some of the present and future implications of Nanotechnology:

Nanomedicine: Programmable nanorobotic devices would allow physicians to perform precise interventions at the cellular and molecular level. Medical nanorobots have been proposed for gerontological applications[9], in pharmaceutical research[10] and clinical diagnosis[11,12], and in dentistry[13,14]. Other applications include mechanically reversing atherosclerosis[15], improving respiratory capacity[16], enabling near instantaneous hemostasis[16], supplementing the immune system[13,18], rewriting[19] or replacing[20] DNA sequences in cells, repairing brain damage[21] and resolving gross cellular insults[19], whether caused by "irreversible" processes[22] or by cryogenic storage of biological tissues[23, 24].

Photothermal antimicrobial therapy: application of laser-activated Carbon Nano Tubes (CNTs) as PhotoThermal (PT) contrast antimicrobial agents has demonstrated its great potential to cause irreparable damages to disease-causing pathogens as well as to detect the pathogens at single bacterium level. This unique integration of laser and nanotechnology may also be used for drinking water treatment, food processing, disinfection of medical instrumentation, and purification of grafts and implants[25].

Avoiding resistant strain production: The disease-causing microbial strains have become resistant to the standard antimicrobial treatments, increasing acute public health risks. Recently, selective photothermal (PT) and photoacoustic (PA) antimicrobial diagnostics and therapy were developed using a combination of pulsed laser energy and strongly light absorbing gold nanoparticles (GNs) conjugated with antibody and their clusters, suggesting excellent potentials of PT-based nanotherapeutics for in vivo antimicrobial treatment and diagnostics. These have also shown promises for cancer therapy.

Virus detection: Nanobiotechnologies possess the potential to be useful in laboratory diagnosis of infections in general and viral infections in particular. Nanosensors are the new contrivance for detection of bioterrorism agents[26].

NanoDiamonds: A team of Northwestern University researchers has introduced nanodiamonds as a novel gene delivery technology that combines key properties in one approach: enhanced delivery efficiency along with outstanding biocompatibility. A low molecular weight polymer called polyethyleneimine-800 (PEI800) currently is a commercial approach for DNA delivery. The combination of PEI800 and nanodiamonds produced a 70 times enhancement in delivery efficiency over PEI800 alone, and the biocompatibility of PEI800 was preserved[27].

Bacterial infection is a major health threat to patients with severe burns and other kinds of serious wounds such as traumatic bone fractures. Recent studies have identified an important new weapon for fighting infection and healing wounds: **Insulin**. At wound site -- skin pH levels can reach very basic levels during the repair and healing process. The researchers found that the insulin, bound firmly to the tiny carbon-based nanodiamonds, is released when it encounters basic pH levels, similar to those commonly observed in bacterially infected wounds. The nanodiamond-insulin clusters, by releasing insulin in alkaline wound areas, could accelerate the healing process and decrease the incidence of infection. Insulin accelerates wound healing by acting as a growth hormone. It encourages skin cells to proliferate and divide, restores blood flow to the wound, suppresses inflammation and fights infection. The nanodiamonds serve as platforms that can successfully bind, deliver and release several classes of therapeutics, which could impact a broad range of medical needs. Nanodiamonds are capable of releasing the chemotherapy agent Doxorubicin in a sustained and consistent manner[28].

Drug delivery: Drug delivery focuses on maximizing bioavailability both at specific places in the body and over a period of time. This will be achieved by molecular targeting by nanoengineered devices[29, 30]. More than $65 billion are wasted each year due to poor bioavailability. Lipid - or polymer-based nanoparticles, can be designed to improve the pharmacological and therapeutic properties of drugs[31]. Nanoparticles have unusual properties that can be used to improve drug delivery. Where larger particles would have been cleared from the body, cells take up these nanoparticles because of their size. Potential nanodrugs will work by very specific and well-understood mechanisms; and will lead to development of completely new drugs with more useful behavior and less side effects.

Protein and peptide delivery: Protein and peptides showing great promise for treatment of various diseases and disorders. These macromolecules are called biopharmaceuticals. Targeted and/or controlled delivery of these biopharmaceuticals using nanomaterials like nanoparticles and Dendrimers is an emerging field called nanobiopharmaceutics, and these products are called nanobiopharmaceuticals.

Cancer: Quantum dots (nanoparticles with quantum confinement properties), when used in conjunction with MRI, can produce exceptional images of tumor sites. Sensor test chips containing thousands of nanowires, able to detect proteins and other biomarkers left behind by cancer cells, could enable the detection and diagnosis of cancer in the early stages from a few drops of a patient's blood[32]. Researchers at Rice University under Prof. Jennifer West have demonstrated the use of 120 nm diameter nanoshells coated with gold to kill cancer tumors in mice. Additionally, John Kanzius has invented a radio machine which uses a combination of radio waves and carbon or gold nanoparticles to destroy cancer cells. Nanoparticles of cadmium selenide (quantum dots) glow when exposed to ultraviolet light. When injected, they seep into cancer tumors. The surgeon can see the glowing tumor, and use it as a guide for more accurate tumor removal.

James Baker, scientist from University of Michigan’s, discovered a dendrimer which has over one hundred hooks. Baker then attaches folic-acid to a few of the hooks. Cancer cells have more vitamin receptors than normal cells, so Baker's vitamin-laden dendrimer will be absorbed by the cancer cell. To the rest of the hooks on the dendrimer, Baker places anti-cancer drugs that will be absorbed with the dendrimer into the cancer cell, thereby delivering the cancer drug to the cancer cell and nowhere else[33].

Neuro-electronic interfaces: Neuro-electronic interfacing is a visionary goal dealing with the construction of nanodevices that will permit computers to be joined and linked to the nervous system. The computers will be able to interpret, register, and respond to signals the body gives off when it feels sensations. The demand for such structures is huge because many diseases involve the decay of the nervous system (ALS and multiple sclerosis). Also, many injuries and accidents may impair the nervous system resulting in dysfunctional systems and paraplegia.

Nanorobots: Nanomedicine[6, 34] would make use of these nanorobots (e.g., Computational Genes), introduced into the body, to repair or detect damages and infections. Carbon would be the primary element used to build these nanorobots.

Cell repair machines: In the future, nanomachine based systems will be built that are able to enter cells, sense differences from healthy ones and make modifications to the structure. Nanocomputers will be needed to guide these machines. These computers will direct machines to examine, take apart, and rebuild damaged molecular structures. Repair machines will be able to repair whole cells by working structure by structure. Then by working cell by cell and tissue by tissue, whole organs can be repaired. Finally, by working organ by organ, health is restored to the body.

Nanodiagnostics: Nanodiagnostics promise increased sensitivity, multiplexing capabilities, and reduced cost for many diagnostic applications as well as intracellular imaging[35].

Magnetic nanoparticles, bound to a suitable antibody, are used to label specific molecules, structures or microorganisms. Gold nanoparticles tagged with short segments of DNA can be used for detection of genetic sequence in a sample. Nanopore technology for analysis of nucleic acids converts strings of nucleotides directly into electronic signatures. DNA nanomachines can function as biomolecular detectors for homogeneous assays.

Nanodentistry: development of nanodentistry will make possible the maintenance of near-perfect oral health through the use of nanomaterials[36, 37]; biotechnology[37-41], including tissue engineering[42, 43] and nanorobotics. Various uses can be:

(a) Inducing anesthesia: One of the most common procedures in dentistry is the injection of local anesthetic, which can involve long waits and varying degrees of efficacy, patient discomfort and complications[44]. Well-known alternatives, such as transcutaneous electronic nerve stimulation[45, 46], cell demodulated electronic targeted anesthesia[47] and other transmucosal[46], intraosseous[46] or topical[48] techniques, are of limited clinical effectiveness. To induce oral anesthesia in the era of nanodentistry, dental professionals will instill a colloidal suspension containing millions of active analgesic micrometer-sized dental nanorobot "particles" on the patient's gingivae. After contacting the surface of the crown or mucosa, the ambulating nanorobots reach the dentin by migrating into the gingival sulcus and passing painlessly through the lamina propriya[49] or the 1- to 3-µm–thick layer of loose tissue at the cementodentinal junction[50]. On reaching the dentin, the nanorobots enter dentinal tubule holes that are 1 to 4 µm in diameter[51-53] and proceed toward the pulp, guided by a combination of chemical gradients, temperature differentials and even positional navigation[11,] all under the control of the onboard nanocomputer, as directed by the dentist.

Assuming a total path length of about 10 mm from the tooth surface to the pulp and a modest travel speed[11] of 100µm/s, nanorobots can complete the journey into the pulp chamber in approximately 100 seconds.

Once installed in the pulp and having established control over nerve-impulse traffic, the analgesic dental nanorobots may be commanded by the dentist to shut down all sensitivity in any tooth that requires treatment. When the dentist presses the icon for the desired tooth on the hand-held controller display, the selected tooth immediately numbs (or later, on command, awakens). After the oral procedures are completed, the dentist orders the nanorobots (via the same acoustic data links) to restore all sensation, to relinquish control of nerve traffic and to egress from the tooth via similar pathways used for ingress; following this, they are aspirated. Nanorobotic analgesics offer greater patient comfort and reduced anxiety, no needles, [54, 55] greater selectivity and controllability of the analgesic effect, fast and completely reversible action, and avoidance of most side effects and complications.[44]

(b) Major tooth repair: Nanodental techniques for major tooth repair may evolve through several stages of technological development, first using genetic engineering, tissue engineering[42, 43, 56-60] and tissue regeneration[43, 56-61] and later involving the growth of whole new teeth in vitro[62, 63] and their installation. Dentition replacement therapy—should become feasible within the time.

(c) Renaturalization procedures. Dentition renaturalization procedures may become a popular addition to the typical dental practice, providing perfect treatment methods for esthetic dentistry. Demand will grow for full coronal renaturalization procedures in which all fillings, crowns and other 20th-century modifications to the visible dentition are removed, with the affected teeth remanufactured to beome indistinguishable from the original teeth.

(d) Dentin hypersensitivity: Dentin hypersensitivity may be caused by changes in pressure transmitted hydrodynamically to the pulp. Many therapeutic agents provide temporary relief for this common painful condition[64] but reconstructive dental nanorobots, using native biological materials, could selectively and precisely occlude specific tubules within minutes, offering patients a quick and permanent cure.

(e) Tooth repositioning. Orthodontic nanorobots could directly manipulate the periodontal tissues, including gingivae, periodontal ligament, cementum and alveolar bone, allowing rapid and painless tooth straightening, rotating and vertical repositioning within minutes to hours. This is in contrast to current molar up righting techniques, which require weeks or months to complete. [65]

(f) Durability and appearance. Tooth durability and appearance may be improved by replacing upper enamel layers with covalently bonded artificial materials such as sapphire[66] or diamond, [14] Pure sapphire and diamond are brittle and prone to fracture if sufficient shear forces are imposed[67] but they can be made more fracture resistant as part of a nanostructured composite material[68] that possibly includes embedded carbon nanotubes. [69]

(g) AntiCaries: Effective prevention has reduced the incidence of caries in children[70] and a caries vaccine may soon be available.[71] However, a subocclusal dwelling nanorobotic dentifrice delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces at least once a day, metabolizing trapped organic matter into harmless and odorless vapors and performing continuous calculus débridement. These almost-invisible (1 to 10 µm) dentifrobots, would be inexpensive, purely mechanical devices that safely deactivate themselves if swallowed. Moreover, they would be programmed with strict protocols to avoid occlusal surfaces. Properly configured dentifrobots could identify and destroy pathogenic bacteria residing in the plaque and elsewhere, while allowing the 500 or so species of harmless oral microflora to flourish in a healthy ecosystem. Dentifrobots also would provide a continuous barrier to halitosis, since bacterial putrefaction is the central metabolic process involved in oral malodor[72.] With this kind of daily dental care available from an early age, conventional tooth decay and gingival disease will disappear.

(h) Nanorobotic dentifrice (dentifrobots)
Subocclusal dwelling nanorobotic dentrifice delivered by mouthwash or toothpaste could patrol all supragingival and subgingival surfaces atleast once a day, metabolising trapped organic matter into harmless and odorless vapors and performing continuous calculus debridement.[64] These invisibly small dentifrobots [1-10 micon], crawling at 1-10 microns/sec, would be inexpensive, purely mechanical devices, that would safely desactivate themselves if swallowed and would be programmed with strict occlusal avoidance protocol.[73]

(i) **Diagnosis of oral cancer[74]**

- NANOELECTROMECHANICAL SYSTEMS (NEMS)
  Convert (bio) chemical to electrical signal
- CANTILEVER ARRAY SENSORS
  Ultrasensitive mass detection technology:
  Picogram (10-12) – bacterium
  Femtogram (10-15) – virus
  Attogram (10-18) – DNA
- MULTIPLEXING MODALITY
  Sensing large numbers of different biomolecules simultaneously in real time

APPLICATIONS

- Diagnosis of diabetes mellitus and cancer
- Detection of bacteria, fungi, and viruses

Nanotechnology- a boon or curse:
One area of concern is the effect that industrial-scale manufacturing and use of nanomaterials would have on human health and the environment, as suggested by nanotoxicology research.

Health and environmental concerns: Some of the recently developed nanoparticle products may have unintended consequences. Researchers have discovered that silver nanoparticles used in socks only to reduce foot odor are being released in the wash with possible negative consequences.[75] Silver nanoparticles, which are bacteriostatic, may then destroy beneficial bacteria which are important for breaking down organic matter in waste treatment plants or farms.[76] A study at the University of Rochester found that when rats breathed in nanoparticles, the particles settled in the brain and lungs, which led to significant increases in biomarkers for inflammation and stress response.[77] A major study published more recently in Nature Nanotechnology suggests some forms of carbon nanotubes could be as harmful as asbestos if inhaled in sufficient quantities. Some of them probably have the potential to cause mesothelioma. A newspaper article reports that workers in a paint factory developed serious lung disease and nanoparticles were found in their lungs.[78]

Laws and regulations for nanotechnology: Groups such as the Center for Responsible Nanotechnology have advocated that nanotechnology should be specially regulated by governments for the above reasons. Berkeley, California is currently the only city in the United States to regulate nanotechnology, Cambridge, Massachusetts in 2008 considered enacting a similar law [79] but ultimately rejected this.[80]

CONCLUSION

Nanomedicine still faces many significant challenges in realizing its tremendous potential. Basic engineering problems run the gamut from precise positioning and assembly of molecular- scale parts, to economical mass-production techniques, to biocompatibility and the simultaneous coordination of the activities of large numbers of independent micrometer-scale robots. In addition, there are larger social issues of public acceptance, ethics, regulation and human safety that must be addressed before molecular nanotechnology can enter the modern medical armamentarium. However, there are equally powerful motivations to surmount these various challenges, although all of these hold immense promises for the future, they are still under development.

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