

**Research and Development into the Field
of Nanotechnology and its Application
to the Recovery of Damaged Nerves**

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PASS WITH DISTINCTION

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ABSTRACT

This paper is based around the new and exciting prospect of nanomedicine, which has the potential to revolutionise the prognosis, diagnosis and treatment for a huge range of diseases and injuries. The paper focuses specifically on research that will possibly be useful for cell repair and replacement in nervous systems. The nervous system can be damaged through injury or disease and it's very difficult to treat because of the tendency of nerve cells being unable to regenerate. Therefore, current sufferers of paralysis and other neurological diseases caused by death of brain cells, who have been told there's no cure, would be given hope if there's possible treatment through new advances in nanotechnology which may return them to full health.

INTRODUCTION

Nanotechnology is technology on a scale of less than 100nm and this essential property means that it can control matter at the atomic scale. This is a unique asset which is very advantageous in the fast paced world of new materials and concepts in science. Medicine is just one of many branches of science that would benefit from this ground-breaking technology.

The complexity of nanotechnology was first materialised from a simple idea of Richard Feynman in 1959 with his speech "There's Plenty of Room at the Bottom". Even though he never directly mentioned the term nanotechnology, the concept of building "infinitesimal machines" was the basis of his speech. He imagined that it would be possible to rearrange atoms by creating "slave hands" that would then go onto create a scaled down version of itself that would then create even smaller "slave hands". The process would repeat itself until there a billions of these tiny "factories". He predicted that laws of physics that affect us at a human level will not apply at an atomic level. Quantum physics means that the molecular sized machines wouldn't interact in the same way as larger version of it would [1].

Feynman's speech was a huge influence on Drexler, who many see as the Godfather of nanotechnology, and other researchers in this field. Drexler is quoted to have said "The revolutionary Feynman vision launched the global nanotechnology race". However, Drexler was the man who "captured the imagination, especially of younger people," since he showed that nanoscale engineering could achieve amazing feats: new materials, removing pollutants and curing diseases (something that will be described more in detail). He published his book, Engines of Creation, in 1981 and was the first time the word nanotechnology was used in this context. He compared nanotechnology to ribosomes in living organisms as they are the "primitive assemblers in the cell". He described his idea of creating nanoscale tools by "snapping" together atoms as if they were like marbles. These tools would act as assemblers which would manipulate other atoms into the shapes needed with atomic precision.

The Foresight institute was founded soon after the book was published in 1986 and has a mission "to ensure the beneficial implementation of nanotechnology". His book sparked interest from scientists across the globe and initiated the real research of nanotechnology during the 1980's and 1990's. New technologies helped further the research into the field. The scanning tunneling microscope (STM) which was invented by Binnig and Rohrer in 1981 is one example as it made nanotechnology testable [2].

The Buckyball (or Buckminsterfullerene) was discovered in 1985 and it's made of 60 carbon atoms arranged into 12 pentagons and 20 hexagons. Its unique hollow spheroid shape means that it can be filled and used for drug delivery. Research by Fred Wudl and co-workers at the University of California, Santa Barbara has shown that a form of the Buckyball can suppress HIV-1 and HIV-2 [3]. The Buckyball fits perfectly into the active site of HIV proteases as it block and disarms HIV protease from cutting proteins without affecting the infecting cells. While this does illustrate the diversity of nanotechnology for medicinal treatments, this particular application is not as effective as current drugs already and more research is needed.

The potential contribution for nanotechnology in medical advancement is huge owing to the way that nanotechnology could interact with the body at the molecular. So called "nanomedicine" would encourage and direct the body to heal itself, faulty proteins being corrected at a cellular level with such precision terminal patients may, in the future, experience a full recovery.

Drexler claimed in Engines of Creation that nanotechnology would "let our minds renew and remake our bodies" [2] which may have been seen as farfetched at the time. However, if technology can match the ideas and concepts many researchers are currently creating, this may be more science fact than science fiction.

DISCUSSION

So far, a lot of the research into applications of nanomedicine shows how nanotechnology can aid the treatment of diseases such as brain cancer. Rice University bioengineers and physician-scientists at Baylor College of Medicine and Texas Children's Hospital tested animals with nanoshells, which are tumor destroying light-activated nanoparticles [4]. The non-invasive treatment could mean future cancer treatment wouldn't involve unwanted side effects of drug and radiation therapies. Patients would have the chance to experience full recovery. Equally however, some conditions may be treatable but leave lasting side-effects which no current medication can cure. Many accidents and diseases associated with the nervous system are simple to treat short term but, usually sufferers will never recover fully. Examples include strokes or road accidents which can leave many disabled because the nervous system is very difficult to regenerate.

Nerve cells (on the whole) are unable to regenerate meaning that damage to the nervous system is permanent. What if it wasn't? What if nanotechnology could be used to encourage these cells to divide and reproduce? What if nanotechnology could replace the damaged nerves with themselves? Nanotechnology may be the perfect opportunity for scientists to create miniscule robots that could either substitute nerves with themselves or direct the cells to multiply. This groundbreaking technology would change many people's lives.

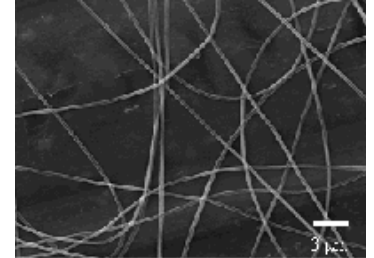


Figure 1 [5]

One approach is to replace the damaged nerves with technology like bio-nanoscaffolding [figure 1]. This technique has been used for burn victims where a sheet is placed over a damaged area of skin (the burn) under which the skin cells are encouraged to grow. The nanoscaffolding prevents infection and the tissue-like paper disintegrates harmlessly after 6 weeks. The sheet is an ultra-fine, 3-dimensional scaffold made from specially developed polymers which looks similar to tissue paper except that it has fibers 100 times finer. Before being placed over the burn, some of the patient's skin cells are attached first. The team of researchers at the University of Sheffield have shown that sometimes simple solutions have the best results [5].

Military researchers in America claim that they will be able to grow limbs and organs using this technology and there has been a case where a soldier lost the end of his finger and the bone, skin and nail grew back with bio-nanoscaffolding [6]. Nanoscaffolding creates a miniscule net which gives tissues in the process of repairing a strong structure on which to base its new cells on. A fluid with tiny fibres can be injected into the damaged site or the nanoscaffolds could be placed directly onto it like in the previous example. The treatment would be perfect if nerve cells could regenerate by themselves but, this is not the case. Therefore something needs to be added to this treatment for it to work [7].

David Nisbet from Monash University's Department of Materials Engineering has combined the use of nanoscaffolding and stem cell research to help with rebuilding damaged nerves. His approach brings together two very exciting but extremely controversial modern medical technologies. Nisbet injected bio-degradable fibres into the site of damaged nerves in a similar way to how nanoscaffolding is used in other tissues. The stem cells can either be integrated into the structure before being injected into the patient or can be added in after. The scaffold prevents stem cells from "floating around" in the patient and as such they are quicker at adapting to the environment and creating new nerve cells. The Mental Health Research Institute of Victoria is using this concept of stem cells and nanoscaffolding for research into repairing damaged brain cells [8].

Future developments into this research may lead to this method being used in many circumstances of nerve damage all over the body. A simple injection could mean that someone would be able to walk again after a terrible accident or a blind person regain their sight. However, such an approach does carry with it a number of ethical issues and complications. Simply using embryonic stem cells will be controversial as this is already a much-debated subject in medicine. Many believe that using stem cells from zygotes is wrong. They see this as a living being and no one has the right to test something that has the potential of human life. These are people who believe that life starts from the moment of conception and that all life is sacred; in essence, embryonic stem cell research is murder.

However, the controversial use of stem cells may not stop nanotechnology. Finding a way for neurons to replicate would mean that research into nanoscaffolding can carry on without being associated with stem cells although many researchers agree that nerve cells don't regenerate under normal conditions [9]. Jonas Frisén recently teamed up with Peter Eriksson's research group from Göteborg University and together with scientists from Australia and America, came to the conclusion that no cell division takes place in the neocortex during the person's life from infancy to adulthood. The hypothesis would usually be tested by determining the age of a nerve cell and since it is remarkably difficult to do so there is a large margin of error. However, what is clear is that it is very

difficult for nerve cells to multiply, if at all, and it is widely accepted that damage to the nervous system and brain is usually permanent.

Cell cycles vary from cell to cell. It can take 10 years for the skeleton to completely regenerate and only 10 days for taste buds. Compared to all the other systems within the body, such as respiratory, digestive or reproductive system the nervous system would benefit most from advances in nanotechnology. Nerve cells are the least capable of recovering by themselves and consequently nanotechnology will be most applicable to them [10].

Different cells are specialized in different ways. They have certain genes “turned on” and “turned off” when embryonic stem cells in a zygote begin the process of differentiation following fertilisation. It is what makes a nerve cell so different to liver cell in appearance and in purpose. Some genes that are active in a liver cell aren’t active in a nerve cell. For example, the ability to create and secrete bile would be coded into the DNA and present in the all types of cells with a nucleus but, only specialised liver cells will transcribe and translate this gene to synthesize the protein that makes up bile. However, there must be a DNA sequence that is switched off in the nerve cell that stops the cell from dividing. Would it be possible to find this gene sequence and switch it back on?

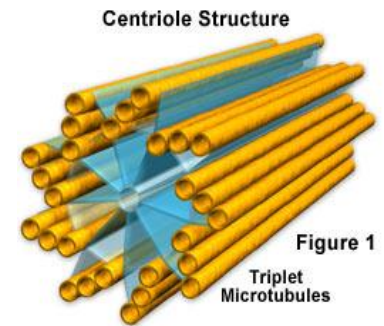


Figure 2 [14]

There are 5 stages in the cell cycle and nerve cells never completes the first stage (first growth G1 stage). The cell rapidly grows before the chromosomes copy themselves in order to split into two nuclei. However, the next stage can never initiate unless the first one is completed because of the cell cycle checkpoints. Research has shown that Protein Kinase C δ can initiate this first stage [11] and this is where nanotechnology could come in.

Nanotechnology has already proven itself useful in modern medicine with nanoscale drug delivery as it's shown to be 15-250 times more efficient at being taken up by cells than similar micro particles in the 1-10 μ m range [12]. The same concept could be used for the Protein Kinase C δ or any other matter that could achieve the same affect of initiating the first stage in the cell cycle. A nanoparticle (similar to the shell structure of a Buckminsterfullerene) could be conjugated with this molecule and would be quickly and efficiently diffused into the targeted cell membrane. In theory, this should start the process of rapid cell growth within the nerve cell.

The next stage should start and this would be the replication of chromosomes within the nucleus. Since every cell within the body has the exact the same set of chromosomes, this part of prophase should not be as much of a problem. However, nerve cells seem to lack centrioles [13] and these are essential in the formation of spindles which is needed for the second stage of the prophase. (However, some experiments show that animal cells can divide without centrioles and plant cells divide without centrioles in the first place) [14]. Centrioles are present in all cells and the lack of them in nerve cells could be another reason it's incapable of dividing.

Centrioles [figure 2] are composed of globular proteins and would therefore be made by protein synthesis in the nucleus. This leads us to believe that the gene responsible for centrioles production was switched off during specialization and would need to be switched back on in order for the cell to create more centrioles for reproduction. Since nanotechnology has already shown it can diffuse into the cell membrane quickly and efficiently, future technology could lead to nanotechnology travelling further into the cell, through the nuclear membrane via pores and into the nucleus where the chromosomes are located.

The reason why the centriole gene would have been turned off is that during specializing of the embryonic stem cells, the pattern of regulated gene expression would have changed [15]. Furthermore, the pattern of regulated gene expression for a nerve cell is to inhibit or to completely switch off the gene used to synthesize centrioles although, promoters can respond to chemical inducers and therefore switch certain genes back on [16]. Mainly this effect is used for research but if this was achieved in a cell of a living organism, the selected genes would possibly be able to take part in transcription and translation.

The next question is how to find this gene and identify the chemical inducer which would switch it back on. It is hoped that this gene will be identified by researchers from The Human Genome Project, whose aim is to sequence the whole of the human genome. Further research could then be done into what can chemically induce this gene into protein synthesis. Once this chemical inducer has been discovered, it can be made part of a nanoparticle similar to protein used for rapid growth in the first stage.

If the centrioles are successfully synthesised, the next stages (metaphase, anaphase and telophase) can start without a problem as the cell cycle checkpoints shouldn't interfere. The spindles will pull the centromeres apart to form chromatids and then two new nuclear envelopes would reform around the two sets of DNA. The last part is cytokinesis and this splits the cell into two by the surface membrane contracting in the middle [17].

Without nanotechnology, this concept would be impossible because it involves interacting with the body systems at not just a cellular level but at the level of the organelles within the cell. This type of treatment would mean that it would be possible to alter the functions of a cell to your advantage instead of replacing them entirely when treating a patient. However it would be important to ensure there was a precise way of making sure that this technology only affects cells that it intends to. This constraint means that the treatment could not be administered orally because the particles would affect any cells that it came into contact with. The nanotechnology would be changing other healthy cell's pattern of regulated gene expression and therefore changing the way the cell would function which could lead to disastrous consequences. It would lead to healthy cells that aren't part of the nervous system possibly going through the process of mitosis too often. Therefore an injection would probably be used for this type of treatment to ensure you are targeting the right cells.

Another very new concept is nanorobots but this hasn't been formally invented yet. Researchers suggest that the public debut of robots that can interact at the virus and bacterium level would be in the next 25 years. [18] The potential of robots small enough to circulate the blood stream with the capability of destroying cancer cells, replacing the immune system of someone with AIDs, synthesising tissues from the most basic building blocks and even fight aging is something that many researchers and scientists are extremely excited about. Such advancement would render invasive and painful treatments like chemotherapy unnecessary in favour of a simple injection.

Nanorobots could build new nerve cells in the spinal cord or where the injury is. They could destroy the faulty nerves and replace them with themselves. However, all these models and ideas are based on a technology that doesn't exist yet but, possibly soon will.

Some people have preconceived ideas about nanotechnology [figure 3] and therefore would be nervous about new developments or even adamantly against it. They may think that nanorobots used in medicine would be built with the ability to replicate. Concerns would arise if the technology is faulty in any way and it would be difficult to eradicate all traces of it from the body. Also, the nanorobots replicating out of control would be alarm anyone going under this treatment. However, these fears are born out of unscientific doomsday ideas created to sensationalize any breakthroughs in this technology. Nanotechnology employed in medicine would not be able to replicate.

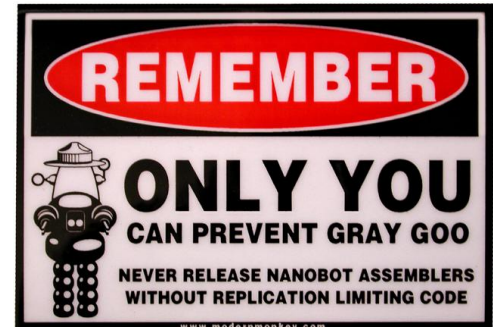


Figure 3 [19]

In Engines of Creation Drexler mentioned the term "grey goo" where nanobots would replicate out of control and consume the planet. It is a scenario many modern scientists don't see as a problem because replicating nanotechnology would be regulated very tightly by all governments.

Some may think that this research is expensive and would see it as a waste of money as they can't see how nanotechnology is benefitting medicine yet. However, this technology wouldn't just extend people's lives, it would improve people's health and well-being; making many people capable of working again or more employable. For example, regaining your sight would mean that you also regain your independence and ability to live alone and earn your own wage. Reducing chances of heart disease with nanorobots destroying any plaque or fatty deposits in the heart would reduce chances of heart attack and therefore taking less time off work. It has already been statistically proven that the medical advances that have benefitted the American economy by trillions of dollars, cost billions of dollars to research. A similar situation is likely with the introduction of nanotechnology [20].

Some may think it would be ethically wrong for artificial robots to be circulating our bloodstream and altering the way our body works. They may consider this a step too far in medicine since we would no longer be in control of our bodies but rather there would be technology behind the scenes. This could also lead to richer, more developed countries being able to cure every disease imaginable while people from undeveloped countries are still unable to feed themselves. The gap of inequality in healthcare will grow and this is uncomfortable for anyone's conscience.

Nanotechnology in medicine can be produced very cheaply and whilst this would be good for public health it would potentially affect businesses involved in drug manufacture and healthcare both of which may adversely affect the economy.

CONCLUSION

The innovative world of nanotechnology in medicine could completely transform healthcare. The way that the technology works at the same scale as biological substances is an extremely important factor into why it could be so radical. This makes it almost perfect to be used in medicine over other scientific disciplines.

The ability to create new neurons wouldn't just benefit people who are paralysed or blind but, people who are suffering from degenerative diseases like MS and Huntington's Disease. This might slow the process as new nerve cells could be created at the same rate as diseased old ones dying. The nervous system affects so much of the body yet it is mainly composed of one type of cell; neurons. If it was possible to find a way to fix this one type of cell, much of this entire system could be treated. Nanotechnology could be the way forward in finding a cure.

Nanotechnology has already proven effective at helping stem cells more efficient at their job by providing support in the form of nanoscaffolding. However, future developments may mean that the controversial use of stem cells would be avoided as nanoparticles could encourage the growth of nerve cells. This technology could even be integrated into the nanoscaffolding system so only the nerve cells surrounding the scaffolding would be affected by this technology.

The possibility of encouraging a cell that originally wouldn't regenerate, to regenerate is down to the fact the technology would be small enough to replace these organelles in the cell that would usually do the job. This would have been impossible with any bigger technology. This shows how well suited nanotechnology is for working with molecular biology and why so many researchers want to take advantage of its attributes.

Like any new technology, new problems, social and ethical, arise as well but, it's difficult to predict to what extent these problems will have on the development of nanotechnology. It could be greeted with open arms by the public or absolute terror.

This paper only highlighted a few elements of how this technology could possibly affect medicine. This may be the very beginning of a new age of medical technology and the implications of being able to change the very nature of cellular biology is something many can scarcely imagine.

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