

## Future Medicine: Nanomedicine

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**Abstract:** Nanotechnology is a field of applied science focused on the design, synthesis, characterization and application of materials and devices on the nanoscale. The application of nanotechnology within medicine has the ability to revolutionize the cure, alleviation and prevention of disease drastically, and ultimately reinforce the restoration and preservation of health through the design, characterization, production and application of nano sized, intelligent materials.

Nanomedicine is the preservation and improvement of human health using molecular tools and molecular knowledge of the human body. Nanomedicine will have extraordinary and far-reaching implications for the medical profession, for the definition of disease, for the diagnosis and treatment of medical conditions including aging, and ultimately for the improvement and extension of natural human biological structure and function. As the science and technology of nanomedicine speed ahead, ethics, policy and the law are struggling to keep up. It is important to proactively address the ethical, social and regulatory aspects of nanomedicine in order to minimize its adverse impacts on the environment and public health and also to avoid a public backlash. At present, the most significant concerns involve risk assessment, risk management of engineered nanomaterials and risk communication. Future applications of nanomedicine will be based on the ability to build nanorobots. These nanorobots could actually be programmed to repair specific diseased cells, functioning in a similar way to antibodies in our natural healing processes. Human health has always been determined on the nanometer scale; this is where the structure and properties of the machines of life work in every one of the cells in every living thing. The practical impact of nanoscience on human health will be huge.

### INTRODUCTION

Nanotechnology consists of the processing of, separation, consolidation, and deformation of materials by one atom or one molecule. More broadly, nanotechnology includes the many techniques used to create structures at a size scale below 100 nm. The biological and medical research communities have exploited the unique properties of nanomaterials for various applications (e.g., contrast agents for cell imaging and therapeutics for treating cancer). Terms such as biomedical nanotechnology, bionanotechnology, and nanomedicine are used to describe this hybrid field. Functionalities can be added to nanomaterials by interfacing them with biological molecules or structures. Nanomaterials can be useful for both in vivo and in vitro biomedical research and applications. The integration of nanomaterials with biology has led to the development of diagnostic devices, contrast agents, analytical tools, physical therapy applications, and drug-delivery vehicles.

### NANOMEDICINE

Nanotechnology has become a new advent of medicine (nano-medicine). The use of nanotechnology in medicine offers some exciting possibilities. Some techniques are only imagined, while others are at various stages of testing, or actually being used today. Two main approaches are used in nanotechnology: one is a "bottom-up" approach where materials and devices are built up atom by atom, the other a "top-down" approach where they are synthesized or constructed by removing existing material from larger entities. Nanotechnology in medicine involves applications of nanoparticles currently under development, as well as longer ranges research that involves the use of manufactured nano-robots to make repairs at the cellular level (referred to as nanomedicine). Nanotechnology-on-a-chip is one more dimension of lab-on-a-chip technology. Biological tests measuring the presence or activity of selected substances become quicker, more sensitive and more flexible when certain nanoscale particles are put to work as tags or labels. The overall drug consumption and side-effects can be lowered significantly by depositing the active agent in the morbid region only and in no higher dose than needed. This highly selective approach reduces costs and human suffering. A targeted or personalized medicine reduces the drug consumption and treatment expenses resulting in an overall societal benefit by reducing the costs to the public health system. Nanotechnology can help to reproduce or to repair damaged tissue. This so

called "tissue engineering" makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors. Tissue engineering might replace today's conventional treatments, e.g. transplantation of organs or artificial implants. There are four entry routes for nanoparticles into the body: they can be inhaled, swallowed, absorbed through skin or be deliberately injected during medical procedures (or released from implants). Once within the body they are highly mobile and in some instances can even cross the blood-brain barrier.

### TYPES OF NANOPARTICLES

Nanoparticle contrast agents are compounds that enhance MRI and ultrasound results in biomedical applications of in vivo imaging. These particles typically contain metals whose properties are dramatically altered at the nano-scale. Gold "nanoshells" are useful in the fight against cancer, particularly soft-tissue tumors, because of their ability to absorb radiation at certain wavelengths. Once the nanoshells enter tumor cells and radiation treatment is applied, they absorb the energy and heat up enough to kill the cancer cells. Positively-charged silver nanoparticles adsorb onto single-stranded DNA and are used for its detection. Many other tools and devices for in vivo imaging (fluorescence detection systems), and to improve contrast in ultrasound and MRI images, are being developed.

In the case of cancer therapies, drug delivery properties are combined with imaging technologies, so that cancer cells can be visually located while undergoing treatment. The predominant strategy is to target specific cells by linking antigens or other biosensors (e.g. RNA strands) to the surface of the nanoparticles that detect specialized properties of the cell walls. Once the target cell has been identified, the nanoparticles will adhere to the cell surface, or enter the cell, via a specially designed mechanism, and deliver its payload.

Once the drug is delivered, if the nanoparticle is also an imaging agent, doctors can follow its progress and the distribution of the cancer cell is known. Such specific targeting and detection will aid in treating late-phase metastasized cancers and hard-to-reach tumors and give indications of the spread of those and other diseases. It also prolongs the life of certain drugs that have been found to last longer inside a nanoparticle than when the tumor was directly injected, since often drugs that have been injected into a tumor diffuse away before effectively killing the tumor cells.

**Molecular nanotechnology** refers to the three-dimensional positional control of molecular structure to create materials and devices to molecular

precision. The human body is comprised of molecules, hence the availability of molecular nanotechnology will permit dramatic progress in human medical services. More than just an extension of "molecular medicine," nanomedicine will employ molecular machine systems to address medical problems, and will use molecular knowledge to maintain and improve human health at the molecular scale. Nanomedicine will have extraordinary and far-reaching implications for the medical profession, for the definition of disease, for the diagnosis and treatment of medical conditions including aging, and ultimately for the improvement and extension of natural human biological structure and function. Nanomedicine is the preservation and improvement of human health using molecular tools and molecular knowledge of the human body.

## APPLICATIONS OF MEDICAL NANOTECHNOLOGY

Applications of medical nanotechnology span across a variety of areas such as in Drugs, Medicines, Therapeutics; in Diagnostics of diseases, abnormal conditions etc., in Surgery, in Medical Robotics, in the general sake of increasing knowledge of the human body, etc.



*Nanoparticles are taking over the world of biomedicine*

### *Applications in Drugs and Medicine*

Nanotechnology can deliver medicine or drugs into specific parts of the human body, thereby making them more effective and less harmful to the other parts of the body. Anti-cancer gold nanoparticles have been found very effective. Gold "nanoshells" are useful to fight cancer because of their ability to absorb radiation at certain wavelengths. Once the nanoshells enter tumor cells and radiation treatment is applied, they absorb the energy and heat up enough to kill the cancer cells. Not only gold but other elements can also be used.

### *Applications in Surgery*

With nanotechnology, minute surgical instruments and robots can be made which can be used to perform microsurgeries on any part of the body. Instead of damaging a large amount of the body, these instruments would be precise and accurate, targeting only the area where surgery should be done. Visualization of surgery can also be improved. Instead of a surgeon holding the instrument, computers can be used to control the nano-sized surgical instruments. "Nanocameras" can provide close up visualization of the surgery. There is less chance of any mistakes or faults. Surgery could also be done on tissue, genetic and cellular levels.

**Nano-robotics**, although having many applications in other areas, have the most useful and variety of uses in medical fields. Future medical nanotechnology expected to employ nanorobots injected into the patient to perform treatment on a cellular level.

The workings of cells, bacteria, viruses etc can be better explored. The causes of relatively new diseases can be found and prevented.

**Restore vision.** Genome sequencing can be made much easier. Biological causes of mental diseases can be monitored and identified. Simple curiosities can be answered.

**Tissue engineering** could also be done using nano-materials. Tissue engineering makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors. Advances in nanotechnology-based tissue engineering could also lead to life extension in humans and other animals.

### *Potential risks*

Potential risks of nanotechnology can broadly be grouped into three areas:

the risk to health and environment from nanoparticles and nanomaterials; the risk posed by molecular manufacturing (or advanced nanotechnology); and societal risks.

### *Economical Issues*

Will "nanomedicine" widen the gap between the rich and the poor in its initial stages like many disruptive technologies of the past? Is there a certain patent for nanomedicine? How much will the ideas of nanomedicine sell for? Will the poor get equal access to nanomedicine and other nanomedical technologies?

## THE FUTURE OF MEDICINE

Study of medical history reveals a long, hard struggle to improve human health, a struggle that will ultimately culminate in a grand victory; the elimination of ill health and suffering in the 21st Century. Assuming that the approximately ten billion people who have ever lived survived an average of 40 years and spent just 2% of their lives in misery and sickness from disease, and then a not inconsiderable price of ~70 trillion man-hours of human suffering will have been paid to achieve this end.

Biotechnology and genetic engineering are comparatively well-known because of their many important successes over the last several decades. But advocates of these approaches often ignore a future post-biotechnology discipline, just now appearing on the 2-3 decade R&D horizon, that can almost guarantee whole-body elimination of biological senescence and the indefinite maintenance of healthy mind and body, while producing few if any unwanted medical side effects. This new technology involves the application of molecular nanotechnology and nanorobotics to human health care. In near future, it will become increasingly clear that all of biotechnology is but a small subset – albeit an important subset – of nanotechnology. Indeed, the 21st century will be dominated by nanotechnology – the engineering and manufacturing of objects with atomic-scale precision – not biotechnology. Humanity is poised at the brink of completion of one of its greatest and most noble enterprises. Early in the 21st century, our growing abilities to swiftly repair most traumatic physical injuries, eliminate pathogens, and alleviate suffering using molecular tools will begin to coalesce in a new medical paradigm called nanomedicine. Nanomedicine may be broadly defined as the comprehensive monitoring, control, construction, repair, defense, and improvement of all human biological systems, working from the molecular level, using engineered nanodevices and nanostructures, molecular machine systems, and – ultimately – nanorobots too small for the eye to see.

**Molecular nanotechnology** refers to the three-dimensional positional control of molecular structure to create materials and devices to molecular precision. The human body is comprised of molecules; hence the availability of molecular nanotechnology will permit dramatic progress in human medical services. More than just an extension of "molecular medicine," nanomedicine will employ molecular machine systems to address medical problems, and will use molecular knowledge to maintain and improve human health at the molecular scale. The body is constantly under assault from the environment, and the immune system is continually waging a silent war against these threats. Toxins, bacteria, fungi, parasites and viruses are all constantly attacking the body and trying to do it harm. Many nanotechnological techniques imagined only a few years ago are today already making remarkable progress toward becoming reality. Scientists are currently exploring how to put to use dendrimers, (branched spherical molecules) carbon buckyballs, and other specifically engineered nanoparticle drugs to combat everything from bacteria and viruses to cancer. Nanoshells could also be used to concentrate infrared (laser) light to heat, and thereby selectively destroy cancerous cells. It may become possible to orally administer drugs that can currently only be delivered by injection. Nanoparticle encapsulation of the drug will help it to easily pass through the stomach lining and into the bloodstream where its payload would be released. Inhaled nanofibers can even stimulate the regeneration of cartilage in damaged joints.

The true potential power of nanomedicine, however, lies in still theoretical,

tiny medical *nanorobots*. "Nanobots" will be devices as small as a microbe, but they will not possess the ability to self-replicate. These engineered nanodevices, or nanomachines, will repair the damage that accumulates as a result of metabolism (being alive) by performing nanorobotic therapeutic procedures on each of the ~75 trillion cells that comprise the human body. They will contain various substructures such as an onboard power supply, nanocomputer, sensors, manipulators, pumps, and pressure tanks. By the early 2020s, molecular manufacturing - the ability to manufacture objects chiefly out of carbon with atomic precision, in very large numbers (through massively parallel assembly) using nanofactories - will enable the first nanobots to be inexpensively produced for use in medicine. Researchers are already beginning to tackle the problem of how to construct such devices.

As doctors begin to use medical nanobots in their daily practice, they will gain the ability to rapidly repair almost any physical injury, cure virtually every known disease that disables and kills people today, and vastly extend human life and health span.

**Respirocytes** are a design for an artificial red blood cell. The human body contains approximately 30 trillion natural red blood cells which circulate in the bloodstream and occupy roughly half of the blood volume. A single disc-shaped red blood cell measures around 6-8  $\mu\text{m}$  in diameter and 2-3  $\mu\text{m}$  thick. Respirocytes will be much smaller - an entire respirocyte will be a 'perfect' sphere measuring only a single  $\mu\text{m}$  in diameter - about the same size as a bacterium. A respirocyte will be an atomically-precise arrangement of 18 billion structural atoms. An onboard nanocomputer controls the loading/unloading of oxygen and carbon dioxide molecules to and from microscopic pressure tanks made of diamondoid crystal via thousands of molecular-scale pumps arranged over its surface. Just 5 ml (or one thousandth of our total blood volume) worth of respirocytes added to a person's blood could double their natural oxygen-carrying and carbon dioxide removing capacity. A single respirocyte will be capable of transporting hundreds of times more bioavailable oxygen than a natural red blood cell, at only a fraction the size. Half a liter - the most respirocytes that could be safely added to a person's blood - would allow them to sprint at top speed for twelve minutes, or remain underwater for up to four hours without taking a single breath. Alternatively, respirocytes would buy valuable time in the event of a heart attack, or drowning, and due to their diminutive form factor they would be able to supply needed oxygen to cells that would otherwise be starved following a crushing or other accident that constricts blood flow.

**Microbivores**, or nanorobotic phagocytes (artificial white blood cells) introduced into the bloodstream would form a synthetic immune system, a search and destroy task-force constantly on patrol for pathogenic microbes, viruses and fungi. Multiple-drug resistant strains of bacteria stand no chance against the microbivore. Even the deadliest of infectious pathogens could be completely cleared from the system within just minutes or hours with no negative effect to the patient, and using only a few milliliters of microbivores. Contrast this with the weeks or months required to achieve similar results (best case scenario) with current antibiotics. Microbivores are expected to be on the order of a thousand times faster acting than even antibiotic-aided natural phagocytes. With additional programming, similar nanobots could be used to detect and selectively destroy cancerous cells, or even clear obstructions from the bloodstream in just minutes, preventing ischemic damage in the event of a stroke.

**Chromalloytes**, one variety of cell-repair nanobot, would enter the nucleus of a cell and extract all of the genetic material (chromosomes) and replace it with a synthetically produced copy of the original that has been manufactured in a laboratory to contain only non-defective base-pairs. The result of this cytosurgical "Chromosome Replacement Therapy" (CRT) process would be the removal of all inherited defective genes, reprogramming of cancerous cells back to a healthy state, and a permanent cure for all genetic diseases, or any combination thereof desired by the patient. CRT will enable us to exchange our old defective chromosomes with digitally-precise new copies of our genes, manufactured in a laboratory by a benchtop size production device, using the patient's genome as the blueprint. By installing new DNA in every tissue cell in the body, this technology will make it possible to arrest and even reverse the effects that aging has on our

biology, and most current causes of natural human death - forever severing the link between calendar age and physiological health. If you are biologically old, and do not wish to be, then for you, aging/being old is a disease, that you deserve to be cured of. Through a combination of nanobot therapies, say once a year or less frequently, accumulated metabolic toxins and other nondegradable material will be cleansed from your body, while chromalloytes delete any genetic mutations or damage. Any remaining structural damage to cells that they are unable to auto-repair such as disabled or enlarged mitochondria will be dealt with using dedicated cellular repair nanobots. These rejuvenation procedures will need to be repeated once a year (or less frequently) to revert all of the damage that occurs on a continual basis as a result of metabolism.

**Clottocytes** are a design for micron-scale, oxygen/glucose-powered, artificial mechanical platelets. Clottocytes would be 100 to 1,000 times faster in response than the body's natural platelets, stopping bleeding almost instantly (within about one second) even in the event of fairly large wounds. The clottocyte is conceived as a two micron diameter, spheroidal nanobot that contains a tightly-folded (biodegradable) fiber mesh payload which, when commanded by its internal nanocomputer, deploys in the general vicinity of a damaged blood vessel. Certain parts of the mesh are designed to dissolve exposing sticky sections upon contact with water in the blood plasma. The overlapping nettings of multiple activated clottocytes trap blood cells and stop bleeding immediately. The clotting function performed by clottocytes is essentially equivalent to that of biological platelets, albeit at just 1/10,000th the concentration in the bloodstream, (or approximately 20 nanobots/cubic centimeter of blood.) and much quicker acting.

DNA can be considered to be biological nanosoftware; ribosomes, large scale molecular constructors. Enzymes are what Nature chose as truly functional molecular sized assemblers. Genetic engineers are not creating new tools per se, but rather, adapting and improvising from what Nature has already provided. Future generations of engineers, armed with molecular engineering techniques, will have a real chance of imitating and perhaps improving upon Nature.

**Nanobots** can also be designed and constructed with absolute atomic precision - a level of perfection that is actually beyond that which say, an entire natural cell operates on. Practically every atom in a nanobot will have a particular function in the overall structure. Intelligent design of the human variety can now be much more direct and efficient than nature - but it took nature to get us this far.

## THE END OF AGING AND DISEASE

The result of these technological advances will be the effective end of aging as well as the reversal of one's current biological age to any new age that is desired. These procedures are anticipated to become commonplace as the technology evolves, a few decades hence. With routine annual checkups/repairs, and the occasional major tune-up, you could remain virtually constantly your ideal biological age. Most people will probably choose to remain perpetually in the prime of their lives - their early twenties - physiologically. People will still die at some point, however most deaths will likely become accidental, rather than "natural." Even if such procedures can keep you "clinically immortal," if you're hit by a flying car, you may still die, though cell repair nanobots and other advanced future medical techniques will be able to repair much more extensive injuries than are now possible. Based on projected rates of accidental death and suicide, a life expectancy of at least one thousand years is expected - if we don't annihilate ourselves in the interim.

Perhaps the most significant danger in curing aging is in the cultural and intellectual stagnation of humankind that may result if the current generation were stopped in time. Aging and Disease result from the molecules in our tissues sliding into disorder, first destroying health, and eventually taking life itself. Nanotechnology will give us numerous novel approaches to repair our aging bodies and undo the disastrous results of the ravages of time. The advancements anticipated in the Nano age offer the first promising hope of a science-based fountain of youth. Radical life (and health) extension will become commonplace.



## DIAGNOSTICS

The high-tech, cutting edge tools required by medicine (especially medical research) are presently very expensive to produce. Building with individual atoms makes it possible to produce entire tools that are incredibly small. Sensors, and indeed entire nanobots, will be made that are tiny enough to fit within living cells.

The complexity of the human body dictates that determination of its state requires the collection of large volumes of data. An analysis of these data will even be available in real-time, (crunched by integrated nanocomputers millions of times faster than current-day computers.) Monitoring the patient's condition continuously, they will construct a detailed model of the patient's body, and apply a predictive approach to both the course of the disease or other ailment and any possible course of action in treating the condition. The sensors/nanocomputers could even provide recommendations based on computation of the probabilities of various potential treatments. The small size and low cost of nanosensors will, for the first time, make gathering this information possible, even in routine diagnosis. With real-time monitoring of a patient's systems, it becomes possible to identify problems much earlier, allowing for a more aggressive and experimental treatment approach. Thousands of medical tests will be combined into a single, inexpensive, hand-held device. This will make diagnosis much more reliable, hence increasing accuracy while reducing malpractice/insurance liability.

## INVINCIBLE MENTAL HEALTH

The single most exciting prospect of molecular nanotechnology is the potential to rewrite the very subjective quality of every moment of our experience itself into something infinitely more fulfilling. Aldous Huxley once said, "If we could sniff or swallow something that would, for five or six hours each day, abolish our solitude as individuals, atone us with our fellows in a glowing exaltation of affection and make life in all its aspects seem not only worth living, but divinely beautiful and significant, and if this heavenly, world-transfiguring drug were of such a kind that we could wake up next morning with a clear head and an undamaged constitution-then, it seems to me, all our problems (and not merely the one small problem of discovering a novel pleasure) would be wholly solved and earth would become paradise." It is possible that our super intelligent posthuman descendants (or perhaps even our future selves) will be animated by gradients of bliss that are literally billions of times richer than anything biologically accessible today.

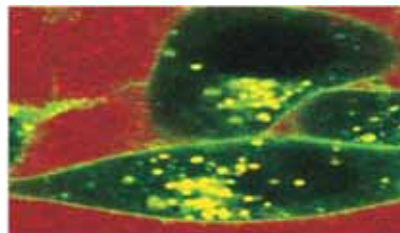
## REENGINEERING THE MAN MADE WORLD

Huge aspirations are coupled to nanotechnological developments in modern medicine (Nanotechnology, Biotechnology, Information Technology & Cognitive Science - NBIC developments). The potential medical applications are predominantly in diagnostics (disease diagnosis and imaging), monitoring, the availability of more durable and better prosthetics, and new drug-delivery systems for potentially harmful drugs.

Nano medicine provides a new avenue for developing ways of combating these stumbling blocks. For instance for many ailments surgery is an inevitability, but surgery can be very damaging to the body. Many patients may have complications after surgery or reductions in quality of life. With Nanotechnology it may be possible to treat disease in a non-invasive way. A prime example of this is the treatment of tumors with a reduction in side-effects, through the development of targeted drug delivery systems negating the need for the poison, slash and burn techniques currently used in medicine for their treatment.

Nanomedicine makes use of various different engineered nanoparticle types and encompasses areas such as nanoparticle drug/ vaccine delivery and in vivo imaging. Nanomedicine also refers to the field of molecular nanotechnology in which nanorobots such as neuro-electronic interfaces and cell repair machines will be used in therapies and surgeries.

The advent of nanotechnology is considered to be the biggest engineering innovation since the Industrial Revolution. Proponents of this new technology promise to re-engineer the man-made world, molecule by



Bright green/yellow showing cancer drug entering a cancerous cell from [purdue.edu](http://purdue.edu)

molecule, sparking a wave of novel revolutionary commercial products from machines to medicine. Nanotechnology opens up a huge range of possibilities for humans but it will also bring huge risks (i.e. misuse and malfunctioning) so there is a need for strong regulation by Governments and International Institutions.

## NANOMATERIALS

There are different kinds of nanoparticles which are suitable to be applicable in drug- and gene- delivery, probing DNA structures, etc, and are categorized as: liposomes, polymer nanoparticles (nanospheres and nanocapsules), solid lipid nanoparticles, nanocrystals, polymer therapeutics such as dendrimers, fullerenes (most common as C60 or buckyball, similar in size of hormones and peptide a-helices), inorganic nanoparticles (e.g. gold and magnetic nanoparticles).

Nanoparticles, being the fundamental elements of nanotechnology, can be applied in various ways such as fluorescent biological markers, as markers for detection of proteins, probing of DNA structures and for separation and purification of biological molecules and cells, and they can also be used for magnetic resonance imaging enhancement, tumour destruction via heating, tissue engineering and drug, gene delivery. Two kinds of nanoparticles that are suitable to be applicable at least in drug-delivery include gold nanoparticles (3-20 nm), that are gold composites with dielectrical cores and golden shells. By choosing the right ratio of core to shell diameters the particle can be tuned to absorb highly in the near infrared, and by irradiation with such wavelength can be heated, even in deeper skin areas. If the particles are embedded in a temperature sensible hydrogen matrix, the matrix will collapse and the included agents will be released at a critical temperature and second, magnetic nanoparticles, with controllable sizes between 2-30 nm that can be coated with biological molecules to make them interact with or bind to a biological entity. They can be made to deliver a package (an anticancer drug, or a cohort of radionuclide atoms) to a targeted region of the body. The magnetic particles can be provided with energy from the exciting external field, and can be heated up making them good hyperthermia agents, delivering toxic amounts of thermal energy to targeted bodies, such as tumours.

For applications to medicine and physiology, these nanomaterials, nanoparticles and devices can be designed to interact with cells and tissues at a molecular (i.e., subcellular) level with a high degree of functional specificity, thus allowing a degree of integration between technology and biological systems not previously attainable. Due to advances in biochemical research and molecular biology diseases can put down to molecular abnormalities. Molecular imaging should detect the corresponding molecular signatures of diseases and use it for medical diagnosis. This should ideally lead to diagnosis and therapy before occurrence of symptoms. In molecular imaging, an imaging molecule is coupled to a transport molecule or particle, which possesses a targeting unit (e.g. special receptors, or peptides). The target finding system should be a specific molecular marker of a certain disease thus the contrast medium accumulates within the sick tissue. Molecular imaging is developed for several diagnostic procedures such as magnetic resonance, ultrasonic imaging, as well as nuclear and optical imaging technologies.

## NANOTECHNOLOGY TOOLS

Different methods for the synthesis of nanoengineered materials and devices can accommodate precursors from solid, liquid or gas phases and encompass a tremendously varied set of experimental techniques. Most synthetic

methods can be classified into two main approaches: “top-down” and “bottom-up” approaches and combinations of them. “Top-down” (photolithography, microcontact printing) techniques begin with a macroscopic material or group of materials and incorporate smaller-scale details into them, whereas “bottom-up” (organic- synthesis, self-assembly) approaches, begin by designing and synthesizing custom-made molecules that have the ability to self-assemble or self-organize into higher order mesoscale and macroscale structures.

Other advanced applications of micro- and nanotechnology in medicine are the microchip-based drug delivery systems, which are devices incorporating micrometer-scale pumps, valves and flow channels. They allow controlled release of single or multiple drugs on demand. Micro- and nanotechnology-based methods (e.g., UV-photolithography, reactive ion etching, chemical vapour deposition, electron beam evaporation) can be used for the fabrication of these silicon-based chips.

Imaging is becoming an ever more important tool in the diagnosis of human diseases. Imaging at cellular, and even sub-cellular and molecular level, is still largely a domain of basic research. However, it is anticipated that these techniques will find their way into routine clinical use. Atomic force microscopy (AFM) and AFM-related techniques (e.g. Scanning Near-Field Optical Microscopy-SNOM) have become sophisticated tools, not only to image surfaces of molecules or sub-cellular compartments, but also to measure molecular forces between molecules. This is substantially increasing our knowledge of molecular interactions.

## APPLICATIONS OF NANOMEDICINE

Nanotechnology provides extraordinary opportunities not only to improve materials and medical devices but also to create new “smart” devices and technologies where existing and more conventional technologies may be reaching their limits.

### *Nanorobots and nanodevices*

The “respirocyte” is expected to be able to deliver more oxygen to the tissues than natural red blood cells and to manage carbonic acidity. Primary medical applications of respirocytes would include transfusable blood substitution; partial treatment for anemia, lung disorders, enhancement of cardiovascular/neurovascular procedures, tumour therapies and diagnostics, prevention of asphyxia, artificial breathing, and a variety of sports, veterinary and battlefield. Microbivores are expected to be up to 1000 times faster acting than either unaided natural or antibiotic assisted biologic phagocytic defenses and able to extend the therapeutic competence of the physician to the entire range of potential bacterial threats, including locally dense infections. Medical “nanorobots” may also be able to intervene at the cellular level, performing in-vivo cytosurgery. The most likely site of pathologic function in the cell is the nucleus – more specifically, the chromosomes. In one simple cytosurgical procedure called “chromosome replacement therapy”, a “nanorobot” controlled by a physician would extract existing chromosomes from a particular diseased cell and insert new ones in their place, in that same cell. If the patient chooses, inherited defective genes could be replaced with non defective base-pair sequences, permanently curing a genetic disease. Engineered bacterial “biobots” (synthetic microbes) may be designed to produce useful vitamins, hormones, enzymes or cytokines in which a patient’s body was deficient or to selectively absorb and metabolize harmful substances such as poisons toxins etc into harmless end products.

### *Biocompatibility and Orthopedic implants*

An important field of application for nanotechnology in medicine is the biomaterials, used for example in orthopedic implants or as scaffolds for tissue engineered products. If the design of a hip implant, for instance, is carried out at nanolevel, it might become possible to construct an implant which closely mimics the mechanical properties of human bone, preventing stress-shielding and the subsequent loss of surrounding bone tissue. Extracellular matrix (ECM) provides an excellent three-dimensional web of

intricate nanofibers to support cells and present an instructive background to guide their behavior. It takes a variety of forms in different tissues and at different stages of development in the same tissue. Nanostructuring of materials provides a powerful mechanism to encourage and direct cell behaviour, ranging from cell adhesion to gene expression, thus enhancing their biocompatibility, by dictating the desirable interactions between cells and materials.

### *Nanotechnology in Cardiology*

Minimally invasive treatments for heart disease, diabetes and other diseases is a desirable goal for scientists, and there is hope for it, because of the use of nanotechnology. Cardiovascular gene therapy could be realized roughly as follows: identification of a protein whose presence causes blood vessels to form, production and packaging of strands of DNA that contain the gene for making the protein and deliverance of the DNA to heart muscle. Of those steps, the last is the most challenging. “Biobots” (a kind of nanorobots), another application of nanotechnology, is the creation of muscle-powered nanoparticles having the ability to transfer information into cells, gives the potential of replacing lost biological function of many tissues such as sinoatrial node. This effect can lead to treatment of diseases which otherwise would be fatal or difficult to cure for human beings and Coronary Artery disease (CAD), by improving the biocompatibility of intracoronary stents and by regulating the main limit factors for Percutaneous Transluminal Coronary Angioplasty (PTCA) at a molecular level via nanoparticles.

Various inhibitors of growth factors secreted by activated platelets such as PDGF, Il-1, TGF- $\beta$  and inhibitors of proinflammatory agents released by leucocytes upon activation (e.g monocyte chemoattractant protein-1) could be used as antithrombotic and antirestenotic agents. It can be concluded that a highly effective molecular coronary intervention by means of nanotechnology may eliminate the need for stents themselves.

Diagnosis of cardiovascular diseases is an application of recent advances in nanotechnology as well. Many monoclonal antibodies, peptides and carbohydrates for non-invasive targeting of atherosclerotic lesions, myocardial necrosis, brain infarction and various tumours can be used for their detection.

The detection of the complementary DNA strand is another application of nanotechnology in the field of cardiology, that is based on the discovery of complexes of single-walled Carbon nanotubes with single-stranded DNA. If a single nucleotide alteration occurs, the association between the carbon nanotube and the complementary DNA strand will be changed, resulting in the detection of single-nucleotide polymorphisms (SNPs). SNPs are sites in the human genome where individuals differ in their DNA sequence, often by a single base. These slight variations in DNA sequences can have a major impact on whether or not a person may develop a disease and even influence the response to drug regimens.

Researchers in public and private sectors are generating SNPs maps which can occur in genes as well as in noncoding regions. Scientists believe that these maps will be used for the identification of the multiple genes associated with complex diseases such as Coronary Artery Disease (for example, ABCA1 gene is susceptible for CAD), hyperlipidaemia, cancer, diabetes mellitus and to detect humans with genetic predisposition to these diseases. By screening tests which are based on the above application of Nanomedicine, individuals that are prone to develop atherosclerosis might be detected and by controlling the main risk factors for CAD (hypertension, diabetes mellitus, smoking, hyperlipidaemia, obesity) a long-term acute coronary syndrome may be avoided.

### *Nanotechnology against Cancer*

Nanotechnology may have an impact on the key challenges in cancer diagnosis and therapy. Diagnosing, treating, and tracking the progress of therapy for each type of cancer has long been a dream among oncologists, and one that has grown closer thanks to parallel revolutions in genomics, proteomics and cell biology. Nanotechnology’s greatest advantage over conventional therapies may be the ability to combine more than one

function.

Recently, there is a lot of research going on to design novel nanodevices capable of detecting cancer at its earliest stages, pinpointing its location within the human body and delivering chemotherapeutic drugs against malignant cells. The major areas in which nanomedicine is being developed in cancer involve: a) early detection of tumour (developing "smart" collection platforms for simultaneous analysis of cancer-associated markers and designing contrast agents that improve the resolution of tumour area comparing with the nearby normal tissues), and b) cancer treatment (creating nanodevices that can release chemotherapeutic agents).

Tumour diagnostics and prevention is the best cure for cancer, but failing that, early detection will greatly increase survival rates with the reasonable assumption that an in situ tumour will be easier to eradicate than one that has metastasized. Nanodevices and especially nanowires can detect cancer-related molecules, contributing to the early diagnosis of tumour. Nanowires having the unique properties of selectivity and specificity, can be designed to sense molecular markers of malignant cells. They are laid down across a microfluidic channel and they allow cells or particles to flow through it.

Nanowires can be coated with a probe such as an antibody or oligonucleotide, a short stretch of DNA that can be used to recognize specific RNA sequences. Proteins that bind to the antibody will change the nanowire's electrical conductance and this can be measured by a detector. As a result, proteins produced by cancer cells can be detected and earlier diagnosis of tumour can be achieved.

Nanoparticle contrast agents are being developed for tumor detection purposes. Labeled and non-labeled nanoparticles are already being tested as imaging agents in diagnostic procedures such as nuclear magnetic resonance imaging<sup>24</sup>. Such nanoparticles are paramagnetic ones, consisting of an inorganic core of iron oxide coated or not with polymers like dextran. There are two main groups of nanoparticles: 1) superparamagnetic iron oxides whose diameter size is greater than 50 nm, 2) ultrasmall superparamagnetic iron oxides whose nanoparticles are smaller than 50nm<sup>25</sup>. Moreover, quantum dots being the nanoscale crystals of a semiconductor material such as cadmium selenide, can be used to measure levels of cancer markers such as breast cancer marker Her-2, actin, microfibril proteins and nuclear antigens. Tumour treatment can be succeeded with nanoscale devices (such as dendrimers, silica-coated micelles, ceramic nanoparticles, liposomes). These devices can serve as targeted drug-delivery vehicles capable of carrying chemotherapeutic agents or therapeutic genes into malignant cells.

The nanoshell-assisted photo-thermal therapy (NAPT), is a non-invasive procedure for selective photo-thermal tumour destruction. It is based on nanoshells that absorb light in the near infrared (NIR) region, which is the wavelength that optimally penetrates tissues. These nanoshells have a core of silica coated with a metallic layer, usually of gold. The metal shell converts the absorbed light into heat with great efficacy. Further specificity can be engineered by attaching antigens on the nanoshells which are specifically recognized by the cancer cells. By supplying a light in NIR from a laser, the particles produce heat, which destroy the tumour. It has been found that, the temperature within the nanoshell-treated tumours rose by about 40°C compared to a rise in 10°C in tissues treated with NIR light alone. The benefit of thermal therapeutics is that most procedures are non-invasive and have the potential to treat tumours which can not be surgically treated.

Gene-, Protein-, Lab-on-a-chip Devices, "Theranostics": Medical devices for in-vitro diagnostics, such as gene-, protein- or lab-on-a-chip devices, do not have any of the safety concerns associated with nanoparticles introduced into the body. Numerous devices and systems for sequencing single molecules of DNA are feasible. Nanopores are finding use as new nanoscale technology for cancer detection enabling ultrarapid and real time DNA sequencers. In general, developments in protein-chips and lab-on-a-chip devices are more challenging compared to gene-chips. These devices are anticipated to play an important role in medicine of the future, as they will be personalised and will combine diagnostics with therapeutics into a new emerging medical area called "theranostics".

The applications of special relevance to improving health and enhancing human physical abilities include the use of virtual environments for training, education, and interactive teaching. This will provide new ways for medical students to visualize, touch, enter, smell, and hear the human anatomy, physiological functions, and medical procedures, as if they were either the

physician or a microscopic blood cell traveling through the body.

The use of nanotechnology in the field of medicine could revolutionize the way we detect and treat damage to the human body and disease in future. Nanofibres can stimulate the production of cartilage in damaged joints. Nano particles may be used, when inhaled, to stimulate an immune response to fight respiratory viruses. Quantum Dots (qdots) may be used in the future for locating cancer tumors in patients and in near term for performing diagnostic tests in samples.

## CONCLUSIONS

The nanotechnology will help to improve health by enhancing the efficacy and safety of nanosystems and nanodevices. Moreover, early diagnosis, implants with improved properties, cancer treatment and minimum invasive treatments for heart disease, diabetes and other diseases are anticipated. In the coming years, nanotechnology will play a key role in the medicine of tomorrow providing revolutionary opportunities for early disease detection, diagnostic and therapeutic procedures to improving health and enhancing human physical abilities, and enabling precise and effective therapy tailored to the patient. Nanomedicine is in infancy, having the potential to change medical research dramatically in the 21st century. Nanomedical devices can be applied for analytical, imaging, detection, diagnostic and therapeutic purposes and procedures, such as targeting cancer, drug delivery, improving cell-material interactions, scaffolds for tissue engineering, and gene delivery systems, and provide innovative opportunities in the fight against incurable diseases. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. Over the next ten to twenty years nanotechnology may fundamentally transform science, technology, and society offering a significant opportunity to enhance human health in novel ways, especially by enabling early disease detection and diagnosis, as well as precise and effective therapy tailored to the patient.

## REFERENCES

1. **Akhlesh Lakhtakia (ed) (2004)**, *The Handbook of Nanotechnology, Nanometer Structures: Theory, Modeling, and Simulation*. SPIE Press, Bellingham, WA, USA. ISBN 0-8194-5186-X[5].
2. **Biology and Medicine** 2005; 1:351
3. **Bonnemai**, "Superparamagnetic agents in magnetic resonance imaging: physicochemical characteristics and clinical applications – a review". *J Drug Target* 1998; 6:167-174
4. **Daniel J. Shanefield (1996)**, *Organic Additives And Ceramic Processing*. Kluwer Academic Publishers. ISBN 0-7923-9765-7/Elwing H. "Protein absorption and ellipsometry in biomaterial research". *Biomaterials* 1998; 19:397; Garcia-Caurel A, Nguyen J, Schwartz L, Drévillon B. "Application of FTIR ellipsometry to detect and classify microorganisms". *Thin Solid Films* 2004; 455:722; "Moving ellipsometry from materials to medicine". *III-Vs Review* 2004; 17:4
5. **Fei Wang & Akhlesh Lakhtakia (eds) (2006)**, *Selected Papers on Nanotechnology – Theory & Modeling (Milestone Volume 182)*. SPIE Press, Bellingham, WA, USA. ISBN 0-8194-6354-X[6].
6. **Going beyond drug-eluting stents".** *Drug Discovery Today: Disease Mechanisms/Cardiovascular diseases* 2005; 2:ii
7. <http://www.ncbi.nlm.nih.gov/pmc/issues/178370> - A link to an official government nanotechnology journal published by NIH (National Institute of Health) – "International Journal of Nanomedicine". The articles are all open-source and updated with the newest developments in biomedical nanotechnology.
8. **Hunt, Geoffrey & Mehta, Michael (eds) (2006)**, *Nanotechnology: Risk Ethics, & Law*. Earthscan, London.
9. **Jong WH de, Roszek B, Geertsma R.E.**, "Nanotechnology in medical applications: possible risks for human health". RIVM report 265001002, 2005. RIVM, National Institute for Public Health and the Environment, Bilthoven, The Netherlands, 2005
10. **Kane JP, Aouizerat BE.** "Novel genetic markers for structural coronary artery disease, myocardial infarction, and familial combined hyperlipidemia: candidate and genome scans of functional SNPs". *Atherosclerosis XIII. Proceedings of the 13th International Atherosclerosis Symposium* 2004; 1262:309-312
11. **Kawasaki ES, Player TA.** "Nanotechnology, nanomedicine, and the development of new, effective therapies for cancer". *Nanomedicine: Nanotechnology, Biology, and Medicine* 2005;1:101-109
12. **Logothetidis S, Gioti M, Lousinian S, Fotiadou S.** "Haemocompatibility studies on carbon-based thin films by ellipsometry". *Thin Solid Films* 2004; 482:126
13. **Nanomedicine; An ESF – European Medical Research Councils (EMRC) Forward Look report** 2005, ([www.nanoforum.org](http://www.nanoforum.org))
14. **Nanomedicine: Nanotechnology, Biology, and Medicine** 2005; 1:326
15. **Robert A. Freitas Jr, JD.** "What is nanomedicine?". *Nanomedicine: Nanotechnology, Biology, and Medicine* 2005; 1:2
16. **Roco M C.** "Nanotechnology: convergence with modern biology and medicine". *Current Opinion in Biotechnology* 2003
17. **Roszek B, Jong WH de, Geertsma RE.** "Nanotechnology for medical applications: state-of-the-art in materials and devices". RIVM report 265001001, 2005. RIVM, National Institute for Public Health and the Environment, Bilthoven, The Netherlands, 2005
18. **Silva G A.**, "Introduction to nanotechnology and its applications to medicine". *Surg Neurol* 2004; 61:216
19. **Service R F.** "Nanotechnology Takes Aim at Cancer". *Science* 2005; 310, No.5751, p.1132; M.M. Stevens, J.H. George, "Exploring and Engineering the Cell Surface Interface". *Science* 2005; 310, No.5751, 1135-33. [www.euronanotechnews.com](http://www.euronanotechnews.com)
20. **Tachung C, Yih PE, Wite C.** "Nanomedicine in cancer treatment". *Nanomedicine: Nanotechnology, Biology, and Medicine* 2005; 1:191-92
21. **Vladimir P, Zharov DSc, Jin-Woo Kim, et al.** "Self-assembling nanoclusters in living systems: application for integrated photothermal nanodiagnoses and nanotherapy".
22. **Zandonella C.** "The tiny toolkit". *Nature* 2003; 423:10-12 24. Brigger É, Dubernet C, Couvreur P. "Nanoparticles in cancer therapy and diagnosis". *Advanced Drug Delivery Reviews* 2002; 54:631-651