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The Promising Future in Medicine: Nanorobots

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Abstract Nanorobotics is an emerging field of nanotechnology which deals with design and construction of devices at an atomic, molecular or cellular level. These hypothetical nanorobots will be extremely small and would transverse inside the human blood. As these nanorobots would have special sensors to detect the target molecules, it can be programmed to diagnosis and treat various vital diseases. The nanorobots such as respirocytes, microbivores and clottocytes are been designed to act as artificial substitutes of blood. The respirocytes are intend designed to mimic all the important functions of red blood cells and also used in treatment of anaemia, heart attack, lung diseases etc where as the clottocyte mimics the natural process of hemostasis and microbivore follows the process of phagocytosis to destroy the blood borne pathogens. This paper will look at how the recent advancements in nanorobotics that have led to the designing and development of these nanorobots which will act as the most efficient blood substitutes.

Keywords: *nanorobots, respirocytes, clottocytes, microbivores, blood substitutes*

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1. Introduction

The essence of nanotechnology is the ability to work at the molecular level, atom by atom, to create large structures with fundamentally new molecular organization [1]. The aim is to exploit these properties by gaining control of structures and devices at atomic, molecular, and supramolecular levels and to learn to efficiently manufacture and use these devices. Nanorobotics that is a part of nanotechnology deals with the study of designing, programming, manufacturing and controlling of robots at nano scale [2]. It refers to hypothetical nanotechnology engineering discipline of designing and constructing nanorobots of size ranging from 0.1-10 µm. A nanorobot is an extremely small robot designed to perform a specific task with precision at nano-scale. They are also known as nanorobots or nanoids. The design of nanorobot is derived from biological models of bacteria. Carbon will likely be the principle element used in construction of nanorobot and comprised probably in the form of diamond/ diamondoid (includes pure diamond and crystalline allotrope of carbon) or fullerence nanocomposites. A nanorobot can be made of mechanical parts such as bearing, gears, motors etc. The outer shell of nanorobot is likely to be constructed using diamondoid material due to their inert properties, high thermal conductivity and strength. The super-smooth surfaces could reduce the chances of triggering the body's immune system. The nanoscale gears and other components designed for special purposes could be constructed using elements like hydrogen, sulfur, oxygen, nitrogen, silicon etc [3].

In 1986, K. Eric Drexler introduced the idea of injecting the small robots into the human body [4]. This idea was designed and simulated as medical nanorobots that could transverse in human body by Robert A. Freitas. Respirocytes (artificial mechanical red blood cell) [5], Microbivores (artificial mechanical white blood cell) [6] and Clottocytes (artificial platelets) [7] were designed by Robert A. Freitas. The respirocyte is designed as an artificial mechanical red blood cell for the exchange of the oxygen and carbon dioxide, the microbivore is designed as an artificial mechanical white blood cell for identifying and digesting pathogens and the clottocyte is designed as an artificial platelet for assisting in primary hemostasis by release of the mesh from clottocyte to the site of injury [8].

"Nanorobots" will be the nanomachines, that will repair the damage which 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. The substructures involved in construction of nanorobot involve onboard power supply, sensors, nanocomputer, pumps, manipulators and pressure tanks [9]. Some of the desirable characteristics to be found in a nanorobot includes - swarm intelligence, Self-assembly & replication, Nano-information processing & programmability and Nano to macro world interface architecture [2]. The application of nanorobots in medicine offers a new range of tools for the treatment of disease and also in improvising human biological system.

Medical nanorobotics [10,11] offers the prospect of powerful new tools for the treatment of various human diseases and the improvement of human biological system. The design of various nanorobots in medicine includes respirocyte, microbivore, clottocyte, Pharmacytes (for nanorobotic drug delivery), dentifrobots (dental nanorobots) and vasculoids (as an artificial nanomechanical vascular system) [12].

The ideal nanorobots will have characteristics to connect to each other, forming a structure with decentralization. They will produce multiple copies of themselves to replace worn out units by a process called self-replication. The doctor administering nanorobot can communicate with it by encoding the messages to acoustic signals at a wave frequency ranging from 1-100 MHz. After the completion of the task, these nanorobots can be retrieved through the usual human excretory channels or can also be removed by active scavenger systems [13,14].

2. Components of Nanorobots

The various components in nanorobot include power supply, fuel buffer tank, sensors, motors, manipulators, onboard computers, pumps, pressure tanks and structural support. The substructures in a nanorobot include:

1. Payload- This void section holds a small dose of drug/medicine. The nanorobots could transverse in the blood and release the drug to the site of infection/injury.
2. Micro camera- The nanorobot may include a miniature camera. The operator can steer the nanorobot when navigating through the body manually [13,15].
3. Electrodes- The electrode mounted on the nanorobot could form the battery using the electrolytes in the blood. These protruding electrodes could also kill the cancer cells by generating an electric current, and heating the cells up to death.
4. Lasers- These lasers could burn the harmful material like arterial plaque, blood clots or cancer cells [15].
5. Ultra sonic signal generators- These generators are used when the nanorobots are used to target and destroy kidney stones.
6. Swimming tail- The nanorobot will require a means of propulsion to get into the body as they travel against the flow of blood in the body.

The nanorobot will have motors for movement and manipulator arms or mechanical leg for mobility. The two main approaches followed in construction of nanorobots are Positional assembly and Self assembly. In self assembly, the arm of a miniature robot or a microscopic set is used to pick the molecules and assemble manually. In positional assembly, the investigators will put billions of molecules together and let them automatically assemble based on their natural affinities into the desired configuration [13,16,17]. Nanorobot Control Design is the software developed for simulating nanorobots in environment with fluids which is dominated by Brownian motion [18]. The nanorobots have chemical sensors which can detect the target molecules.

The nanorobots are provided with swarm intelligence for decentralization activity. Swarm intelligence techniques are the algorithms designed for artificial intelligence of the nanorobot. The swarm intelligence technique is been inspired by the behaviour of social animals such as ants, bees and termites which work collaboratively without a centralized control. The three main types of swarm intelligence techniques deigned are ant colony optimization (ACO), artificial bee colony (ABC) and particle swarm optimization (PSO) [8].

3. Types of Nanorobots

The types of nanorobots designed by *Robert A. Freitas Jr* as artificial blood are:

i. Respirocytes.
ii. Microbivores.
iii. Clottocytes.

3.1. Respirocytes

Respirocytes are the nanorobots designed as artificial mechanical red blood cells which are blood borne spherical 1 µm diameter sized (Figure 1). The outer shell is made of diamondoid 1000 atm pressure vessel with reversible molecule-selective pumps [19,20]. Respirocytes carry oxygen and carbon dioxide molecules throughout the body.

The respirocyte is constructed of 18 billion atoms which are precisely arranged in a diamondoid pressure tanks that can store up to 3 billion oxygen and carbon dioxide molecules [19]. The respirocyte would deliver 236 times more oxygen to the body tissues when compared to natural red blood cells.

The respirocyte could manage the carbonic acidity which will be controlled by gas concentration sensors and an onboard nanocomputer [20].

The stored gases are released from the tank in a controlled manner through molecular pumps. The respirocytes exchange gases via molecular rotors. The rotors have special tips for particular type of molecule [21].

Figure 1. An artificial red cell—the respirocyte designed by Robert A.Freitas Jr

Each respirocyte consists of 3 types of rotors. One rotor releases the stored oxygen while travelling through the body. The second type of rotor captures all the carbon dioxide in the blood stream and release at the lungs while the third rotor takes in the glucose from blood stream as fuel source [5,21]. There are 12 identical pumps which are laid around the equator; oxygen rotors on the left, water rotors in the middle and carbon dioxide rotors in the left. There are gas concentration sensors on the surface of respirocyte.

When the respirocyte passes through the lung capillaries, O_2 partial pressure will be high and CO_2 partial pressure will be low, therefore the onboard nanocomputer commands the sorting rotors to load in oxygen and release the carbon dioxide molecules [15]. The water ballast chambers aid in maintaining buoyancy. The respirocytes can be programmed to scavenge carbon monoxide and other poisonous gases from the body.

The respirocyte works as an artificial erythrocyte by mimicking the oxygen and carbon dioxide transport functions (Figure 2). A 5 cc therapeutic dose of 50% respirocyte saline suspension containing 5 trillion nanorobots would exactly replace the gas carrying capacity of the patient's entire 5.4 litres of blood.

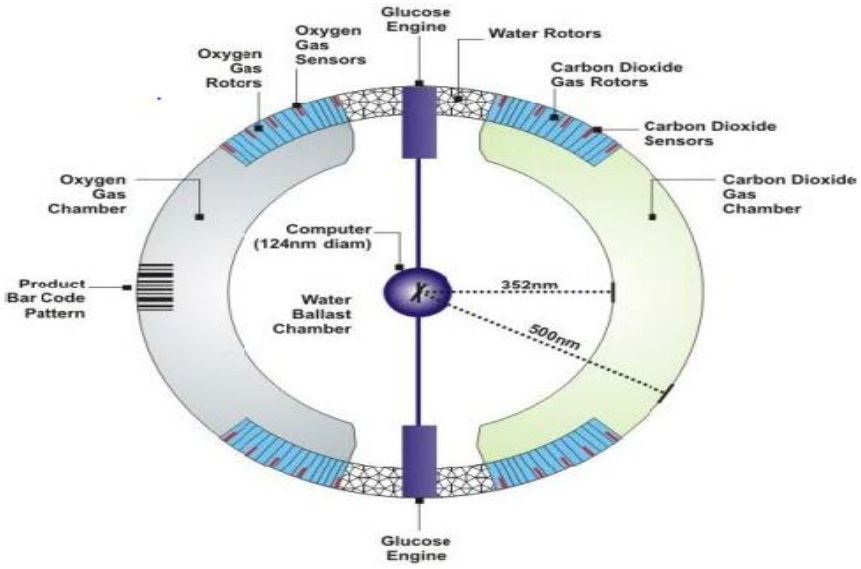

Figure 2. Internal cutaway view of respirocyte—equatorial view

Once the therapeutic purpose is served, the respirocyte may be extracted from circulation, requiring respirocyte activating protocol. During this protocol called nanapheresis, the blood to be cleared would be passed from the patient to a specialized centrifugation apparatus where the ultrasonic transmitters command the respirocyte to maintain neutral buoyancy. There are no other solid blood components that can maintain neutral buoyancy; hence those components are precipitate outwards during centrifugation. The blood components are added back to filtered plasma. The filtered plasma is recombined with centrifuged solid blood components and then returned undamaged to the patient's body [6].

3.2. Microbivores

Microbivores are the nanorobot which functions as artificial white blood cell and also known as nanorobotic phagocytes. The microbivore is a spheroid device made up of diamond and sapphire which measures 3.4 μm in diameter along its major axis and 2.0 μm diameter along minor axis and consists of 610 billion precisely arranged structural atoms. It traps in the pathogens present in the blood stream and break down to smaller molecules. The main function of microbivore is to absorb and digest the pathogens in the blood stream by the process of phagocytosis. The microbivore consist of 4 fundamental components:

i. An array of reversible binding sites.
ii. An array of telescoping grapples.
iii. A morcellation chamber.
iv. Digestion chamber [22].

During the cycle of operation, the target bacterium binds to the microbivore surface via species-specific reversible binding site. A collision between the bacterium and the microbivore brings in the surface into intimate contact, allowing the reversible binding site to recognize and weakly bind to the bacterium. A set of 9 different antigenic markers should be specific and confirm the positive binding event confirming the presence target microbe. There would be 20,000 copies of the 9 marker sets distributed in 275 disk shaped regions across microbivore. When the bacterium is bound to the binding site, the telescopic robotic grapples rise up from the surface and attach to the trapped bacterium thereby establishing a secure anchorage. The grapple's handoff motion can transport the bacterium from binding site to the ingestion port. Further the bacterium is internalized into the morcellation chamber where in the bacterium is minced into nanoscale pieces (Figure 3). The remains are pistoned into the digestion chamber which consists of a pre-programmed set of digestive enzymes.

These enzymes are injected and extracted 6 times during a single digestion cycle, where in the morcellate is progressively reduced into amino acids, mononucleotides, free fatty acid and simple sugars. These small molecules are then discharged into the blood stream through the exhaust port. After the destruction of pathogens the microbivores exits the body through the kidneys and are then excreted in urine.

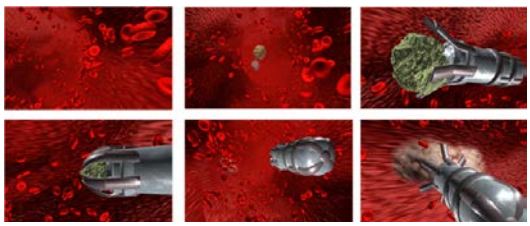

Figure 3. Mechanism of phagocytosis by microbivore

An entire cycle of phagocytosis by microbivore will be completed in 30 seconds. There are no chances of septic shock or sepsis as the bacterial components are internalized and digested into non-antigenic biomolecules [22]. The microbivore is 1000 times faster acting than antibiotic aided white blood cells and the pathogen stand no chance of multiple drug resistance. They can also be used to clear respiratory, cerebrospinal bacterial infection or infections in urinary fluids and synovial fluids.

3.3. Clottocytes

Hemostasis is the process of blood clotting when there is damage to the endothelium cells of blood vessels by platelets. These platelets can be activated by collision of exposed collagen from damaged blood vessels to the

platelets. The whole process of natural blood clotting can take 2-5 minutes. The nanotechnology has shown the capabilities of reducing the clotting time and reducing the blood loss. In certain patients, the blood clots are found to occur irregularly. This abnormality is treated using drugs such corticosteroids. The treatment with corticosteroids is associated with side effects such as hormonal secretions; blood/platelet could damage lungs and allergic reactions [8].

The theoretically designed clottocyte describes artificial mechanical platelet or clottocyte that would complete hemostasis in approximately 1 sec [6]. It is spherical nanorobot powered by serum-oxyglucose approximately 2 µm in diameter containing a fiber mesh that is compactly folded onboard. The response time of clottocyte is 100-1000 times faster than the natural hemostatic system [22]. The fiber mesh would be biodegradable and upon release, a soluble film coating of the mesh would dissolve in contact with the plasma to expose sticky mesh [6].

Reliable communication protocols would be required to control the coordinated mesh release from neighboring clottocytes and also to regulate multidevice-activation radius within the local clottocyte population. As clottocyte-rich blood enters the injured blood vessel, the onboard sensors of clottocyte rapidly detects the change in partial pressure, often indicating that it is bled out of body. If the first clottocyte is 75 µm away from air-serum interface, oxygen molecules from the air diffuse through serum at human body temperature. This detection would be broadcasted rapidly to the neighbouring clottocytes through acoustic pulses. This allows rapid propagation of a carefully controlled device-enablement cascade. The stickiness in the fiber mesh would be blood group specific to trap blood cells by binding to the antigens present on blood cells (Figure 4). Each mesh would overlap on the neighboring mesh and attract the red blood cells to immediately stop bleeding [22].

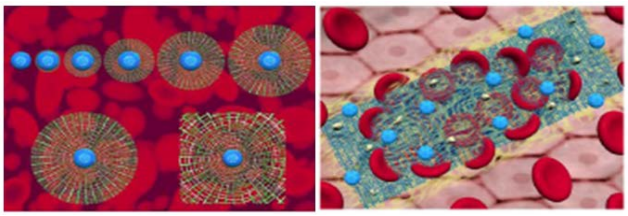

Figure 4. Blood clotting mechanism of clottocytes

The clotting function by clottocyte is essentially equivalent to that of natural platelets at about 1/10,000th the concentration in the blood stream i.e. 20 clottocytes per cubic milimeter of blood [23]. The major risk associated with the clottocytes is that the additional activity of the mechanical platelets could trigger the disseminated intravascular coagulation resulting in multiple micro thrombi [22].

4. Onboard Computers of Nanorobots

Functions that are controlled by the onboard computer include:

1. Pumping- Molecular pumps would be a primary system in nanorobots like respirocyte and pharmacyte. Single-molecule recognition, sorting and pumping via molecular sorting rotors to allow molecule-by-molecule exchange with in the environment.

2. Sensing- Chemical, pressure, temperature sensors, electromagnetic, magnetic, optical sensors, gravity, position/orientation sensors, molecular recognition sites. The nanorobot of approximately 1 micron diameter could employ approximately 10^4-10^5 sensors of various kinds for controlling the device.

3. Configuration- Control of device shape; gas-driven extensible bumpers to maintain physical contact among adjacent device, control of internal ballasting for nanapheresis and control of chemical ligands for hull displays, for controlled adhesion regulation of external surfaces.

4. Energy- Control of onboard power generation or power receiver systems including thermal, mechanical, acoustic, chemical, electrical, photonic, or nuclear sources; management of onboard energy storage; controlling the transduction, conditioning, and conversion of tethered energy sources; and control of internal power distribution and load balancing throughout a nanorobotic device.

5. Communication- Control of communications hardware including receivers and transmitters, whether chemical, acoustic, electromagnetic, or other modality; interpretation of received signals as new commands from the physician; replacement of existing operating parameters with new ones and out messaging, coordination of nanorobot populations to accurately transfer information directly to or from the patient.

6. Navigation- Establishing absolute or relative physical position across many regimes including bloodstream, tissues, organs, and cells; positional navigation by dead reckoning, cartotaxis, macro/micro transponder networks.

7. Manipulation- Deployment and actuation of manipulators including ciliary, pneumatic, or telescoping systems; stowage, retrieval, selection, installation, use, and detachment of tooltips and other end-effectors; management of tool and manipulator garages; management of coordinated manipulator arrays; and control of onboard disposal or disassembly systems including morcellation, grinding, sonication, thermal or chemical decomposition systems.

8. Locomotion- Control of specific in vivo locomotion systems including ciliary or grapple systems, surface deformation, inclined planes/screws, volume displacement, and viscous anchoring systems; control of locomotion across cell-coated tissue surfaces, amoeboid motion or inchworm locomotion [22].

5. Applications of Nanorobots in Medicine

Medical nanorobots can perform wide range of tasks in diagnosis, monitoring and treating vital diseases. These nanorobots are capable of delivering medicine or drugs into specific sites/targets in the human body.

The potential applications of nanorobots include:

1. Drug delivery- Pharmacytes are the nanorobots designed for the action of drug delivery. The dosage of drug will be loaded into the payload of the pharmacyte. The pharmacyte will be capable of precise transport and targeted delivery of drug to specific cellular targets. The pharmacytes upon arriving at the vicinity of tumor or any

target cell would release the drug via nanoinjection or by progressive cytopenetration until the payload delivery is reached [20].

2. Body surveillance: Monitoring continuously of vitals and wireless transmission could be possible using nanorobots, leading to a quantum leap in diagnostics. This would also help in quick response in case of sudden change in vitals, or could warn against a possibile risk, such as high blood glucose in case of diabetics [24].

3. Dentistry- The nanorobots designed for dental treatment are referred to as dentifrobots. These nanorobots can induce oral analgesia, desensitize tooth, manipulate the tissues to realign and straighten irregular set of teeth [25].

4. In surgery- The surgical programmed nanorobot can act as a semi-autonomous onsite surgeon inside the body. It would perform various functions such as detection of pathology, diagnosing, correcting lesions by nano-manipulation coordinated by an on-board computer.

5. Cancer detection and treatment- The nanorobots are made with a mixture of polymer and a protein known as transferrin which is capable of detecting tumor cells. The nanorobots would consist of embedded chemical biosensor that can be used in detection of tumor. The medical nanorobots with chemical biosensors can be programmed to detect different levels of E-cadherin and beta-catenin, aiding in the target identification and drug delivery. The nanorobot could also carry the chemicals employed in chemotherapy to treat the cancer at the site [26]. The robots could either attack tumors directly using lasers, microwaves or ultrasonic signals or as a part of a chemotherapy treatment, delivering medication to the cancer site.

6. Diagnosis and treatment of diabetes- The glucose molecules are carried through the blood stream to maintain the human metabolism. The hSGLT3 molecule can define the glucose levels for diabetes patients. The glucose monitoring nanorobot uses the chemo sensor which involves in the modulation of hSGLT3 protein gluco-sensor activity [25]. These chemical sensors can effectively determine the need of insulin in the body and inject.

7. Delicate surgeries: Nanorobots could be soon used for performing micro surgery of the eye as well as surgeries of the retina and surrounding membranes. In addition, instead of injecting directly into the eye, nanorobots could be injected elsewhere in the body and delivery of the drug can be guided to the eye. Foetal surgery, one of the most risky surgeries today because of the high mortality rate of either the baby or the mother, could soon have a 100% success rate, due to the fact that nanorobots can provide better access to the required area inducing minimal trauma. Similarly, other difficult surgeries could also benefit from advances in nanorobotics [24].

8. Gene therapy- The medical nanorobot can treat genetic diseases by comparing the molecular structure of both DNA and proteins found in the cell. The chromosome replacement therapy can carried out using chromallocytes [9].

6. Conclusion

The nanorobots used in medicine are predicted to provide a wealth of promise. When the severe side effects of the existing therapies are been considered, the nanorobots are found to be more innovative, supportive to the treatment and diagnosis of vital diseases. The respirocytes would be 236 times quicker when compared to normal red blood cells. The nanorobotics are found to exhibit strong potential to diagnose and treat various medical conditions like cancer, heart attack, diabetes, arteriosclerosis, kidney stones etc. The nanorobot can allow us a personalized treatment, hence achieving high efficacy against many diseases.

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