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Review Paper

NANOROBOTICS IN ADVANCES IN PHARMACEUTICAL SCIENCES

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ABSTRACT

Nanorobotics is the technology of creating machines or robots at or close to the scale of a nanometre (10-9 metres), machines constructed at the molecular level (nanomachines) may be used to cure the human body of its various ills. This application of nanotechnology to the field of medicine is commonly called as nanomedicine.Nanotechnology promises futuristic applications such as microscopic robots that assemble other machines or travel inside the body to deliver drugs or do microsurgery. Taking inspiration from the biological motors of living cells, chemists are learning how to utilize protein dynamics to power microsize and nanosize machines with catalytic reactions. Nanorobot's toolkit contains features like ***medicine cavity*** *containing medicine,* ***probes***, ***knives*** *and* ***chisels*** *to remove blockages and plaque,* ***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.To cure skin diseases, a cream containing nanorobots may be used which remove the right amount of dead skin, remove excess oils, add missing oils, apply the right amounts of natural moisturising compounds, and even achieve the elusive goal of 'deep pore cleaning'.other fields of applications are to clean the wounds,to break the kidney stones, to treat gout, for parasite removal, for cancer treatment, treatment of arteriosclerosis.*

Introduction: A new approach within advanced graphics simulations is presented for the problem of nano-assembly automation and its application for medicine. The problem under study concentrates its main focus on nanorobot control design for molecular manipulation and the use of evolutionary agents as a suitable way to enable the robustness on the proposed model. Thereby the presented works summarize as well distinct aspects of some techniques required to achieve successful integrated system design and 3D simulation visualization in real time[1].

Figure-1

Nanorobotics is the technology of creating machines or robots at or close to the scale of a nanometre (10-9 metres). More specifically, nanorobotics refers to the still largely theoretical nanotechnology engineering discipline of designing and building nanorobots. Nanorobots (nanobots or nanoids) are typically devices ranging in size from 0.1-10 micrometres and constructed of nanoscale or molecular components. As no artificial non-biological nanorobots have so far been created, they remain a hypothetical concept at this time. Another definition sometimes used is a robot which allows precision interactions with nanoscale objects, or can manipulate with nanoscale resolution.

Following this definition even a large apparatus such as an atomic force microscope can be considered a nanorobotic instrument when configured to perform nanomanipulation. Also, macroscale robots or microrobots which can move with nanoscale precision can also be considered nanorobots[2].

Initial uses of nanorobots to health care are likely to emerge within the next ten years with potentially broad biomedical applications. The ongoing developments of molecular-scale electronics, sensors and motors are expected to enable microscopic robots with dimensions comparable to bacteria. Recent developments on the field of biomolecular computing has demonstrated positively the feasibility of processing logic tasks by bio-computers, which is a promising first step to enable future nanoprocessors with increasingly complexity. Studies in the sense of building biosensors and nano-kinetic devices, which is required to enable nanorobots operation and locomotion, has been advanced recently too. Moreover, classical objections related to the real feasibility of nanotechnology, such as quantum mechanics, thermal motions and friction, has been considered and resolved and discussions about the manufacturing of nanodevises is growing up. Developing nanoscale robots presents difficult fabrication and control challenges. The control design and the development of complex integrated nanosystems with high performance can be well analysed and addressed via simulation to help pave the way for future use of nanorobots in biomedical engineering problems[3].

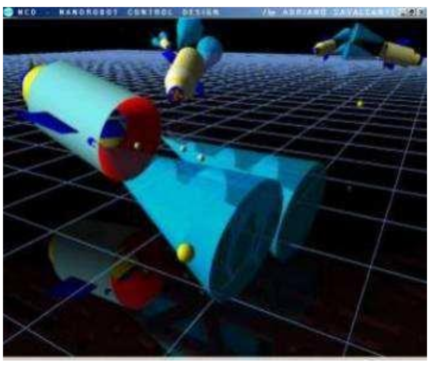


Figure-2

Nanorobotics is the technology of creating machines or robots at or close to the microscopic scale of a nanometer (10^{-9}meters). More specifically, nanorobotics refers to the still largely hypothetical nanotechnology engineering discipline of designing and building **nanorobots**, devices ranging in size from 0.1-10 micrometers and constructed of nanoscale or molecular components. As no artificial non-biological nanorobots have yet been created, they remain a hypothetical concept. The names **nanobots**, **nanoids**, **nanites** or **nanomites** have also been used to describe these hypothetical devices. Another definition is a robot that allows precision interactions with nanoscale objects, or can manipulate with nanoscale resolution. Following this definition even a large apparatus such as an atomic force microscope can be considered a nanorobotic instrument when configured to perform nanomanipulation. Also, macroscale robots or microrobots that can move with nanoscale precision can also be considered nanorobots.

Figure-3

Nanomachines are largely in the research-and-development phase, but some primitive molecular machines have been tested. An example is a sensor having a switch approximately 1.5 nanometers across, capable of counting specific molecules in a chemical sample. The first useful applications of nanomachines, if such are ever built, might be in medical technology, where they might be used to identify cancer cells and destroy them. Another potential application is the detection of toxic chemicals, and the measurement of their concentrations, in the environment. Recently, Rice University has demonstrated a single-molecule car developed by a chemical process and includes buckyballs for wheels. It is actuated by controlling the environmental temperature and by positioning a scanning tunneling microscope tip. Since nanorobots would be microscopic in size, it would probably be necessary for very large numbers of them to work together to perform microscopic and macroscopic tasks. These nanorobot swarms, both those incapable of replication (as in utility fog) and those capable of unconstrained replication in the natural environment (as in grey goo and its less common variants), are found in many science fiction stories, such as the Borg nanoprobes in *Star Trek*. The word "nanobot" (also "nanite", "nanogene", or "nanoant") is often used to indicate this fictional context and is an informal or even pejorative term to refer to the engineering concept of nanorobots. The word nanorobot is the correct technical term in the nonfictional context of serious engineering studies. Some proponents of nanorobotics, in reaction to the grey goo scare scenarios that they earlier helped to propagate, hold the view that nanorobots capable of replication outside of a restricted factory environment do not form a necessary part of a purported productive nanotechnology, and that the process of self-replication, if it were ever to be developed, could be made inherently safe. They further assert that free-foraging replicators are in fact absent from their current plans for developing and using molecular manufacturing. Nanotechnology promises futuristic applications such as microscopic robots that assemble other machines or travel inside the body to deliver drugs or do microsurgery. These machines will face some unique physics. At small scales, fluids appear as viscous as molasses, and Brownian motion makes everything incessantly shake. Taking inspiration from the biological motors of living cells, chemists are learning how to utilize protein dynamics to power microsize and nanosize machines with catalytic reactions[4].

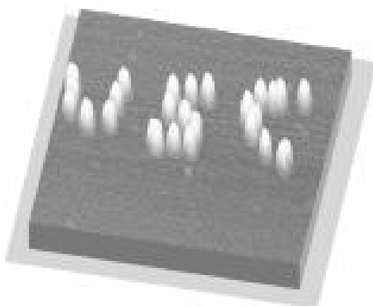
NANOROBOTS: MEDICINE OF THE FUTURE

The above statement raises the interesting possibility that machines constructed at the molecular level (nanomachines) may be used to cure the human body of its various ills. This application of nanotechnology to the field of medicine is commonly called as nanomedicine.

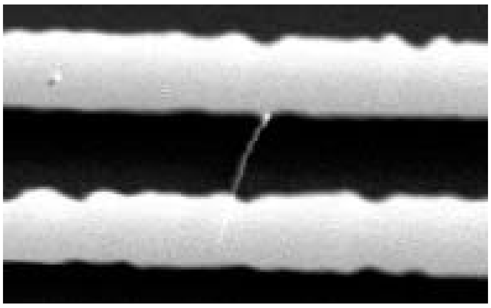
NANOROBOTS: WHAT ARE THEY?

Nanorobots are nanodevices that will be used for the purpose of maintaining and protecting the human body against pathogens. They will have a diameter of about 0.5 to 3 microns and will be constructed out of parts with dimensions in the range of 1 to 100 nanometers. The main element used will be carbon in the form of *diamond / fullerene nanocomposites* because of the strength and chemical inertness of these forms. Many other light elements such as oxygen and nitrogen can be used for special purposes. To avoid being attacked by the host's immune system, the best choice for the exterior coating is a passive diamond coating. The smoother and more flawless the coating, the less the reaction from the body's immune system. Such devices have been designed in recent years but no working model has been built so far. The powering of the nanorobots can be done by metabolising local glucose and oxygen for energy. In a clinical environment, another option would be externally supplied acoustic energy. Other sources of energy within the body can also be used to supply the necessary energy for the devices. They will have simple onboard computers capable of performing around 1000 or fewer computations per second. This is because their computing needs are simple. Communication with the device can be achieved by *broadcast-type acoustic signalling.*

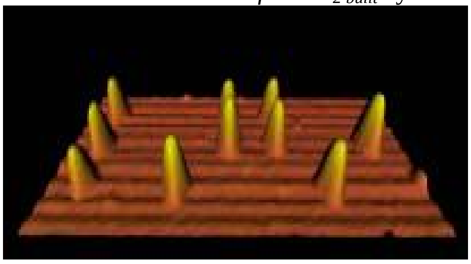
Nanorobotics Examples



Pattern of 15 nm Au particles built by AFM manipulation



In2O3 nanowire sensor for NO_2 built by CVD



NanoCD: LMR in ASCII encoded in the positions of nanomanipulated 15nm Au particles

Figure-4

A navigational network may be installed in the body, with stationkeeping navigational elements providing high positional accuracy to all passing nanorobots that interrogate them, wanting to know their location. This will enable the physician to keep track of the various devices in the body. These nanorobots will be able to distinguish between different cell types by checking their surface antigens (they are different for each type of cell). This is accomplished by the use of chemotactic sensors keyed to the specific antigens on the target cells[5].

When the task of the nanorobots is completed, they can be retrieved by allowing them to exfuse themselves via the usual human excretory channels. They can also be removed by active scavenger systems. This feature is design-dependent.

FIELDS OF APPLICATION:

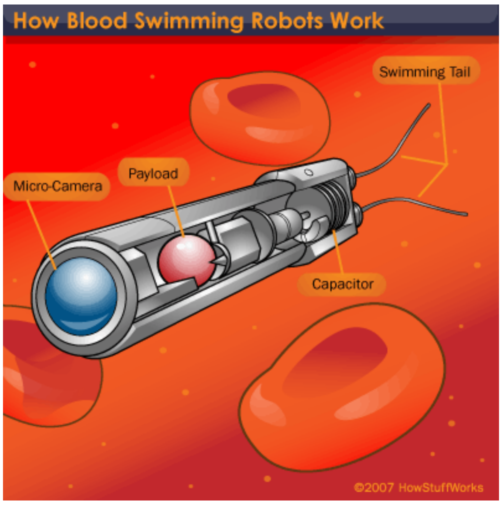
Some possible applications using nanorobots are as follows:

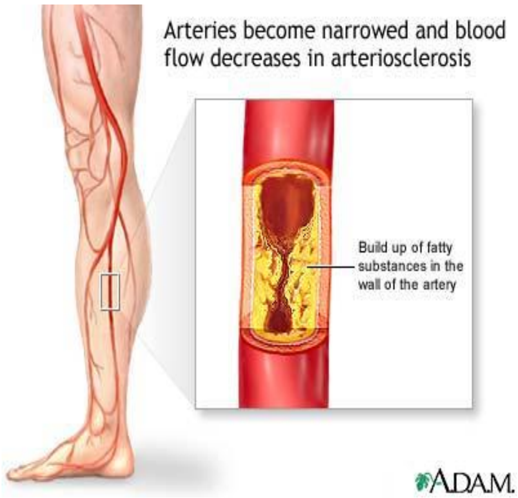
1. To cure skin diseases, a cream containing nanorobots may be used. It could remove the right amount of dead skin, remove excess oils, add missing oils, apply the right amounts of natural moisturising compounds, and even achieve the elusive goal of *'deep pore cleaning'* by actually reaching down into pores and cleaning them out. The cream could be a smart material with smooth-on, peel-off convenience.
2. A mouthwash full of smart nanomachines could identify and destroy pathogenic bacteria while allowing the harmless flora of the mouth to flourish in a healthy ecosystem. Further, the devices would identify particles of food, plaque, or tartar, and lift them from teeth to be rinsed away. Being suspended in liquid and able to swim about, devices would be able to reach surfaces beyond reach of toothbrush bristles or the fibres of floss. As short-lifetime medical nanodevices, they could be built to last only a few minutes in the body before falling apart into materials of the sort found in foods (such as fibre).
3. Medical nanodevices could augment the immune system by finding and disabling unwanted bacteria and viruses. When an invader is identified, it can be punctured, letting its contents spill out and ending its effectiveness. If the contents were known to be hazardous by themselves, then the immune machine could hold on to it long enough to dismantle it more completely.
4. Devices working in the bloodstream could nibble away at arteriosclerotic deposits, widening the affected blood vessels. Cell herding devices could restore artery walls and artery linings to health, by ensuring that the right cells and supporting structures are in the right places. This would prevent most heart attacks.

Introduction to How Nanorobots Will Work

Imagine going to the doctor to get treatment for a persistent fever. Instead of giving you a pill or a shot, the doctor refers you to a special medical team which implants a tiny robot into your bloodstream. The robot detects the cause of your fever, travels to the appropriate system and provides a dose of medication directly to the infected area.

Surprisingly, we're not that far off from seeing devices like this actually used in medical procedures. They're called nanorobots and engineering teams around the world are working to design robots that will eventually be used to treat everything from hemophilia to cancer. As you can imagine, the challenges facing engineers are daunting. A viable nanorobot has to be small and agile enough to navigate through the human circulatory system, an incredibly complex network of veins and arteries. The robot must also have the capacity to carry medication or miniature tools. Assuming the nanorobot isn't meant to stay in the patient forever, it also has to be able to make its way out of the host. In this article, we'll learn about the potential applications of nanorobots, the various ways nanorobots will navigate and move through our bodies, the tools they will use to heal patients, the progress teams around the world have made so far and what theorists see in the future. Properly realized, nanorobots will be able to treat a host of diseases and conditions. While their size means they can only carry very small payloads of medicine or equipment, many doctors and engineers believe the precise application of these tools will be more effective than more traditional methods. For example, a doctor might deliver a powerful antibiotic to a patient through a syringe to help his immune system. The antibiotic becomes diluted while it travels through the patient's bloodstream, causing only some of it makes it to the point of infection. However, a nanorobot or team of nanorobots could travel to the point of infection directly and deliver a small dose of medication. The patient would potentially suffer fewer side effects from the medication. Several engineers, scientists and doctors believe that nanorobot applications are practically unlimited[6]. Some of the most likely uses include:





Nanorobots may treat conditions like arteriosclerosis by physically chipping away the plaque along artery walls

Figure-5

Treating arteriosclerosis: Arteriosclerosis refers to a condition where plaque builds along the walls of arteries. Nanorobots could conceivably treat the condition by cutting away the plaque, which would then enter the bloodstream

- **Breaking up blood clots**: Blood clots can cause complications ranging from muscle death to a stroke. Nanorobots could travel to a clot and break it up. This application is one of the most dangerous uses for nanorobots the robot must be able to remove the blockage without losing small pieces in the bloodstream, which could then travel elsewhere in the body and cause more problems. The robot must also be small enough so that it doesn't block the flow of blood itself.

- **Fighting cancer**: Doctors hope to use nanorobots to treat cancer patients. The robots could either attack tumors directly using lasers, microwaves or ultrasonic signals or they could be part of a chemotherapy treatment, delivering medication directly to the cancer site. Doctors believe that by delivering small but precise doses of medication to the patient, side effects will be minimized without a loss in the medication's effectiveness.

- **Helping the body clot**: One particular kind of nanorobot is the **clottocyte**, or artificial platelet. The clottocyte carries a small mesh net that dissolves into a sticky membrane upon contact with blood plasma. According to Robert A. Freitas, Jr., the man who designed the clottocyte, clotting could be up to 1,000 times faster than the body's natural clotting mechanism [source: Freitas]. Doctors could use clottocytes to treat hemophiliacs or patients with serious open wounds.
- **Parasite Removal**: Nanorobots could wage micro-war on bacteria and small parasitic organisms inside a patient. It might take several nanorobots working together to destroy all the parasites.
- **Gout**: Gout is a condition where the kidneys lose the ability to remove waste from the breakdown of fats from the bloodstream. This waste sometimes crystallizes at points near joints like the knees and ankles. People who suffer from gout experience intense pain at these joints. A nanorobot could break up the crystalline structures at the joints, providing relief from the symptoms, though it wouldn't be able to reverse the condition permanently.

Breaking up kidney stones: Kidney stones can be intensely painful the larger the stone the more difficult it is to pass. Doctors break up large kidney stones using ultrasonic frequencies, but it's not always effective. A nanorobot could break up kidney stones using a small laser.

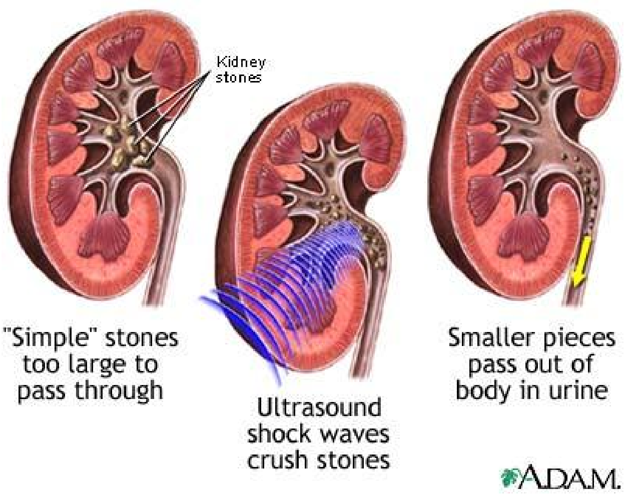


Figure-6

Cleaning wounds: Nanorobots could help remove debris from wounds, decreasing the likelihood of infection. They would be particularly useful in cases of puncture wounds, where it might be difficult to treat using more conventional methods. There are three main considerations scientists need to focus on when looking at nanorobots moving through the body **navigation**, **power** and how the nanorobot will move through blood vessels. Nanotechnologists are looking at different options for each of these considerations, each of which has positive and negative aspects. Most options can be divided into one of two categories: external systems and onboard systems.

External navigation systems might use a variety of different methods to pilot the nanorobot to the right location. One of these methods is to use **ultrasonic signals** to detect the nanorobot's location and direct it to the right destination. Doctors would beam ultrasonic signals into the patient's body. The signals would either pass through the body, reflect back to the source of the signals, or both. The nanorobot could emit pulses of ultrasonic signals, which doctors could detect using special equipment with ultrasonic sensors. Doctors could keep track of the nanorobot's location and maneuver it to the right part of the patient's body. Using a Magnetic Resonance Imaging (MRI) device, doctors could locate and track a nanorobot by detecting its magnetic field. Doctors and engineers at the Ecole Polytechnique de Montreal demonstrated how they could detect, track, control and even propel a nanorobot using MRI. They tested their findings by maneuvering a small magnetic particle through a pig's arteries using specialized software on an MRI machine. Because many hospitals have MRI machines, this might become the industry standard -- hospitals won't have to invest in expensive, unproven technologies.

Some scientists plan to control and power nanorobots using MRI devices like this one

Figure-7

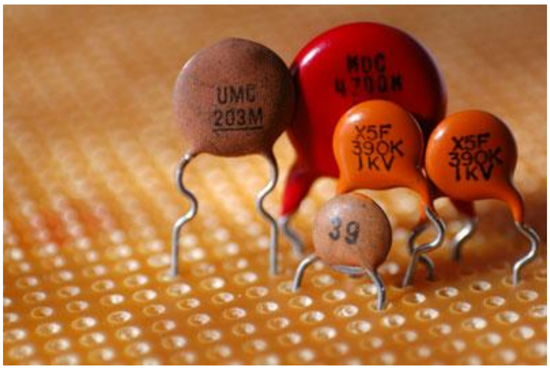
Doctors might also track nanorobots by injecting a radioactive dye into the patient's bloodstream. They would then use a fluoroscope or similar device to detect the radioactive dye as it moves through the circulatory system. Complex three-dimensional images would indicate where the nanorobot is located. Alternatively, the nanorobot could emit the radioactive dye, creating a pathway behind it as it moves through the body[7].

Other methods of detecting the nanorobot include using X-rays, radio waves, microwaves or heat. Right now, our technology using these methods on nano-sized objects is limited, so it's much more likely that future systems will rely more on other methods.

Onboard systems, or internal sensors, might also play a large role in navigation. A nanorobot with chemical sensors could detect and follow the trail of specific chemicals to reach the right location. A spectroscopic sensor would allow the nanorobot to take samples of surrounding tissue, analyze them and follow a path of the right combination of chemicals. Hard as it may be to imagine, nanorobots might include a miniature television camera. An operator at a console will be able to steer the device while watching a live video feed, navigating it through the body manually. Camera systems are fairly complex, so it might be a few years before nanotechnologists can create a reliable system that can fit inside a tiny robot. In the next section, we'll look at nanorobot power systems.

Powering the Nanorobot:

Just like the navigation systems, nanotechnologists are considering both external and internal power sources. Some designs rely on the nanorobot using the patient's own body as a way of generating power. Other designs include a small power source on board the robot itself. Finally, some designs use forces outside the patient's body to power the robot. Nanorobots could get power directly from the bloodstream. A nanorobot with mounted electrodes could form a battery using the electrolytes found in blood.



Engineers are working on building smaller capacitors that will power technology like nanorobots.

Figure-8

Another option is to create chemical reactions with blood to burn it for energy. The nanorobot would hold a small supply of chemicals that would become a fuel source when combined with blood. A nanorobot could use the patient's body heat to create power, but there would need to be a gradient of temperatures to manage it. Power generation would be a result of the **Seebeck effect**. The Seebeck effect occurs when two conductors made of different metals are joined at two points that are kept at two different temperatures. The metal conductors become a thermocouple, meaning that they generate voltage when the junctures are at different temperatures. Since it's difficult to rely on temperature gradients within the body, it's unlikely we'll see many nanorobots use body heat for power[8].

While it might be possible to create batteries small enough to fit inside a nanorobot, they aren't generally seen as a viable power source. The problem is that batteries supply a relatively small amount of power related to their size and weight, so a very small battery would only provide a fraction of the power a nanorobot would need. A more likely candidate is a capacitor, which has a slightly better power-to-weight ratio.

Another possibility for nanorobot power is to use a nuclear power source. The thought of a tiny robot powered by nuclear energy gives some people the willies, but keep in mind the amount of material is small and, according to some experts, easy to shield [source: Rubinstein]. Still, public opinions regarding nuclear power make this possibility unlikely at best. External power sources include systems where the nanorobot is either tethered to the outside world or is controlled without a physical tether. Tethered systems would need a wire between the nanorobot and the power source. The wire would need to be strong, but it would also need to move effortlessly through the human body without causing damage. A physical tether could supply power either by electricity or optically. Optical systems use light through fiber optics, which would then need to be converted into electricity on board the robot. External systems that don't use tethers could rely on microwaves, ultrasonic signals or magnetic fields. Microwaves are the least likely, since beaming them into a patient would result in damaged tissue, since the patient's body would absorb most of the microwaves and heat up as a result. A nanorobot with a piezoelectric membrane could pick up ultrasonic signals and convert them into electricity. Systems using magnetic fields, like the one doctors are experimenting with in Montreal, can either manipulate the nanorobot directly or induce an electrical current in a closed conducting loop in the robot. In the next section, we'll look at nanorobot propulsion systems[9].

Nanorobot Locomotion:

Assuming the nanorobot isn't tethered or designed to float passively through the bloodstream, it will need a means of propulsion to get around the body. Because it may have to travel against the flow of blood, the propulsion system has to be relatively strong for its size. Another important consideration is the safety of the patient -- the system must be able to move the nanorobot around without causing damage to the host. Some scientists are looking at the world of microscopic organisms for inspiration. Paramecium move through their environment using tiny tail-like limbs called **cilia**. By vibrating the cilia, the paramecium can swim in any direction. Similar to cilia are **flagella**, which are longer tail structures. Organisms whip flagella around in different ways to move around.

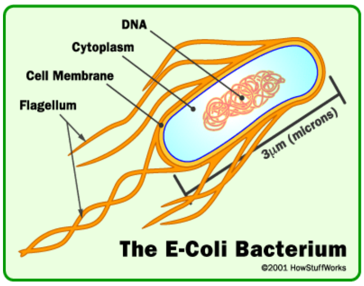
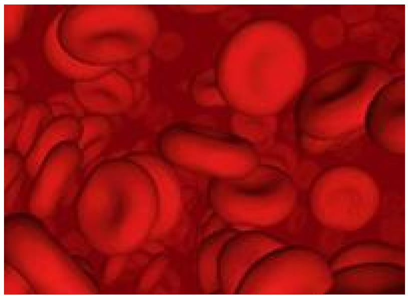


Figure-9



Nanorobot tools will have to be small enough to manipulate cells like RBC

Figure-10

Scientists in Israel created **microrobot**, a robot only a few millimeters in length, which uses small appendages to grip and crawl through blood vessels. The scientists manipulate the arms by creating magnetic fields outside the patient's body. The magnetic fields cause the robot's arms to vibrate, pushing it further through the blood vessels. The scientists point out that because all of the energy for the nanorobot comes from an external source, there's no need for an internal power source. They hope the relatively simple design will make it easy to build even smaller robots.

Other devices sound even more exotic. One would use capacitors to generate magnetic fields that would pull conductive fluids through one end of an **electromagnetic pump** and shoot it out the back end. The nanorobot would move around like a jet airplane. Miniaturized **jet pumps** could even use blood plasma to push the nanorobot forward, though, unlike the electromagnetic pump, there would need to be moving parts.

Another potential way nanorobots could move around is by using a vibrating membrane. By alternately tightening and relaxing tension on a membrane, a nanorobot could generate small amounts of thrust. On the nanoscale, this thrust could be significant enough to act as a viable source of motion. In the next section, we'll look at the tools nanorobots might carry to fulfill their medical missions:

Teeny, Tiny Tools

Current microrobots are only a few millimeters long and about a millimeter in diameter. Compared to the nanoscale, that's enormous, a nanometer is only one-billionth of a meter, while a millimeter is one-thousandth of a meter. Future nanorobots will be so small, you'll only be able to see them with the help of a microscope. Nanorobot tools will need to be even smaller. Here are a few of the items you might find in a nanorobot's toolkit:

- **Medicine cavity** a hollow section inside the nanorobot might hold small doses of medicine or chemicals. The robot could release medication directly to the site of injury or infection. Nanorobots could also carry the chemicals used in chemotherapy to treat cancer directly at the site. Although the amount of medication is relatively miniscule, applying it directly to the cancerous tissue may be more effective than traditional chemotherapy, which relies on the body's circulatory system to carry the chemicals throughout the patient's body.
- **Probes**, **knives** and **chisels** to remove blockages and plaque, a nanorobot will need something to grab and break down material. They might also need a device to crush clots into very small pieces. If a partial clot breaks free and enters the bloodstream, it may cause more problems further down the circulatory system.
- **Microwave emitters** and **ultrasonic signal generators** to destroy cancerous cells, doctors need methods that will kill a cell without rupturing it. A ruptured cancer cell might release chemicals that could cause the cancer to spread further. By using fine-tuned microwaves or ultrasonic signals, a nanorobot could break the chemical bonds in the cancerous cell, killing it without breaking the cell wall. Alternatively, the robot could emit microwaves or ultrasonic signals in order to heat the cancerous cell enough to destroy it.
- **Electrodes** two electrodes protruding from the nanorobot could kill cancer cells by generating an electric current, heating the cell up until it dies.
- **Lasers** tiny, powerful lasers could burn away harmful material like arterial plaque, cancerous cells or blood clots. The lasers would literally vaporize the tissue.

The two biggest challenges and concerns scientists have regarding these small tools are making them effective and making them safe. For instance, creating a small laser powerful enough to vaporize cancerous cells is a big challenge, but designing it so that the nanorobot doesn't harm surrounding healthy tissue makes the task even more difficult. While many scientific teams have developed nanorobots small enough to enter the bloodstream, that's only the first step to making nanorobots a real medical application. Teams around the world are working on creating the first practical medical nanorobot. Robots ranging from a millimeter in diameter to a relatively hefty two centimeters long already exist, though they are all still in the testing phase of development and haven't been used on people. We're probably several years away from seeing nanorobots enter the medical market. Today's microrobots are just prototypes that lack the ability to perform medical tasks[10].

This 2-cm-long robot is an impressive achievement, future robots will be hundreds of times of smaller (Yoshikazu Tsuno/AFP/Getty Image)

Figure-11

Future footsteps of nanorobotics: In the future, nanorobots could revolutionize medicine. Doctors could treat everything from heart disease to cancer using tiny robots the size of bacteria, a scale much smaller than today's robots[11]. Robots might work alone or in teams to eradicate disease and treat other conditions. Some believe that semiautonomous nanorobots are right around the corner doctors would implant robots able to patrol a human's body, reacting to any problems that pop up. Unlike acute treatment, these robots would stay in the patient's body forever[12]. Another potential future application of nanorobot technology is to re-engineer our bodies to become resistant to disease, increase our strength or even improve our intelligence. Dr. Richard Thompson, a former professor of ethics, has written about the ethical implications of nanotechnology. He says the most important tool is communication, and that it's pivotal for communities, medical organizations and the government to talk about nanotechnology now, while the industry is still in its infancy[13]. Will we one day have thousands of microscopic robots rushing around in our veins, making corrections and healing our cuts, bruises and illnesses? With nanotechnology, it seems like anything is possible.

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12) *www.iopscience.iop.org www.nano-biology.net*

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