

Importance of nanorobots in pharma and medical field

Saksham Guha, Vinod M Thakare, Vaibhav P Uplanchiwar and Renuka K Mahajan *

Nagpur College of Pharmacy, Wanadongri, Hingna Road, Nagpur-441110, Maharashtra, India.

World Journal of Advanced Research and Reviews, 2023, 20(01), 191–201

Publication history: Received on 11 August 2023; revised on 26 September 2023; accepted on 28 September 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.20.1.1954>

Abstract

Machines built at the molecular level (referred to as "nanomachines") may be utilized to treat the human body of its numerous diseases. Nanorobotics is the science of building machines or robots at or near the scale of a nanometre (10⁻⁹ meters). Nanomedicine is the term used to describe this application of nanotechnology to the field of medicine. Future-looking uses for nanotechnology include minuscule robots that can build other machines, navigate inside the body to distribute drugs, or do microsurgery. Chemists are discovering how to use protein dynamics to power micro and nano size machines using catalytic processes, drawing inspiration from the biological motors of live cells. The toolkit for nanorobots includes items like a cavity for storing medication, probes, blades, and chisels to remove plaque and obstructions, microwave emitters, and ultrasonic signal generators to destroy cancerous cells, two electrodes generating an electric current, heating the cell up until it dies, powerful lasers could burn away harmful material like arterial plaque. A cream incorporating nanorobots that remove the proper amount of dead skin, remove excess oils, add missing oils, apply the right amounts of natural moisturizing ingredients, and even accomplish the elusive objective of "deep pore cleaning" may be utilized to treat skin problems. Other uses include the treatment of gout, kidney stones, gouty arthritis, parasite elimination, cancer treatment, and arteriosclerosis treatment.

Keywords: Nanomachines; Nanorobots; Medicine; Microsurgery; M. education

1. Introduction

The best way to define nanotechnology is as a description of atomic and molecular level activities that have practical uses. One billionth of a meter, or around 1/80,000 of the diameter of a human hair, or 10 times the diameter of a hydrogen atom, is referred to as a nanometer.

The capacity to measure, manipulates, and construct matter with features on the scale of 1-100 nm is the size-related issue. Automating molecular production will be crucial for nanotechnology to become cost-effective. The engineering of molecular goods requires the use of nanorobots, which are miniature robotic machines. This review chapter concentrates on the current state of the field of nano robotics, its applications, and briefly explores some of the fundamental characteristics and dynamical laws that make this field more difficult and distinctive than its macro size cousin. In response to the grey goo scare scenarios, some supporters of nano robotics hold the opinion that self-replicating nanorobots do not necessarily make up a purportedly productive nanotechnology, and that the process of self-replication, if it were ever developed, could be made inherently safe. They also claim that free-foraging replicators are not part of their current intentions for creating and utilizing molecular manufacturing. Nano robots made entirely of artificial components are still a dream. The focus of current study in this field is largely on molecular robots, which are heavily influenced by nature's nanoscale processes [2]. Mother Nature has her own set of molecular tools that have been in operation for eons and have been improved for functionality and shape over time. We now see a potential of employing the natural machines or building synthetic ones from scratch using elements from nature as our knowledge and comprehension of these countless devices continues to grow. In the field of molecular machines, the fundamental

* Corresponding author: Renuka K Mahajan

objective is to use numerous biological components whose action at the cellular level generates motion, force, or a signal as a machine components. In response to the unique physiochemical stimuli, these components carry out their preprogrammed biological activity, but in an artificial environment. In this manner, proteins and DNA may function as sensors, mechanical joints, or transmission components. These many parts may create nanodevices with multiple degrees of freedom that could apply forces and manipulate objects in the nanoscale universe if they were put together in the right ratio and orientation. The benefit of employing natural machine parts is that they are incredibly efficient and dependable.

1.1. Types and design of nanobots

1.1.1. Tiniest engine ever built

German physicists from the University of Mainz recently produced the tiniest engine ever built out of just one atom. It turns energy into movement like all alternative engines do, but it does it on a smaller scale than is typical.

1.1.2. Desoxyribonucleic acid-based 3D-motion nanomachines

Mechanical engineers at Ohio State University have created advanced nanoscale mechanical components using "DNA origami," demonstrating that the same fundamental design principles that apply to typical full-size machine components can currently be applied to DNA. These advanced, controllable components may be used to create nanorobots in the future.

1.1.3. Nanoswimmers

Researchers from the Technion and ETH Zurich have created an elastic "nanoswimmer" polypyrrole (Ppy) nanowire that is about two hundred nanometers thick and fifteen micrometers long, and it can move through biological fluid environments at a speed of almost fifteen micrometers per second. The magnetically controlled nanoswimmers may be functionalized to carry medicine and swim through the blood to target cancer cells.

1.1.4. An ant-like nanoengine with a force per unit weight that is 100 times greater

than any motor or muscle was created by researchers at the University of Cambridge. According to the researchers, the new nano-engines could eventually produce nanorobots that are small enough to infiltrate living cells and combat disease. The research's principal investigator, academician Jeremy Baumberg of the Cavendish Laboratory, gave the gadgets the term "actuating nanotransducers" (ANTs). Like actual ants, they generate enormous forces to support their weight.

1.1.5. Sperm-inspired microrobots

Researchers at the German University in Cairo (Egypt) and the University of Twente (Netherlands) have developed sperm-inspired microrobots that can be guided by intermittent mild magnetic fields. They perform specialized medical aid tasks and sophisticated micromanipulation.

1.1.6. Bacteria-powered robots

Drexel University engineers have created a method for employing electrical fields to assist tiny bacteria-powered robots in detecting and avoiding obstacles in their environment. Delivering medication, directing stem cell growth, or creating a microstructure are a few examples of applications. 17,

1.1.7. Nanorockets

By fusing nanoparticles with biological molecules, numerous research teams have recently created a high-speed, pilotless nanoscale rocket. The goal of the researchers is to perfect the rocket so that it may be used anywhere, such as to deliver medicine to a specific region of the body.

2. Chemotherapy drug delivery using nanorobots in cancer treatment

More effective targeted drug administration has been made possible by recent developments in medication delivery, which use nanosensors to identify specific cells and smart medications to control discharges. Traditional chemotherapeutic agents work by destroying rapidly multiplying cells, which is a key characteristic of cancerous cells. The majority of anticancer drugs have a narrow therapeutic window and frequently cause cytotoxicity to normal stem cells that proliferate quickly, including those in the bone marrow, macrophages, gastrointestinal tract (GIT), and hair

follicles. This results in side effects like myelosuppression (lower production of WBCs, which produces immunosuppression), mucositis (inflammation of the GIT lining), alopecia (hair loss), organ dysfunction, thrombocytopenia/anaemia, and haematological side effects, among other things. Doxorubicin is a drug used to when paired with Hodgkin's disease, several types of malignancy, including To reduce its toxicity, use additional anti-cancer medications. A medication is paclitaxel. It treats breast cancer by being administered intravenously. several of the major negative consequences consist of increasing bone marrow suppression. neurotoxicity. An alkylating medication called cisplatin causes intra-DNA binding filament. Giddiness and severe vomiting are some of its side effects, and it can be nephrotoxic. By blocking type 1 topoisomerases, an enzyme necessary for cellular duplication of genetic material, camptothecin is used to treat neoplasia. Numerous projects have been started with the intention of using nanotechnology to create DDS that can lessen the side effects of conventional therapy.

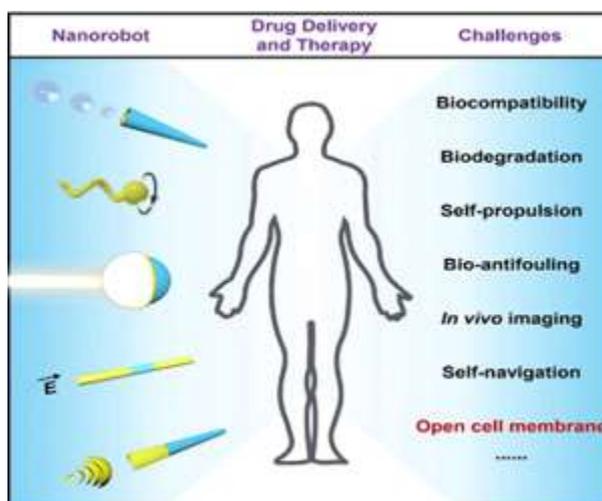


Figure 1 Challenges of nanorobots in drug delivery

This image throws light on the various challenges that different shaped nanorobots face when employed for drug delivery

3. Future of nanotechnology in the area of medicine

Numerous traditional scientific disciplines, including medicine, chemistry, physics, materials science, and biology, have come together to establish the developing field of nanotechnology in order to combine the necessary cooperative skills to produce these novel technologies. A wide range of potential uses for nanotechnology exist (Figure 2) [39], ranging from enhancements to current procedures to the development of whole new tools and abilities. The interest in nanotechnology and related research has grown exponentially over the past few years, which has sparked the discovery of new uses for the technology in medicine and the birth of a cutting-edge subfield termed nanomedicine. It includes the science and technology of identifying, treating, and preventing disease, traumatic injury, and pain relief; preserving and improving human health through the use of nanoscale architected materials, biotechnology, and genetic engineering; and ultimately, complex machine systems and nanorobots, known as "nanomedicine"

Nanotechnology assisted in the discovery of nanoparticles, which has resulted in a variety of applications in the field of medicine. The newly produced nanoparticle has a variety of applications, including the production of nanoimplants, tissue engineering for drug delivery systems, gene delivery systems, drug screening, theranostics, cancer therapy, biomarker mapping, illness detection, and bio-imaging.

In several areas of pre-clinical and clinical medicine, nanorobots are used. Nanorobots are used in pre-clinical medicine for bioimaging, different drug delivery methods, gene therapy, living cells, and inorganic therapies. Similar to this, nanorobots are widely utilized in clinical practice for tissue collection, biofilm destruction, illness diagnostics, and sampling [41].

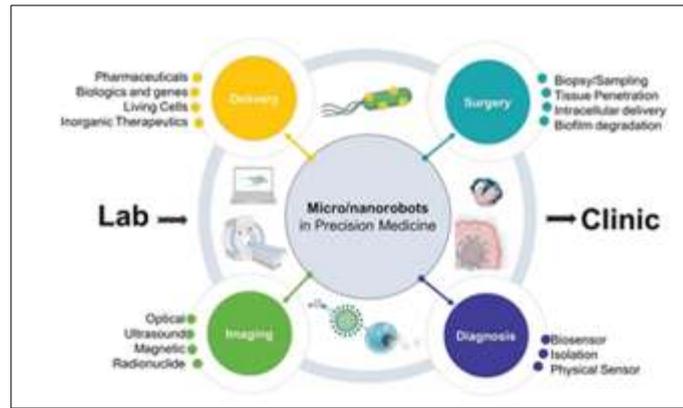


Figure 2 Schematic diagram of the current trends of micro/nanorobotics in precision medicine

3.1. Medical application of nano robots

Nano robots are anticipated to make it possible for people suffering from various ailments to receive new treatments, which will signal a significant advancement in medical history. Recent advancements in the field of biomolecular computing are a promising first step toward enabling more complicated nanoproducts in the future. Research has also advanced on creating the biosensors and nano-kinetic tools needed for medical nano robotic operation and locomotion. The use of nanorobots could progress biomedical intervention through minimally invasive procedures, assist patients who require ongoing body function monitoring, or even enhance treatment efficacy through the early detection of potentially fatal diseases. For instance, the nano robots may be used to attach on moving immune cells or white blood cells, enabling them to reach injured regions more quickly and aid in their recovery. Nano robots will be used in chemotherapy to treat cancer by administering exact chemical dosages; a similar strategy might be used to make nano robots capable of delivering antiHIV medications. Nano robots could be utilized as auxiliary equipment for damaged organs to process certain chemical reactions in the human body. Nano robots may be used for monitoring diabetes and regulating glucose levels for patients.

3.1.1. Nano robots in cancer treatment

With the state-of-the-art therapeutic methods and medical technologies, cancer can be successfully treated. The likelihood that a cancer patient would survive, however, is significantly influenced by how quickly the disease was discovered. If at all possible, a tumour should be found at least before metastasis has started. The development of effective targeted drug delivery to lessen the side effects of chemotherapy is a crucial component of achieving a successful treatment for patients. Nanorobots have the ability to go through the bloodstream, which makes them useful for such crucial components of cancer therapy. The early phases of tumor cell formation can be detected inside the body of the patient using nanorobots with chemical biosensors inserted. To measure the strength of the E-cadherin signals, integrated nanosensors can be used. In order to apply nanorobots for cancer therapy, a hardware architecture based on nano bioelectronics is given here. Real-time 3D simulation is used to produce the analyses and findings for the proposed model.

3.1.2. Nano robots in gene therapy

By comparing the molecular structures of the DNA and proteins found in the cell to desired or known reference structures, medical nano robots can quickly correct hereditary disorders. Then, any errors can be fixed or the appropriate changes can be made and put in place. Chromosome replacement therapy may occasionally be more effective than CY to repair a damaged chromosome. A human cell's nucleus is home to an assembler-built repair vessel that carries out certain genetic upkeep. The nano machine gently pulls an unwound strand of DNA through an aperture in its prow for analysis after stretching a super coil of DNA between its lower set of robot arms. While this is happening, upper arms pull. The larger nano computer, located outside the nucleus and linked to the cell-repair ship through a communications link, is used to compare the molecular structures of DNA and proteins to data recorded in its database.

The repair vessel would be smaller than the majority of bacteria and viruses, yet capable of therapies and cures far beyond the reach of modern doctors. If irregularities found in either structure are corrected and the proteins are reattached to the DNA chain, which re-coils into its original form with a diameter of only 50 nanometers, the repair vessel would be smaller than most bacteria and viruses. regulatory proteins away from the chain and deposit them in an intake port. Internal medicine would gain new significance when a patient's bloodstream contained trillions of these

devices. By attacking disease at the molecular level, conditions like cancer, viral infections, and arteriosclerosis could be cured.

3.1.3. Nano robot for brain aneurysm

The brain aneurysm prognostic nano robot uses computational nanotechnology to prototype medical equipment. Equipment prototyping, the manufacturing process, and inside-body transduction are the three key components of this. Computing-based nanotechnology makes equipment prototyping a critical tool for the rapid and efficient production of nanorobots, assisting in the examination of crucial issues with medical instrumentation and device prototyping. Industry previously used a similar strategy to construct race cars, aircraft, submarines, ICs, and medical gadgets. The development and study of medical nanorobots might now profit from the same. The manufacturing process used to create the nano robot should be incorporated into a biochip device. Along with a description of the nano robot design, novel materials, photonics, and nano bioelectronics are introduced. Additionally, the parameters for the inside-body interactions and nanorobot morphology are based on cell morphology, microbiology, and proteomics. Medical prognosis is based on changes in chemical gradients and telemetric instruments, with the nano robots activated depending on proteome over expression. These three ideas make up the essential components needed to enhance the creation and application of medical nano robots, as they are described in the study. Nano robots must monitor vessel endothelial damage before a subarachnoid hemorrhage happens in order to determine the prognosis of brain aneurysms. The nano robots are directed by these variations in chemical concentration to find developing brain aneurysms (Figure 2). The robot uses chemical nano biosensor contact to identify the bio molecules because they are too small to be detected accurately. The primary morphologic characteristics of brain aneurysms are used as models for the investigation of nanorobot interaction and sensing within the distorted blood artery. Intracranial NOS concentrations are low, and pNOS's positive interactions with N-oxide can even lead to occasional false positives. Along with the fluid low, cells and nanorobots frequently enter one end of the workspace. The setup for sensing and control activation can be changed for different values, such as modifying the detection thresholds, in order for the nano robots to detect protein over expression. When a nano robot is inside the workplace but doesn't reply, we assume that they didn't detect any signals, thus they follow the fluid out of the workspace. The electrochemical sensor on the nano robot produces a feeble signal of less than 50 nA when it detects NOS in small quantities or within a typical gradient. In this scenario, the nano robot disregards the NOS concentration on the grounds that it is within the range of expected intracranial NOS values. Each time the cell phone has received at least a total of 100 nano robots higher proteomic signal transduction as a practical threshold for medical diagnosis, to prevent noise distortions and produce a higher resolution, the model deems this to be strong indication of an intracranial aneurysm. When the sensors on the nano robots are turned on, they also show where they were when they noticed a high concentration of NOS protein, giving important details on the location and size of the vessel bulb.

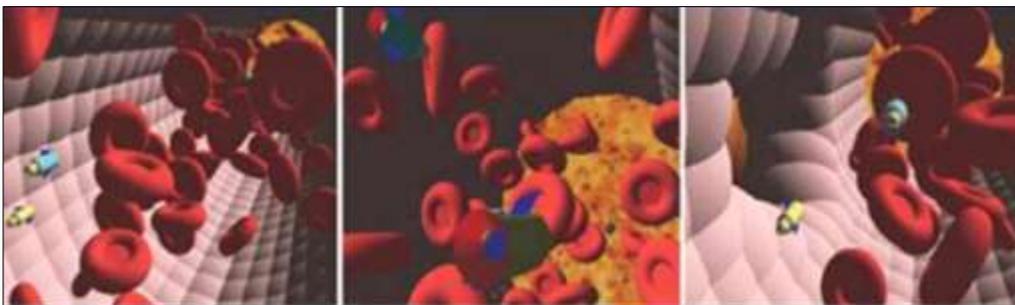


Figure 3 Working of brain aneurysm

3.1.4. Nano robots in dentistry

Nano dentistry is a new field that has emerged as a result of the increased interest in the potential dental uses of nanotechnology. Nano robots use oral analgesia, tooth desensitization, and tissue manipulation to realign and straighten an uneven set of teeth as well as to increase the durability of teeth. Furthermore, it is described how preventive, restorative, and curative treatments are carried out by nanorobots. For extensive tooth repair, nano dental techniques include numerous tissue engineering operations. To replace the entire dentition, a biologically autologous full replacement tooth that has both mineral and cellular components is made and installed primarily using nanorobotics. The endurance and aesthetics of teeth have been improved by sapphire, a nanostructured composite material, thanks to nanomedicine. By covalently bonding artificial material, such as sapphire, the upper enamel layers are replaced. This substance possesses a hardness and failure strength that are 100 to 200 times greater than those of ceramic. Similar to enamel, sapphire is a little vulnerable to acid corrosion. Sapphire has the top-tier aesthetic option to whitening sealants.

Nano composites are a new kind of restorative substance that will make teeth more durable. To create this, discrete nanoparticles are nano-agglomerated and uniformly dispersed in resins or coatings to create nanocomposites. Alumina silicate powder with a 1:4 ratio of alumina to silica and a mean particle size of roughly 80 nm is included in the nano-iller. The nano iller has a refractive index of 1.503, exceptional hardness, a superb color density, translucency, aesthetic appeal, high polish, and a 50% decrease in illing shrinkage. They outperform traditional composites and more closely resemble natural tooth structure.

4. Importance of nanorobotics in pharma manufacturing field

4.1. Nanomedicine

The use of nanotechnology in medicine is known as nanomedicine. Utilizing molecular techniques and human anatomy knowledge, it is the preservation and advancement of human health. Targeting certain tissues and organs is now possible with the help of precisely designed nanoparticles like nanorobots, dendrimers, carbon fullerenes (buckyballs), and nanoshells. These nanoparticles could be used as therapeutic, diagnostic, and antiviral, antitumor, and anticancer drugs. Drug distribution and Nubots: A variety of novel technologies made possible by nanotechnology can be used to provide specialized solutions that improve the delivery of pharmaceutical drugs. Drugs must be safeguarded while being transported to the target action site in the body while keeping their biological and chemical properties in order to be therapeutically effective. Some medications are extremely toxic, and they can have severe adverse effects and a diminished therapeutic impact if they break down while being administered. The transit duration and delivery difficulties can range significantly depending on where the medications will be absorbed (colon, small intestine, etc.), and whether or not certain natural defensive mechanisms, including the blood brain barrier, need to be passed through. Drugs must be delivered at the right rate once they reach their target in order to be effective. The medicine may not be entirely absorbed if it is released too quickly, or it may induce gastrointestinal discomfort and other negative effects. The rate of ingestion, distribution, metabolism, and excretion of the drug or other substances in the body must be favourably impacted by the drug delivery system. Nubot stands for "nucleic acid robot," in short. At the nanoscale, nubots are organic molecular machines. DNA-based biological circuit gates have been created as molecular machineries to enable in-vitro drug delivery for targeted medical issues. The nubots are capable of carrying out complex and exact duties like shutting off the blood supply to malignant tumors, imaging probes, and cargo delivery vehicles.



Figure 4 Nubots

4.2. Mouthwash manufacturing

4.2.1. Prevention of tooth decay

Smart nanomachines in mouthwash could recognize and eliminate harmful bacteria while promoting the growth of the mouth's beneficial flora in a stable environment. Additionally, the tools would recognize food, plaque, or tartar particles and lift them off teeth so they could be rinsed away. Devices would be able to reach surfaces that are out of the reach of toothbrush bristles or floss fibers because they are suspended in liquid and may swim about. Dentifrice-delivered subocclusally residing nanorobots patrol all supra-gingival and sub-gingival surfaces while metabolizing trapped organic debris and continuing calculus debridement. They guard against tooth decay and act as a permanent halitosis barrier.

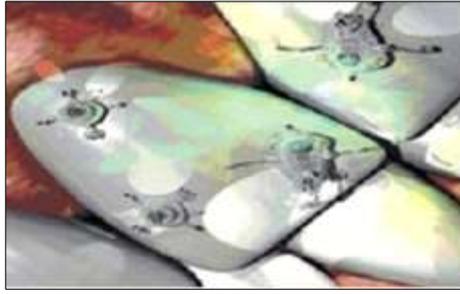


Figure 5 Nanorobotics in dental application

4.2.2. Cavity Preparation and Restoration

For cavity preparation and tooth repair, several invisible nanorobots may be used that cooperate on the patient's teeth. The most sound tooth structure is preserved by carefully limiting the cavity preparation to the demineralized enamel and dentin.



Figure 6 Cavity preparation and restoration

5. Nanorobots in medical treatment field

5.1. Artificial Blood and Respiration

Medical nanorobots can help and expand natural human respiratory capacity by acting as artificial oxygen carriers in the blood. As the patient inhales deeply, hundreds of inhaled nanorobots rush past a significant bronchial junction on their way further into the lungs.

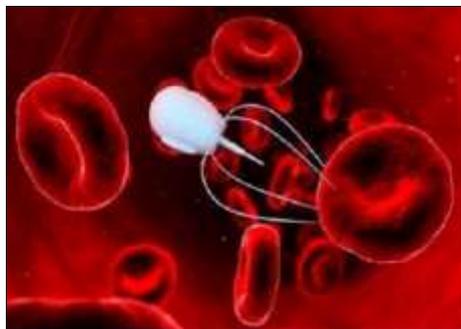


Figure 7 Artificial blood and respiration

5.2. Aging

Chromosome segments that are broken or incorrectly coded can be repaired or replaced by DNA repair machinery. Other medical nanorobots with cell healing capabilities can clean up unhealthy collected debris from human tissue cells and restore these cells to their youthful vigor.



Figure 8 Nanorobots repairing damaged cells

5.3. Treating Arteriosclerosis

Fatty buildup on artery walls is the root cause of this. It ought to be possible for the equipment to take it out of the artery walls. The problem might be treated by nanorobots by removing the plaque, which would then enter the bloodstream.



Figure 9 Nanorobots in Arteriosclerosis

5.4. Tumor

Nanorobots with integrated chemical biosensors can be used to find tumor cells inside a patient's body when they are still in the early stages of growth. The method is designed to be able to treat cancers like deep brain tumors, which are difficult to reach during traditional surgery.

5.5. Fighting cancer

Nanorobots may be used by doctors to treat cancer patients. The robots may either be used as part of a chemotherapy treatment, delivering medication straight to the cancer location, or they could attack tumors directly using lasers, microwaves, or ultrasonic sounds. Given that nanorobots may move through the blood as bloodborne devices, they can assist with such crucial parts of cancer therapy.



Figure 10 Nanorobots helping the body clot

aiding in blood clotting Nanorobots might move to a clot and dislodge it. One of the most intricate and advanced uses of Sofna No Robots is this application. The clottocyte, often known as an artificial platelet, is one particular type of nanorobot. A tiny mesh net that the clottocyte carries turns into a sticky membrane when it comes into touch with blood plasma.

6. Conclusion

The primary goal of producing this review was to present an overview of the technological advancement of nanotechnology in medicine by creating a nanorobot and utilizing it as a novel method of drug delivery in the treatment of cancer. A growing number of people are being diagnosed with cancer each year, which is a group of diseases characterized by the body's malignant cells developing and spreading out of control. Cancer treatment is most likely what inspired the development of nanorobotics; it can be successfully treated with current medical technology and therapeutic tools, with nanorobotics playing a vital role. The following considerations should be taken into account when determining a cancer patient's prognosis and chances of survival: If the progression of the disease is time-dependent and a prompt diagnosis is established, a better prognosis can be obtained. Another crucial element is developing effective targeted drug delivery methods to lessen the adverse effects of chemotherapy on patients. Doctors could administer precise treatment with the use of programmable nanorobotic devices that operate at the cellular and molecular level. In the field of medicine, these nanorobots have been proposed for use in various branches of dentistry, research, and near-instant homeostasis in addition to resolving gross cellular insults caused by irreversible mechanisms or to the biological tissues stored cryogenically, mechanically reversing the process of atherosclerosis, enhancing the immune system, replacing or re-writing the DNA sequences in cells at will, improving total respiratory capacity, and achieving near-instant homeostasis. The ideal objective of doctors, medical professionals, and every healer throughout recorded history would be accomplished once nanomechanics became feasible. Medical professionals would be able to work at the cellular and molecular levels to heal and execute rehabilitative procedures thanks to microscale robots with programmable and controllable nanoscale components made with nanometre accuracy. Since the finest treatments are those that intervene the least, nanomedical doctors of the twenty-first century will continue to make good use of the body's own healing capabilities and homeostatic systems.

Compliance with ethical standards

Acknowledgments

We would like to acknowledge and express our gratitude to the management for providing us with the necessary facilities and support. We would like to extend our heartfelt thanks to Dr. Narendra R. Dighade, principle of Nagpur college of pharmacy. Nagpur.

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

- [1] Vaughn JR. "Over the Horizon: Potential Impact of Emerging Trends in Information and Communication Technology on Disability Policy and Practice". National Council on Disability, Washington DC, 2006; 1–55.
- [2] Ghosh, A.; Fischer, P. "Controlled Propulsion of Artificial Magnetic Nanostructured Propellers". *Nano Letters*, 2009; 9.
- [3] Tarakanov, A. O.; Goncharova, L. B.; Tarakanov Y. A. "Carbon nanotubes towards medicinal biochips". *Wiley Interdisciplinary Reviews: Nanomedicine and Nanobiotechnology*, 2009; 2(1): 1–10.
- [4] Robert A, Freitas Jr. What is nanomedicine? *Nanomedicine: Nanotechnology, Biology, and Medicine*, 2005; 1: 1-8.
- [5] http://www.fractal.org/Bio-Nano_Robotics/Nanorobotics
- [6] Rosen J, Hannaford B, Satava RM. *Surgical Robotics: Systems Applications and Visions*. Springer, 2011.
- [7] Hess, Henry; Bachand, George D.; Vogel, Viola. "Powering Nanodevices with Biomolecular Motors". *Chemistry: A European Journal*, 2004; 10(9): 2110–2116.

- [8] Fisher, B. "Biological Research in the Evolution of Cancer Surgery: A Personal Perspective". *Cancer Research*, 2008; 68(24): 10007–10020.
- [9] Lavan, D. A.; McGuire, T.; Langer, R. "Small-scale systems for in vivo drug delivery". *Nature Biotechnology*, 2003; 21(10): 1184–91.
- [10] Vartholomeos, P.; Fruchard, M.; Ferreira, A.; Mavroidis, C. "MRI-Guided Nanorobotic Systems for Therapeutic and Diagnostic Applications" (PDF). *Annu Rev Biomed Eng*, 2011; 13: 157–84
- [11] Nanorobotics By ummat A , Dubey.A, Sharma.G, Mavroidis Department of Mechanical and Industrial Engineering, Northeastern University ,. Department of Mechanical and Aerospace Engineering, Rutgers University.
- [12] Wang J (2009) "Can Man-Made Nanomachines Compete with Nature Biomotors?". *ACS Nano* 3: 4–9.
- [13] Cale TS, LuJ-Q, Gutmann RJ (2008) "Three-dimensional integration in microelectronics: Motivation, processing, and thermomechanical modeling". *Chemical Engineering Communications* 195: 847–888.
- [14] Couvreur P, Vauthier C (2006) "Nanotechnology: Intelligent Design to Treat Complex Disease". *Pharmaceutical Research* 23: 1417–1450.
- [15] Cavalcanti A, Freitas Jr RA, Kretly LC (2004) "Nanorobotics Control Design: A Practical Approach Tutorial". In *Proc ASME 28th Biennial Mechanisms and Robotics Conference*, Salt Lake City, Utah, USA. ,
- [16] Cui Y, Wei Q, Park H, Lieber CM (2001) Nanowire nanosensors for highly sensitive and selective detection of biological and chemical species. *Science* 293: 1289–1292.
- [17] Robert A, Freitas Jr (2005) Current Status of Nanomedicine and Medical Nanorobotics. *J Comput Theor Nanosci* 2: 1-25.
- [18] Cavalcanti A, Shirinzadeh B, Freitas RA Jr, Hogg T (2008) Nanorobot architecture for medical target identification. *Nanotechnology* 19: 015103.
- [19] Cavalcanti A, Shirinzadeh B, Zhang M, Kretly LC (2008) Nanorobot hardware architecture for medical defense. *Sensors* 8: 2932–2958.
- [20] Chau R, Doyle B, Datta S, Kavalieros J, Zhang K (2007). Integrated nanoelectronics for the future. *Nature Materials* 6: 810–812.
- [21] Fisher B (2008) "Biological Research in the Evolution of Cancer Surgery: A Personal Perspective". *Cancer Research* 68: 10007–10020.
- [22] Hill C, Amodeo A, Joseph JV, Patel HRH (2008) "Nano_ and microrobotics: how far is the reality?". *Expert Review of Anticancer Therapy* 8: 1891–1897.
- [23] Adleman LM (1996) "On Constructing A Molecular Computer", *DNA Based Computers II: Dimacs Workshop*, Jun. 10-12, (Dimacs Series in Discrete Mathematics and
- [24] *Theoretical Computer Science*, V. 44), American Mathematical Society 1-21.
- [25] Hamdi M, Ferreira A, Sharma G, Mavroidis C (2008) Prototyping bio-nanorobots using molecular dynamics simulation and virtual reality. *Microelectronics Journal* 39:190–201.
- [26] Genov R, Stanacevic M, Naware M, Cauwenberghs G, Thakor NV (2006) 16-Channel integrated potentiostat for distributed neurochemical sensing. *IEEE Transactions on Circuits and Systems I—Regular Papers* 53: 2371–2376.
- [27] Cavalcanti (2003) Assembly Automation with Evolutionary Nanorobots and Sensor-Based Control Applied to Nanomedicine". *IEEE Transactions on Nanotechnology* 2: 82-87.
- [28] Hogg T (2007) Coordinating microscopic robots in viscous fluids. *Auton Agent Multi Agent Syst* 14: 271–305.
- [29] Cavalcanti A, Freitas Jr RA (2002) "Autonomous Multi- Robot Sensor-Based Cooperation for Nanomedicine", *Int'l J. Nonlinear Science Numerical Simulation* 3: 743-746.
- [30] Buchanan JR, Kleinstreuer C (1998) "Simulation of Particle-Hemodynamics in a Partially Occluded Artery Segment with Implications to the Initiation of Microemboli and Secondary Stenoses". *J Biomech Eng* 120: 446-454.
- [31] Casal A, Hogg T, Cavalcanti A (2003) "Nanorobots as Cellular Assistants in Inflammatory Responses", in *Proc. IEEE BCATS Biomedical Computation at Stanford 2003 Symposium*, IEEE Computer Society, Stanford CA, USA.

- [32] Elder JB, Hoh DJ, Oh BC, Heller AC, Liu CY, et al. (2008) “The future of cerebral surgery: a kaleidoscope of opportunities”. *Neurosurgery* 62: 1555–1582.
- [33] Elder JB, Liu CY, Apuzzo MLJ (2008) *Neurosurgery in the realm of 10_9, Part 2: Applications of nanotechnology to neurosurgery-present and future*. *Neurosurgery* 62: 269–285.
- [34] Freitas RA Jr (2005) What is nanomedicine? *Nanomedicine: Nanotechnology Biology and Medicine* 1: 2–9.
- [35] Fukuda S, Hashimoto N, Naritomi H, Nagata I, Nozaki K, et al. (2000) Prevention of rat cerebral aneurysm formation by inhibition of nitric oxide synthase. *Circulation* 101: 2532–2538.
- [36] Fukuda T, Kawamoto A, Arai F, Matsuura H (1995). Steering mechanism and swimming experiment of micro mobile robot in water. *Micro Electro Mechanical Systems* 300–305.
- [37] Cavalcanti A (2003) Assembly automation with evolutionary nanorobots and sensor-based control applied to nanomedicine. *IEEE Transactions on Nanotechnology* 2: 82–87.
- [38] Martel S, Mohammadi M, Felfoul O, Lu Z, Poupponeau P (2009). “Flagellated Magnetotactic Bacteria as Controlled MRITrackable Propulsion and Steering Systems for Medical Nanorobots Operating in the Human Microvasculature”. *International Journal of*
- [39] *Robotics Research* 28: 571–582. 28. Cavalcanti A (2009) “Nanorobot Invention and Linux: The Open Technology Factor - An Open Letter to UNO General Secretary”. CANNXS Project 1.
- [40] Vaughn JR (2006) “Over the Horizon: Potential Impact of Emerging Trends in Information and Communication Technology on Disability Policy and Practice”. *National Council on Disability* 1–55.
- [41] Drexler KE (1992) “Nanosystems: molecular machinery, manufacturing, and computation”. Wiley & Sons.
- [42] Fishbine G (2001) “The investor’s guide to nanotechnology & micromachines”. Wiley & Sons.
- [43] FLUENT, Fluent Inc.
- [44] Freitas Jr RA (1999) “Nanomedicine, Vol. I: Basic Capabilities”, Landes Bioscience