REVIEW ARTICLE

Chinese Journal of Medical Research
Chinese J Med Res 2020; 3(1):23-27

ISSN(e): 2618-091X
ISSN(p): 2663-8053

# Nanotechnology and Artificial Blood; Future Revolution in Modern Transfusion Medicine

**Muhammad Y[1], Liya S[2], Saeed S[3,4], Yakubu A[4], Habeeb A[4], Muh'd BK[5], Abdullahi M[6], Zainab I[4], Shehu Z[7]**

*1 Department of Chemical Pathology, Rasheed Shekoni Teaching Hospital Dutse, Dutse, Nigeria*

*2 Department of Biological Sciences, School of Pure and Applied Sciences, Mount Kenya University Thika, Kenya*

*3 Department of Haematology, 44 Nigerian Army Reference Hospital, Kaduna, Nigeria*

*4 Department of Hematology and Blood Bank, Rasheed Shekoni Teaching Hospital Dutse, Dutse, Nigeria*

*5 Department of Biotechnology, Federal University Dutse, Dutse, Jigawa State, Nigeria*

*6 Department of Chemical Pathology, Federal Medical Center, Katsina, Nigeria*

*7 Department of Science Lab Tech., Jigawa State Polytechnic, Dutse, Nigeria*

*Corresponding Author: Dr. Muhammad Y, Department of Chemical Pathology, Rasheed Shekoni Teaching Hospital Dutse, Dutse, Nigeria.

Email: yahyoukhan@gmail.com; Tel: +2348064731241

**Received:** February 28, 2020; **Accepted:** March 11, 2020

## Abstract

It has been recently reported by World Health Organization reported that currently world is suffering an extreme shortage of donor blood. A possible future solution to this problem could be the promising virgin area of nanorobotics; an aspect of nanotechnology that deals with designing and manufacturing of nanorobots ranging in size from 0.1-10 micrometers. It's all began in the 19th century when a researcher named Robert A. Frietas at the Institute for Molecular Manufacturing (IMM) designed mechanical artificial RBC called a "Respirocyte" and mechanical platelets called Clottocytes that will have an improved physiological function of the natural RBCs and platelets respectively. Chemically inert element such as diamond or fullerene nanocomposite may be central and principal in the manufacturing of these medical nanoparticles.

**Keywords:** Nanotechnology, Nanobots, Blood Transfusion, Respirocyte, Clottocyte.

## INTRODUCTION

Nanobot is made up of two words Nano and Bots. Nano is word prefix meaning one billionth of and Bot is short for robot, a machine which may be programmed to carry out certain functions independently or operated by remote control [1]. Nanorobotics is an engineering and manufacturing aspect of nanotechnology that deals with designing and building nanorobots ranging in size from 0.1-10 micrometers and constructed of nanoscale or molecular components [2]. These Nanoparticles might function in molecular manufacturing and self-replication process [3]. Eric Drexler first brought the concept of injecting nanoparticles into the human body in the year 1986, the idea was later transcribed by the researcher named Robert A. Frietas at the Institute for Molecular Manufacturing (IMM) who designed and simulated the medical nanoparticles that could transverse in human body and this could shape the way into the future of artificial blood [4]. Respirocytes (artificial mechanical red blood cell) [5], Microbivores (artificial mechanical white blood cell) [6] and Clottocytes (artificial platelets) were designed by Robert A. Freitas [1].

### *Chemical elements of nanorobots*

Carbon probably would be an indispensable and principal element comprising the bulk of a medical nanorobot, may be in the form of diamond or fullerene nanocomposite. Elements which are light such as hydrogen, sulfur, oxygen, nitrogen, fluorine, silicon, etc. will be used for special functions. Diamond has been proved as scientifically inert based on the culturing of peritoneal macrophages from mouse on DLC, which revealed no excess release of beta N-acetyl-Dglucosaminidase or lactate dehydrogenase [7].

### RESPIROCYTES

It's all started by Robert Freitas who designed respirocytes as an artificial mechanical RBC that humans are not yet currently capable of manufacturing [8]. These nano medical robots are hypothetical artificial RBC with capabilities of exerting same physiological functions as natural human RBCs. They are micron-scale spherical measuring 1µm in diameter, they could

be used to replace the entirety of human RBC as a carrier of oxygen and carbon dioxide having potential capacity for oxygen 2366 times greater than hemoglobin [9]. In blood transfusion medicine the primary function of red blood cells (RBC) is the transport of oxygen and carbon-dioxide to and from tissues by virtue of binding the gases to haemoglobin molecule within the RBC [10]. The morphology and physico-mechanical properties of RBC play an important role in their collisional interactions under haemodynamic flow environment and thereby able to carry oxygen to tissue. Based on these observations, recent research approaches have tried to mimic the shape, size, function and flexibility of red blood cell in nanomedicine design [11].

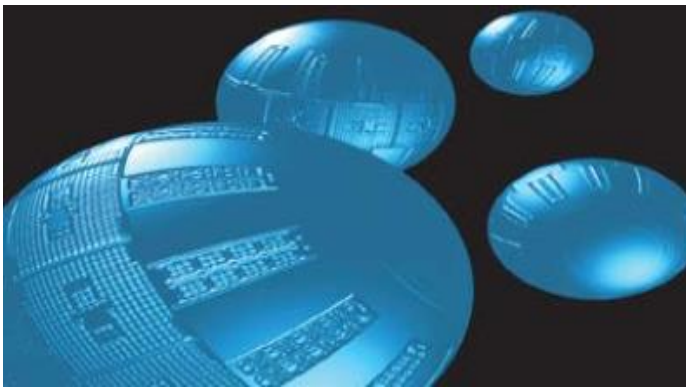

**Figure 1:** An artificial red cell- the respirocyte designed by Robert A. Freitas Jr.

### *Overview of Respirocytes Cell*

The critical aspect of respirocyte construction is the overall size of the device; the artificial RBC must be small enough to pass unhindered within the biological system [12]. In order to achieve this, Robert designed respirocyte in such a way that the size is 6-8 size lower than normal RBC (1µm in diameter), this attribute pave the way for respirocyte to freely pass into the smallest capillaries, where red blood cells can normally get stuck and only move very slowly [5]. The combine use of rotors in respirocyte and its nano size would allow for much more efficient oxygen delivery to tissue than is normal RBC [5]. For a perfect construction of respirocyte outer shell, small units of sapphire (which is similar to diamond in structure) would be needed and this would allow the nano medical erythrocyte to contain gases at incredibly high pressures, up to 100,000 atmospheres. With this capability, the device could hold 2366 times more oxygen and carbon dioxide than a red blood cell [9].

### *Components of Respirocyte*

***Molecular rotors***: A functional respirocyte would need the rotors built from around 100,000 atoms [13] to pump gases in and out of the pressurized storage chambers, and collect glucose for energy. These would be functionalized with selective binding sites, restricting them from pumping all but one type of molecule at a time.

***Power generator***: generator would probably be similar in operation to a fuel cell to utilize glucose captured by a selective pump rotor to generate enough energy for powering the whole device.

***Water ballast chambers***: these would be responsible for control and maintaining the neutral buoyancy.

***Sensors:*** various types of sensors would be used to determine the concentrations of oxygen and carbon dioxide in the local areas well monitoring the pressure within the gas storage tanks.

***Interpretation device:*** a tiny computer would be needed to interpret input from the sensors, and use the data to govern gas flow rates and power distribution.

***Receiver:*** Pressure transducers on the outside of the structure have been proposed as a receiver for programming instructions, sent by a physician via an encoded series of compression pulse [13].

### *Working Principle of Respirocyte*

The respirocytes are designed to operate molecularly. Each respirocyte is between 0.2 to 1µ in diameter consisting of 18 billion precisely arranged structural atoms plus 9 billion temporary residents molecules [4]. There are three types in respirocyte. First one releases the stored oxygen as the robot travels through the body; the second one captures oxygen and all the carbon dioxide in the blood stream and releases it when needed while the third rotor takes in the glucose from blood stream as a source of energy [14]. Inside the lungs, where the partial pressure of oxygen is high and low partial pressure of carbon, the onboard nanocomputer controls the sorting rotors to capture and load oxygen in exchange with carbon dioxide molecules [15]. The water ballast chamber is tasked with responsibility of maintaining flexibility. Other poisonous gases and carbon monoxide can be scavenged from the body through the help of programmed respirocyte [16].

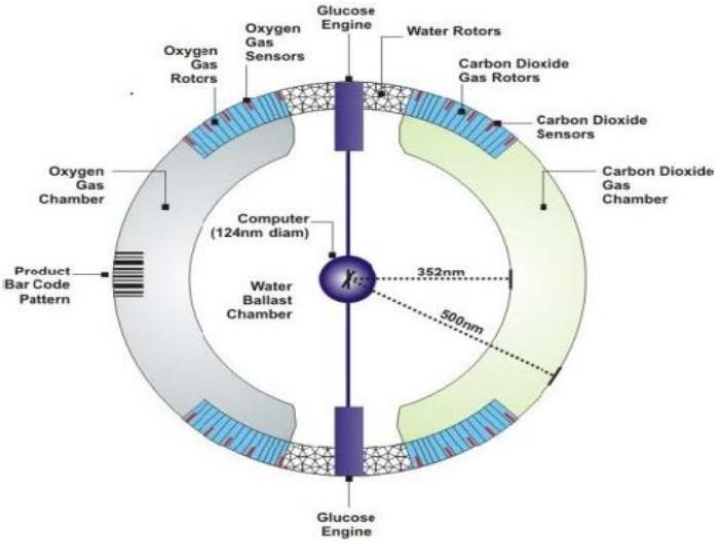


**Figure 2:** Internal cutaway view of respirocyte - equatorial view

### *Pharmacological Dose of a Respirocytes*

In human blood, there are approximately 28.5 trillion red blood cells. Each of these red blood cells comprises of about 270 million haemoglobin molecules capable of transporting oxygen to the tissues. Within the arterial circulation, normally haemoglobin molecules operates between 95% while 70% of these molecules operate in venous circulation but only 25% of the stored oxygen can reached the body tissue. Respirocyte can store up to 1.51 billion oxygen molecules, all are accessible to the tissues these make them a promising development in the field of modern transfusion medicine as an alternative to red blood cell transfusion [14].

For the respirocyte to serve as an alternative to red blood cell transfusion the desired pharmacological dose of 5cc respirocyte in saline suspension containing 5 trillion nanorobots should be prescribed in order to replace the oxygen carrying capacity of the patient's blood. To meet the body oxygen requirement, 5.36 trillion nanorobot respirocyte is needed to be administered either by hypodermal injection or transfusion. The pharmacological dose of a respirocyte has the potential to completely replace oxygen carrying capacity of the patient blood and to further extend natural bone marrow erythropoiesis [16].

***Removal of Respirocytes***

Once the respirocyte exert its physiological function, it may be removed from the circulation. A specialized centrifugation apparatus is used to remove the nanorobots from the patient circulatory system. During the centrifugation process the entire blood component except the respirocyte cannot maintain neutral buoyancy so those components will precipitate outward and are added back to the filtered plasma on the other side of the centrifuge machine [17]. The patient plasma contains most of the suspended respirocyte with few other solids which are passed through a micro filter after reaching the desired centrifugation periods. The centrifuged solid blood component will be combined with the filtered plasma component and returned undamaged to the patient's blood. The respirocyte are therefore removed from the circulation [9].

***Application of respirocytes in modern blood transfusion medicine***

Currently in our health facilities, human blood has never been more in demand than it is today. Non-existence of national blood transfusion centers, increase elective surgery, poor infrastructures, lack of trained personnel and financial resources to support the running of a voluntary non-remunerated donor transfusion service, burden from new viral infections such as hepatitis A, B C; HIV, Syphilis, VDRL have all conspired to ensure that all human blood remains very much a vital but limited asset to healthcare delivery particularly in Nigeria [10]. Human blood transfusion has many adverse effects, this justify the need to develop an alternative to human blood transfusion [18]. The development of respirocyte as an alternative to red blood cell transfusion has provided an exciting opportunity in the field of modern transfusion medicine [12]. These nano- particles is free of diseases vectors like HIV, hepatitis and venereal diseases therefore eliminating the risk of transfusion transmissible infections. Respirocyte are readily available with no need for blood grouping and cross-matching before issuing it's for transfusion. The storage nanorobot is indefinite thereby eliminating the risk of storage related changes associated with human red blood cell [9]. Immediately after bone marrow transplantation, respirocytes could be used as a long-term perfusant to increase oxygen delivery to the tissues [19]. In modern medical practices, these nanorobots can be used in the management of all forms of anemia since they can increase the oxygen carrying capacity of human blood [20].

***Respirocyte and their future use in other field of medicine***

During coronary angioplasty, congenital heart disorders, maternal hypoxia, in utero asphyxia, underwater rescue operations, carbon monoxide poisoning, respirocyte can be used as a perfusant to increase oxygen delivery to the tissue [12].

***Anticipated Challenges with the Use of Respirocytes***

Respirocyte reduces the ability of the kidney to produce erythropoietin hormone in low oxygen tension. These suppress the bone marrow ability to produce red blood cells. The human blood cells could be damage due to continuous movement of the respirocyte rotors leading haemolysis and release of certain chemicals in the circulation. Macrophage can identify respirocyte as a foreign body through the reticuloendothelial system; the main obstacle is that nanoparticles cannot be metabolized inside the macrophages leading to blockage of phagocytic system [21].

**CLOTTOCYTES**

The human body actualizes the process of hemostatsis by corporate functions of coagulation factors, prostaglandins, enzymes, proteins as well as the main players i.e. platelets, these factors works collectively to form fibrin clot and ultimately arrest blood loss [12,22]. The whole process of blood clotting from vasoconstriction to hemostatic plague formation takes approximately 2-5 minutes [23], but the emerging field of nanotechnology has the potentiality of producing metallic nanoparticles that can achieve hemostatsis within approximately one second [6]. The theoretically designed nanoparticle by Dr Robert Frietas Jr called clottocyte or artificial mechanical platelet is spherical nanorobot same as natural platelets in size (2 microns in diameter) and works based on the same principle [24].

***Basic principle of clottocytes mechanism of actions***

Once the blood containing clottocytes find itself in an injured location, a change of partial pressure would be detected immediately often indicating that it is bled out of body. The oxygen molecules from air will enters into the human body via air-serum interface and this is only possible when the first clottocytes is at least 75 μm away from air-serum interface. The information would be disseminated rapidly to neigbouring clottocytes via acoustic pulses. These processes would bring about propagation of cascade, the capabilities of fibre mesh in the integral functions of clottocytes cannot be undermine. The stickiness in the fibre mesh would be blood group specific to trap blood cells by binding to the antigens present on blood cells (Figure 3). Each mesh would overlap on the neigbouring mesh and attract the red blood cells to immediately achieve hemostatsis [9].

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].

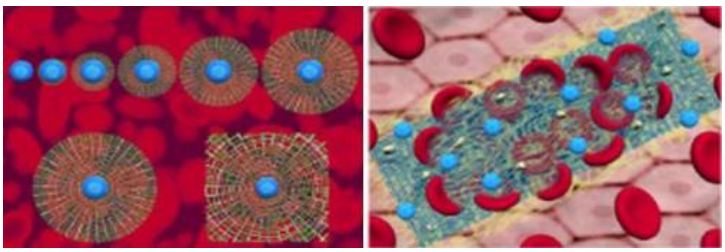

**Figure 3:** Blood clotting mechanism of clottocytes

***Component and Functionality of Clottocytes***

Clottocytes comprises of a compact fibre mesh that is folded onboard. Surface sensors would be task with the responsibility of detecting the serum levels of some plasma proteins which includes fibrinogen, plasminogen, alpha$_2$antiplasmin,

antithrombin III, factor VII, protein C, protein S. The computer sends signal and command the clottocytes to unfold its mesh packet in the immediate local environment of an exposed or injured blood vessels. And this is principally achieved by efficient communication protocols in regulating the coordinated biodegradable mesh release from neighboring clottocyte and controlling the multidevice-activation radius within the local clottocyte population [6]. Upon coming in contact with plasma, a soluble but thin film would be dissolved revealing sticky sections complimentary to blood group antigens. Blood cells are instantly trapped by local activated clottocytes and consequently arrest bleeding [8].

The major anticipated risk associated with the clottocytes is that the additional activity of the mechanical platelets could trigger the disseminated intravascular coagulation [25].

***Applications of clottocytes in modern transfusion medicine***

The advent of platelet transfusions into medical science can be trace back in 1950s and 1960s [26,27]. Platelet transfusions can be used to increase the number of functional platelets for patient with low platelets count or poor platelets function and therefore decrease the risk of problems associated with bleeding [28]. The standard platelet dosing for a thrombocytopaenic patient is by pooling at least 4-6 whole bloods from random donors or from one plateletpheresis donation (apheresis platelets) and this is expected to raise platelets count to 50,000u/L [29]. The proposed nanorobot that can mimic functional platelet has been termed as an artificial mechanical platelet, or “clottocyte [1]. These nanorobots may have applicability in haemostasis. Haemostasis is a complex process involving several steps with a number of promoters and inhibitors balancing thrombosis and fibrinolysis thereby maintaining normal physiologic process within the vascular system [30]. Its takes about five minutes for these natural haemostatic processes to arrest bleeding, which can be improved upon by clottocytes [31]. Additionally, the transfusion of human platelets has several limitations which include the risks of infection with pathogens and the potential of triggering an immune response. These can be eliminated with the transfusion of clottocyte as in the case of thrombocytopaenia [32].

## CONCLUSION

As our technology advances, we explore more nanorobotics devices making it possible to gain control of the world around us. The era of nanotechnology is poised to change many of the paradigms while exploring the field of modern blood transfusion medicine. This field of nanomedicine will significantly reduce the need of human blood for transfusion thereby eliminating all the challenges associated with human blood transfusion like shortages associated with the supply of human blood for transfusion, risk of transfusion transmissible infection. At the other hand these devices increase the oxygen carrying capacity of the blood (respirocyte) and reduce the bleeding time to 1 second (clottocytes). This review provided detailed information on respirocyte and clottocyte with their potential application in modern transfusion medicine. Nanorobots can be used in the management of anaemia and several bleeding disorders, therefore expanding a wide range of treatment option available while also improving the patient condition. It is certainly possible within a generation of time that the use of nanorobotics technology would be ubiquitous in blood transfusion medicine.

**Conflict of Interest**

We declare that we have no conflict of interest.

**Financial Support**

None declared.

## REFERENCES

1. Freitas Jr RA. Clottocytes: Artificial mechanical platelets. IMM Report 18: Nanomedicine. Institute for Molecular Manufacturing, Palo Alto, CA. 2000.
2. Ghosh A, Fischer P. Controlled propulsion of artificial magnetic nanostructured propellers. Nano letters. 2009 Jun 10;9(6):2243-5.
3. Yarin AL. Nanofibers, nanofluidics, nanoparticles and nanobots for drug and protein delivery systems. Scientia Pharmaceutica. 2010 Sep;78(3):542.
4. Drexler KE. Engines of Creation 2.0: The Coming Era of Nanotechnology. 20th anniversary ed., Oxford University Press, Oxford, 2006.
5. Frcitas RA. Exploratory design in medical nanotechnology: a mechanical artificial red cell. Artificial Cells, Blood Substitutes, and Biotechnology. 1998 Jan 1;26(4):411-30.
6. Freitas Jr RA. Microbivores: artificial mechanical phagocytes using digest and discharge protocol. J Evol Technol. 2005 Apr;14:1-52.
7. Freitas Jr RA. Is Diamond Biocompatible With Living Cells. Foresight Update. 1999 Dec 30(39):7-9.
8. Freitas RA. Current status of nanomedicine and medical nanorobotics. Journal of computational and theoretical nanoscience. 2010 Mar 1;2(1):1-25.
9. Satyaveni M, Sai Sowjanya M, Sreenivasulu K, Sreekanth N, Baburao C. Respirocytes: Mechanical artificial Red blood cells. International Journal of Biological, Pharmaceutical Research. 2013;4(4):297-301.
10. Carson JL, Hill S, Carless P, Hébert P, Henry D. Transfusion triggers: a systematic review of the literature. Transfusion medicine reviews. 2002 Jul 1;16(3):187-99.
11. Hillyer CD. Blood banking and Transfusion Medicine. Churchill Livingstone Elsevier 2007; 2:14-15.
12. Shabnashmi PS. NKS, Vithya V., Vijaya Lakshmi B. And jasmine R. Therapeutic applications of Nanorobots-Respirocytes and Microbivores. J Chem Pharm Res. 2016;8(5):605-609.
13. Merkle RC. Nanotechnology and Medicine. In: KlatzRm, Ed. Advances In Anti-Aging Medicine, Vol. 1, Liebert Press: 1992. 277-286.
14. Jaiswal A, Thakar H, Atanukumar B, Krunali T, Meshram DB. Nanotechnology revolution: respirocytes and its application in life sciences. Innovative Journal of Life Sciences. 2013;1(1):8-13.
15. Mishra J, Dash AK, Kumar R. Nanotechnology challenges; nanomedicine; nanorabots. International Research Journal of Pharmaceuticals. 2012;2(4):112-9.
16. Manjunath A, Kishore V. The promising future in medicine: nanorobots. Biomedical Science and Engineering. 2014;2(2):42-7.
17. Fahy GM. Possible medical applications of nanotechnology. In: Crandall BC, Lewis J,eds. Nanotechnology: Research and Perspectives, Cambridge MA: MIT Press. 1992:251-267.
18. Erhabor O, Adias TC. Transfusion Made Easy for Students of Allied Medical Sciences and Medicine. 2012;128:131.
19. Kale PB, Sklar GE, Wesolowicz LA, DiLisio RE. Fluosol: therapeutic failure in severe anemia. Annals of Pharmacotherapy. 1993 Dec;27(12):1452-4.
20. Youngson C, Nurse C, Yeger H, Cutz E. Oxygen sensing in airway chemoreceptors. Nature. 1993 Sep;365(6442):153-5.

21. Golkar Z, Bagasra O, Pace DG. Bacteriophage therapy: a potential solution for the antibiotic resistance crisis. The Journal of Infection in Developing Countries. 2014 Feb 13;8(02):129-36.
22. Thachil J. The elusive diagnosis of disseminated intravascular coagulation: does a diagnosis of DIC exist anymore? InSeminars in thrombosis and hemostasis 2019;45(1):100-107. Thieme Medical Publishers.
23. Boonrong P, Kaewkamnerdpong B. Canonical PSO based nanorobot control for blood vessel repair. World Academy of Science, Engineering and Technology. 2011 Oct 25;58:511-6.
24. Save N, Deshpande S. Nanorobot A Prospective Outlook in Medicine. Biochem Ind J. 2017;11(1):114.
25. Kannan TT, Lal AH, Ganesan M, Baskaran R. Study and Overview About Molecular Manufacturing System. International Journal of Mechanical Engineering and Robotics Research. 2013;2(1):193-201.
26. Hillyer CD. Blood Banking and Transfusion Medicine: Basic Principles & Practice. Elsevier Health Sciences. 2007. pp. 308–310.
27. Das PC, Smit-Sibinga CT, Halie MR. Supportive therapy in haematology. Springer Science & Business Media.2012. p. 190.
28. Brass L. Understanding and Evaluating Platelet Function. Hematology Am Soc Hematol Educ Program. 2010.387-96
29. Slichter SJ, Kaufman RM, Assmann SF, McCullough J, Triulzi DJ, Strauss RG et al. Dose of prophylactic platelet transfusions and prevention of hemorrhage. New England Journal of Medicine. 2010 Feb 18;362(7):600-13.
30. Hassouna HI. Blood stasis, thrombosis and fibrinolysis. Hematol Oncol Clin North Am. 2000;14(2):xvii–xxii. doi:10.1016/s0889-8588(05)70134-9
31. Sahoo SK, Parveen S, Panda JJ. The present and future of nanotechnology in human health care. Nanomedicine: Nanotechnology, Biology and Medicine. 2007 Mar 1;3(1):20-31.
32. Schreiber GB, Busch MP, Kleinman SH, Korelitz JJ. The risk of transfusion-transmitted viral infections. New England journal of medicine. 1996 Jun 27;334(26):1685-90.