How Could Nanotechnology Further Influence Medicine?

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ABSTRACT

Nanotechnology is a revolutionary scientific breakthrough, and already it is being used to further medical knowledge and progression. Nanotechnology is the ability to build machines at the subatomic level. In order for us to manipulate the atoms in such a way that medical advances can be made via nanotechnology, we must understand how the body reacts to the treatments that are currently available. By fully understanding the processes that occur between a drug and the body, it is possible to design nanorobots that can carry out the functions of the drug in a more efficient and side effect free manner.

INTRODUCTION

Nanotechnology was brought to the forefront of research in the 1980's with the birth of cluster science and the invention of the scanning tunneling microscope (STM) [1] by Gerd Binnig and Heinrich Rohrer. However, the Richard Feynman speech of 1959, namely '*There's Plenty of Room at the Bottom',* was when the phenomenon was first brought about. Feynman suggested the possibility of making nanoscale machines that "arrange the atoms the way we want", and do chemical synthesis by mechanical manipulation [2]. It was this hypothesis that sparked interest in molecular manufacturing.

During the 1980's, Dr. K. Eric Drexler explored the handling of individual atoms and molecules and promoted the technological significances of nano-scale phenomena and devices through the book *Engines of Creation: The Coming Era of Nanotechnology* [4].

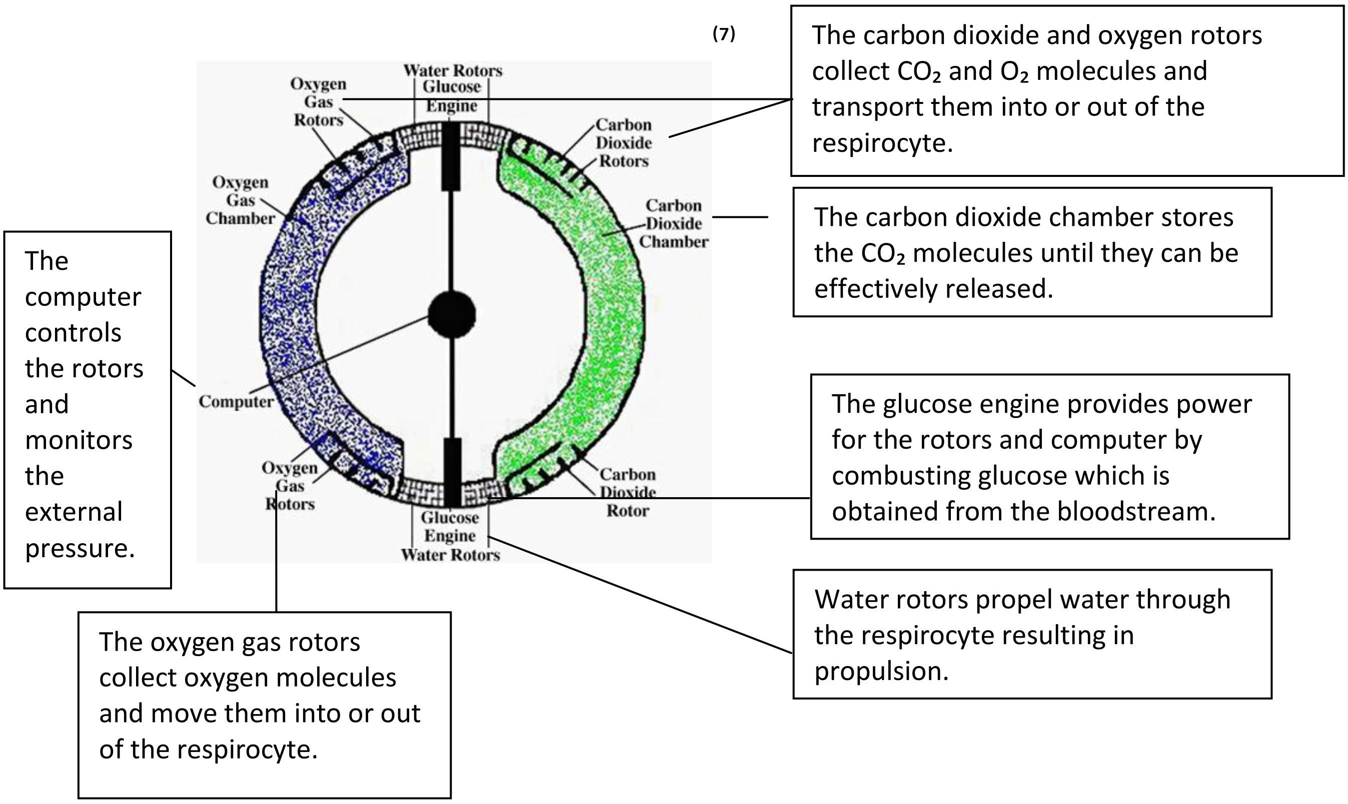
The development of the STM was an immense breakthrough in the 1980's and is an instrument which is able to image surfaces at an atomic level. Cluster science and the STM led to the development of fullerenes in 1985 followed closely by the development of carbon nanotubes. A fullerene is a molecule that is composed of just carbon atoms in the shape of a sphere, ellipsoid or tube. Spherical fullerenes are known as '*buckyballs'* which have undergone intense research due to their unusual shape and chemistry. Cylindrical fullerenes are called nanotubes and due to its properties (high tensile strength, high electrical conductivity, high ductility, high heat conductivity, and relative chemical inactivity[3]); it too has undergone intense research. The properties of fullerenes have not been fully established, however, much research is taking place to investigate the possible large scale uses. For example C_{60}, known as an optical limiter, it turns dark instantaneously when light is shined upon it. This property could be used for protective goggles for people who work with lasers and so protect their eyes as only a small amount of laser light can lead to permanent eye injuires[14]. In 1996 the buckminster-fullerene was discovered by Kroto, Curl, and Smalley. This fullerene is particularly useful in nanotechnology as it possesses delocalised electrons which allow the fullerene to conduct electricity. Consequently, the minuteness of the buckminster-fullerene and its ability to conduct electricity make it useful in nanotechnology. This development is potentially extremely beneficial in cardiac medicine as it may be possible to replace pace makers with the buckminster-fullerene.

At present, drug delivery systems are of great importance within medicine. As a result of nanoparticles being so diminutive, cells can easily uptake them as opposed to larger molecules which would not be up taken. Complex drug delivery mechanisms are being developed, including the ability to get drugs through cell membranes and into cell cytoplasm.[5] However, it is only recently that advances within drug delivery systems have been made.

<u>DISCUSSION</u>

There are many possible developments of nanotechnology, many of which are being explored and in some cases refined. However, I am personally engaged in the more immediate discoveries of nanotechnology within medicine and their potential. The possibility of effective treatment to cure such ailments as cancer and diabetes is incredible and extremely beneficial and nanotechnology is a technology that can be developed to further extents. Furthermore, nanotechnology can provide aid to less economically developed countries and improve water supplies, improve sanitation and lessen the effects of global warming. This could help to almost eradicate diseases that have already, all but, been eradicated in more economically developed countries. Thousands of people die each day due to water related diseases such as cholera, which could be completely preventable if nanotechnology became the 'norm' across the world. Nanotechnology is a technology that can refine current medical procedures such as transplants and be almost one hundred percent effective. Nanotechnology may also improve oxygen content in the blood due Robert A. Freitas's design of an artificial red blood cell called a respirocyte. Despite this only being a theory at present, a respirocyte has huge potential.

A respirocyte is a spherical nanorobot that is approximately the same size as a bacterium. It is compounded by approximately eighteen billion atoms that are arranged in a crystalline structure to form a miniature pressure tank. This miniature pressure tank would be able to contain approximately nine billion oxygen molecules and approximately nine billion carbon dioxide molecules[6]. When the respirocytes become in vivo via injection and enter the recipient's blood stream, sensors on the surface of the respirocyte would immediately detect oxygen and carbon dioxide levels in the blood. Depending on the oxygen and carbon dioxide levels, the respirocyte will decide whether to load or unload oxygen and carbon dioxide. A respirocyte is more advantageous than an ordinary red blood cell as it is able to transport two hundred times more gas.

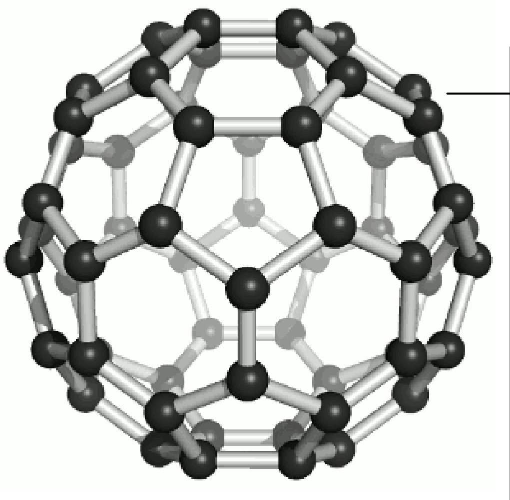


The benefits of respirocytes can be reaped by many people such as those suffering from the effects of lung diseases such as asthma, emphysema and pulmonary fibrosis where a lack of oxygen is the main issue; smokers or ex-smokers could also benefit as would people involved in recreational fields such as climbing and sport. The efficiency of the gas exchange in the lung would be improved in all cases where the reduced surface area in the lungs impinges on efficient gas exchange; i.e. when the total supply of oxygen is short of its maximum capacity. However, by using respirocytes in vivo, more oxygen can be transported within the human body helping to supplement the shortness of breath often experienced by high altitude climbers and smokers. It takes approximately 10-15 years on average for tar to be removed from the lungs (depending on how many cigarettes were smoked) thus even those people who have quit smoking can still be short of breath and suffer difficulty in their breathing. Whist suffering from shortness of breath, the patient will most likely be fighting against the addiction thus high stress levels can be a side effect. Nonetheless, respirocytes may aid the ‘quitting’ process by stabilising breathing consequently there may be a decrease in the number of smokers – a major benefit to overall health. Those persons who engage in recreational activities may also benefit from an increase in oxygen supply as muscle recovery will improve. Those that enter areas of high altitude should be able to breathe easily despite the harsh conditions. The lower atmospheric pressure affects humans because of a decrease in the partial pressure of oxygen. This lack of oxygen can cause various illnesses, some being potentially fatal, illnesses such as altitude sickness, high altitude pulmonary edema (fluid accumulation in the lungs) or high altitude cerebral edema (swelling of the brain) [8].

The Buckminster-Fullerene is a spherical molecule with the molecular formula C_{60}. As a result of them being hollow, fullerenes are very light molecules with respect to their hardness. They also have the ability to absorb light and can release it at a different frequency, as heat or transfer it to another molecule. This means that they can act as optical limiters. The more light that is shone through a C_{60} solution, the more light C_{60} molecules will absorb as the concentration of the excited form of C_{60} increases and also because the excess light is emitted as heat. C_{60} fullerenes can also lose energy to other molecules. When the C_{60} fullerenes are shone on with light, toxic excited oxygen is formed. Therefore in the presence of light and air C_{60} is highly toxic.

The method in which C_{60} molecules arrange themselves result in gaps forming between one another. These gaps can then be filled with group one and group two metals, some of which can provide superconducting properties at very low temperatures. For example, if Rubidium fills all of these holes, below 28K, this material conducts electricity with zero resistance. The Rubidium molecule donates an electron forming the salt $[Rb^{+}]_{3}[C_{6}0_{3}^{-}]$ which has a delocalised electron that can carry an electrical current [9].

[10]



High symmetry of the 12 pentagonal and 20 hexagonal faces arranged to form a football shape. Each carbon atom in the structure is bonded covalently with 3 others. Carbon atoms have 6 electrons, meaning their electronic configuration is $1S_2$ $2S_2$ $2P_2$. In order to become stable, the carbon atom needs 8 electrons in its outer shell and covalently bonding with 3 other atoms will only make 7 electrons in its outer shell. This means that the one unbonded electron on every carbon atom is delocalised and free to move around the molecule. The delocalised electron is able to carry electrical charge therefore the buckminster-fullerene is a very good conductor of electricity. This, because of its size, makes it very useful in nanotechnology. [11]

The Buckminster-fullerene is yet to be used comprehensively in medicine, however, given its properties and the current knowledge of the molecule, there is huge potential for development. The fact that the Buckminster-fullerene can absorb light and can give out that energy to nearby molecules could prove to be incredibly useful in the treatment of cancer. If C_{60} is present in the bloodstream around a tumour and light is shone on that tumour, toxic excited oxygen will be formed and will attack the cancer in that localised area. However, this theory is not yet perfected; but much research is underway in order to perfect it.
Another potential utilisation of the Buckminster-fullerene is perhaps as a potential replacement for pacemakers or perhaps as an attempt to improve the heart's electrical activity. Pacemakers are usually prescribed when a patient has bradycardia or heart block. Bradycardia is when the patient has a slower than normal heartbeat. Heart block is where there is a problem with the heart's electrical system. Heart block occurs when the electrical signals are slowed or disrupted as it moves through the heart. This can happen due to ageing, previous damage to the heart or any other conditions that may interfere with the heart's electrical activity. A pacemaker consists of a battery, a computerised generator and wires with electrodes on one end. The battery powers the generator which is surrounded by a metal box. The wires are connected to the heart. The electrodes monitor the heart's electrical activity and can consequently control the number of electrical impulses that are sent to the heart. Although the probability of contracting any problems during pacemaker surgery is low, the risks remain nonetheless. However, perhaps by injecting Buckminster-fullerenes in vivo, cardiac surgery could be prevented as the C_{60} molecules improve the heart's electrical activity by being programmed to stimulate or carry the electrical current needed for the heart to beat. As a result the risks associated with cardiac surgery would without doubt be lower.

One of the most significant developments due to nanotechnology is the development of targeted drug delivery systems. These will be of huge importance to the pharmaceutical industry in the future as the potential profits from targeted drug delivery will be vast. The main issue with current drugs is that we are not able to deliver them straight to the intended area. In traditional drug delivery systems such as oral ingestion or intravascular injection, the medication is distributed throughout the body through the systemic blood circulation. For most therapeutic agents, only a small portion of the medication reaches the organ to be affected. Targeted drug delivery seeks to concentrate the medication in the tissues of interest while reducing the relative concentration of the medication in the remaining tissues. This improves efficacy while reducing side effects.[(12)]
Researchers are contemplating using magnetic nanoparticles containing the drug to be delivered to specific parts of the human body by means of magnetic field. Drugs can also be attached to nano-ligand (a substance that forms a complex around a central metal atom or ion), the role of which would be to deliver the drug only to target tissue whilst at the same time reducing its side effects [(6)].
Scientists from the California Nanosystems Institute and Northwestern University have developed a new method of targeted drug delivery. The university has developed a *nanovalve* which can release its content under specific conditions such as different pH levels, such as to cells which differ in their physiological characters or to cells which are expressing certain enzymes. For example, this can be incredibly useful in the treatment of cancer as an unhealthy cancer cell will express different enzymes to the healthy cells surrounding it. The nanovalve is composed of a minute honey-comb shaped enclosure which is covered by another molecule. The covering molecule is attached to the honey-comb structure by strong electrostatic forces which create a closed complex. At pH less than or equal to seven (neutral or acidic pH), the

covering molecule remains attached to the honey-comb shaped container. Conversely, when there is a pH greater than seven (basic), the electrostatic forces holding the structure together are weakened and the contents released. This way, the drug is only delivered that are of a basic environment.
As opposed to other nano systems that are soluble only in organic compounds, the nanovalve was designed to be water-soluble allowing it to be used for medical purposes. Tests have been conducted and involve the transportation of paint molecules within water. However tests are yet to be conducted in vivo. The nanovalve is approximately 400 nanometers in diameter making it good for targeted drug delivery. The nanovalve could be further developed to be triggered in response to other conditions such as in response to specific enzymes present in cells affected by disease [(13)].
Given that targeted drug delivery systems are able to reduce side effects, therefore by using a targeted drug delivery system, the drug can be transported directly to the site in smaller doses whilst not limiting the use of other drugs. Analgesia could be a good example of this where pain could be targeted specifically rather than targeted via the circulatory system.

Some drugs have the issue of having poor water solubility and consequently are not one hundred percent absorbed into the human body. However, this problem has been solved by The NanoSystems Company which has developed a process named 'nanonization' [(6)]. Nanonization begins with the drug crystals being reduced in size until they are particles of less than four hundred nanometres in diameter. In order to stabilise the newly formed particles and prevent them from aggregating, a thin layer of polymeric surface modifiers is absorbed onto crystal surfaces resulting in a suspension that operates like a solution. The suspension can then be utilised in various dosage forms including: pills, sprays and creams. Obtaining drugs that are soluble in water is extremely beneficial to humans as the human body is approximately eighty percent water. The blood and water circulation systems carry the nutrients and drugs hence improving a drug's solubility will allow for faster absorption. By improving absorption rates lower doses can be used which is advantageous to the economy as money is saved on the production of drugs and on importing drugs. It is advantageous to the human body as the recipient is not exposed to as much artificial chemicals.

Another major benefit from nanotechnology is the improvement in diabetes treatments. Mauro Ferrari from Ohio State University and Tejal Desai from Boston University have created what could be considered a major treatment to diabetes. A miniature silicon box which contains pancreatic beta cells is taken from animals. The silicon box is surrounded by a material which has a nanopore size of approximately 20 nanometres in diameter. These pores allow the passage of glucose molecules and the hormone insulin but impede the passage of larger immune system molecules. The silicon boxes can be implanted under the skin of the patient and could frequently correct the body's glucose levels without the need of immunosuppressant drugs, large injections of insulin and the annoyance of monitoring your diet [(6)].
Another form of treatment is a device called Long Term Sensor System (LTSS) which comprises of an implantable glucose mini sensor and a miniature insulin pump. However, there is a remaining problem of how to translate glucose levels into appropriate insulin dosages[(6)]. Much research is being carried out in order to solve this complication.
Another potential treatment called 'SmartCell' is undergoing development. A SmartCell is programmed to have its structure broken down when blood glucose levels rise. As the protein matrix is decomposed, the content (insulin) is released. Testing on rats has commenced and preliminary results have proved to be promising [(6)].

In opposition to the improvements of medicine via improvements and development in nanotechnology are those people who perceive nanotechnology to be unethical. It is thought that using nanotechnology is against nature and is therefore unnatural. It is questionable that by using nanotechnology we are controlling life and death. It is also argued that we are implementing miniature 'robots' in our body and that they are programmed `to control our body parts. In correlation to whether nanotechnology is unnatural or not is that we are already using man made devices in our body, for example pacemakers. Some people are afraid of what they do not know and do not trust new technology. Furthermore nanotechnology is likely to be only available to the rich initially and if national health services begin to use nanotechnology then taxes will rise. A raise in taxes is likely to generate political pandemonium given the fact that the world is currently suffering an economic crisis. It is suggested that it is 'unfair' for doctors to aid people who have caused their own problem for example smokers and ex-smokers as the money used to provide for these people originates from the tax payers. In reference to the development of SmartCell, animal testing is perceived to be cruelty to animals in people's opinions but equally science is only able to advance via testing on a whole organism. This ethical issue is argued against by the prevention of an incident similar to that of the thalidomide incident where the drug was incorrectly tested and resulted in many birth defects. Such consequences for nanotechnology may prove to be even more severe.

CONCLUSIONS

I believe that nanotechnology is the path of the future and that it will revolutionise medicine entirely. This is because much of the necessary basics of nanotechnology are understood by experts and much research is on the penultimate stages and some is being put into practice already.
By utilising nanotechnology medical procedures such as heart surgery can be made less complex or potentially unnecessary but even more importantly some diseases such as cholera, which is prevalent is less economically developed countries can be eradicated. The main source of hindrance originates from people who have a fear of the unknown and the idea that man made 'machines' in the human body is unwise when clearly it is a progression of current medicine. For example, nanotechnology could perhaps be used to replace transplants.

Nanotechnology is not far away from becoming a reality and is indeed tests are being carried out on organisms such as rats and are proving to be successful. Ultimately, I believe nanotechnology will further influence medicine in such a way that it will revolutionise medical industries for the better. Albeit a new branch of medicine, however nanotechnology could prove to be a successful life saving technology. Using nanotechnology to cure malignant cancer tumours and other such life threatening diseases could prove to be one of the greatest treatments in history.

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