An investigation into the possible Applications of Nanotechnology In Medical Science

by

Guy Niblett

PASS WITH MERIT

RESEARCH PAPER
BASED ON
PATHOLOGY LECTURES
AT MEDLINK 2010

Abstract
Nanotechnology is a newly emergent area of science. It is not yet fully defined: it is a field of exciting possibilities and opportunities. This paper presents ideas for how nanotechnology could be applied to medical science focussing mainly on drug delivery and cancer treatment. In so doing greatly nanotechnology will enhance the treatment techniques available to patients. While much of what I will be writing about in this paper is not currently possible, and much may never be achieved, I aim to present possibilities for future research and development. Nanotechnology could be applied in a huge variety of ways, and could greatly expand the borders of what is possible in healthcare.

Introduction

Nanotechnology is a subject that has fascinated and intrigued both scientist and science fiction writers for the best part of a century. It is concerned with the science of building structures and machines on a nanoscopic scale, i.e. with dimensions between 1 and 100 nanometres. For a long time this area of science was deemed to be impossible to access, but recent discoveries and inventions have opened up an incredible range of possible uses of nanotechnology and applications to the real world.

The first of these discoveries was made by Smalley and Kroto in 1985, when they produced a third allotrope of Carbon: a spherical molecule containing 60 carbon atoms arranged in hexagons and pentagons. They named this molecule buckminsterfullerene (or a Buckyball) after the famous architect Buckminster Fuller, whose work included many domes of similar structures to this. [1]

This discovery sparked a huge amount of interest in this field and led to the second great discovery. Sumio Iijima, a Japanese scientist who had previously done work in the same field as Smalley and Kroto realised the link between buckminsterfullerene and some of the phenomena he had previously observed, and went on to isolate nanotubes. Nanotubes are cylinders made up of carbon atoms in hexagonal and pentagonal patterns. These are likely to be the most useful component of many nanotechnological devices. [1]

The next invention that has made practical usage of nanotechnology seem possible is the Scanning Tunnelling Microscope (STM), which was developed in the IBM laboratory in Zurich. This device has revolutionised the field of nanotechnology. It essentially works by moving a very fine needle or probe across the surface of the sample that is being analyzed, and by measuring the electronic interactions between the surface of the sample and the probe an incredibly high resolution image can be produced, showing even the individual atoms. [1]

However, this is not its only application. By taking advantage of the forces between the probe and the atoms or molecules in the sample, scientists can use this device to move individual atoms and molecules around. This was a turning point in nanotechnological science, as for the first time it provided a way in which molecules themselves can be manipulated into position to create nanoscopic scale machines. [1]

It is my opinion that nanotechnology could be applied to medicine to achieve astonishing results. This is because so much of what makes medical treatment hard in some situations is the size of the cells in the human body and the impossibility of humans interacting with them directly. With technology on a nanoscopic scale we would be able to directly combat diseases and conditions at the level of individual cells.

So far the applications of nanotechnology to medicine have been fairly limited, mainly due to the practical difficulties that have not yet been overcome. The main application of nanotechnology in medicine has been the encasing of drugs in lipid micelles or buckyballs. Usually this helps to protect the drug while it enters the bloodstream, e.g. protecting the drug as it passes through the stomach if it is administered orally. This

technique has been applied to many types of drug for various conditions, including several cancers (e.g. Kaposi's sarcoma) and oestrogen hormone treatment. [2]
While this has greatly improved delivery systems by protecting the drug from the body, and sometimes the body from the drug (in the case of some chemotherapeutic drugs) it does not help specifically target drugs to particular cells that require it.
Another application of nanotechnology in medicine that has been developed, although it is not yet widely in use, is known as Nanotube Tattooing for diabetics. This is where nanotubes are wrapped in glucose sensitive polymers and then inserted under the patient's skin as a tattoo. These nanoparticles can then change colour depending on the concentration of glucose in the blood, and give an easy to read, cheap and continuous flow of information on the patient's blood sugar levels.
However, I think that there is a huge potential in the application of nanotechnology to medicine that has not yet been exploited. I will discuss three possible applications in this paper: use of nanotubes for improved drug delivery, use of nanocontainers for enhanced drug targeting to specific cells, and the use of nanoscopic scale machines in the body.

Discussion

One simple and possibly quite easily achievable advance in medical technology is the more widespread use of nanotubes for various processes. Nanotubes have already been mounted on STMs and used as probes to insert Quantum Dots into cells. Quantum Dots (QDs) are nanoscopic inorganic crystals that have been designed to be tracked by scientists, either by fluorescence or by other means. These can then be used to observe cellular activity. [3]
I propose that bundles of nanotube fibres could in the future replace all or most hypodermic needles. The advantages they could bring would be tremendous.
The diameter of nanotubes depends on how they are synthesised. Thus they can be at smallest 3nm in diameter [4]. Thus they could be designed to be large enough to allow the drug molecules to pass through their lumens, but too small for anything larger, e.g. viruses or bacterial cells. This could dramatically decrease the rates of infection in patients both in hospitals and perhaps more importantly in non aseptic situations, since the holes left behind by the nanotube bundle would be too small to allow any pathogens to enter the blood stream. Furthermore these nanotube needles would make extremely precise delivery of drugs to specific regions of the body possible.
However there are several issues that would have to be overcome before this could become a viable option. Firstly the nanotubes used for this would have to be extremely long, longer than any that have yet been produced. In addition current nanotube production technologies are very expensive, and so would not be practical for use on the industrial scale that would be required if the nanotubes were put to this use. Finally the precision required to use these needles would be phenomenal, because it would be very easy to damage their fine tips during insertion. Hence either only highly trained professionals would probably be able to administer them, or the process would have to be machine driven.

Building on this point I believe that nanotechnology could be used to improve drug delivery even further, beyond the introduction of the drugs into the body. I think that it could be used to target drugs directly to the cells where they are needed. Current drug delivery systems involving nanotechnology are quite basic. At the moment they are just simple micelles designed to encase the drug and protect it as it enters the body before breaking down [5]. By copying nature we could apply nanotechnology to design a drug delivery system that administers the drug directly and specifically to the cells where it is required. The natural procedure that I think we should imitate is that of receptor endocytosis. This is the process by which cells can engulf and absorb material from outside the cell. The molecules that are to be absorbed by the cell bind onto specific proteins called receptors on the cell's surface. The binding of the molecule onto these receptors cause them to change shape and form depressions called clathrin-coated pits. These pits then enlarge or 'invaginate' pulling the molecule into the cell. Eventually the membrane pinches off around it, sealing the molecule in a vesicle inside the cell. [6]

Thus I propose that the following mechanism would allow drugs to be delivered directly to specific cells. The drug would be stored inside balls of buckminsterfullerene or alternatively larger phospholipid micelles, which would act as the storage device or transport. To the surface of the transport container would be attached molecules specifically designed and manufactured to mimic a molecule that would bind to the membrane of the cells that we wish to target (e.g. mammary cells in the case of breast cancer). These nanocontainers would be injected into the blood stream, and when they encounter the cell they were designed to fuse with, the binding molecules on the transport's surface would interact with the specific receptors on the membrane of the cell. The whole device would then be absorbed into the cell and the drug would be released.

This elegant solution, inspired by nature, could be incredibly useful for the treatment of various conditions, as it would drastically reduce the side effects of certain treatments. For example, chemotherapeutic drugs for treating cancer are designed to kill cancerous cells, but are usually not specific in the cells they damage, hence can cause very serious side effects by damaging cells they encounter even if they are not cancerous. An example of this is Amsacrine, a chemotherapy drug often used in conjunction with others in the treatment of leukaemia, which can cause weakening of the immune system (making the patient vulnerable to other diseases), anaemia, reduced platelet count, ulceration and heart arrhythmias. By utilising nanotechnology in this way these side effects could be radically reduced. [7]

Unfortunately this technique for drug delivery is far from within our reach based on current technology. To transport drugs directly to the target cells like this, firstly scientists would have to engineer and produce molecules of the right shape to interact with the cells, and manipulate them into position on the surface of the buckminsterfullerene molecule or micelle structure (depending on which was being used). This would be extremely expensive and perhaps impractical using current techniques.

A third and final possible application of nanotechnology to medicine is perhaps the one which is furthest away from achievement and yet is by many considered to be the ultimate goal of nanotechnology. This application is the creation of nanoscopic scale robots which would be inserted into the body (probably into the bloodstream) and then would travel around the body fixing cells and fighting diseases. As farfetched as this might seem, it is not entirely impossible.

One method of controlling these nanoscopic scale robots would be to use silicon based computer chips. Since the creation of computer systems there has been a remarkably consistent trend of miniaturisation, of approximately 13% each year [1]. The computing giant Intel recently announced that they were able to produce a silicon chip with gaps as small as 32nm between memory cells. Given that the processing capabilities of these nano-robots would not need to be that great, relatively few of these memory cells would be required, so chips like these (and even smaller ones in the future) could possibly revolutionise the nanotechnology industry. Giving the nano-robots computer chips like this would enable them to interact with the environment around them. For example nano-robots could be used to detect and combat viruses. When a virus invades a cell it takes over the cell's processes and organelles and forces them to replicate the virus. When the cell fills with viruses it bursts, releasing water and other chemicals into the bloodstream. If a nano-robot in the blood were to detect through its sensors a higher than usual water concentration, or perhaps an unusually high concentration of potassium ions (as K^+ are found more frequently inside cells than in the blood, it would be able to react to that, perhaps by searching for the cause, or releasing an antiviral agent. The procedures carried out by these chips would not have to be very complex at all, little more than receiving a signal and responding to it in a prearranged fashion. Another option would be to use other non silicon based computing devices. These could possibly be smaller and cheaper to produce.

The next issue to be overcome is that of movement. In many situations it would probably be acceptable to have these nano-robots as free floating devices in the blood stream that would just be pumped around by the heart with the blood cells, randomly encountering cells and obstacles. However in other situations a nano-robot might need to be designed to be able to travel at its own instigation. The simple solution would be to attach a motor and propeller to the robot, as one would with a ship or submarine. However the problem is encountered with powering it. In the normal world we would use an exothermic reaction (i.e. the combustion of fossil fuels) to produce heat which could then be transferred into rotary motion. Unfortunately, on the nanoscopic scale any heat produced would be dissipated by the vibration of the molecules immediately, before it could be harnessed as useful energy. [1]

A relatively simple solution to this problem would be to use an oscillating chemical reaction (one that causes the reactants to change into products and vice-versa regularly) which changes the pH, for example the Landolt pH-oscillator which is based on the reaction between bromate, sulphite, and ferrocyanide compounds, in conjunction with a pH sensitive polymer that changes in volume depending on the pH of its environment. [9] The changing pH would cause the polymer to swell or shrink, each time in so doing it would displace fluid and push the robot forward. [1]

Unfortunately there are several other physical issues with the deliberate movement of nano-robots through liquid. Firstly due to the relative size of the robot, it would experience much greater resistance forces due to the viscosity of the medium through which it was travelling. This would mean that any progress it does make would be very slow and energy wasteful. Secondly there is the problem of Brownian Motion. This is the random movement of free floating particles caused by collisions with other particles. While this does not affect larger objects because of relative size differences, a nano-robot would experience noticeable forces (due to the smaller size and the momentum changes caused by each collision), which would make general movement difficult and controlled or precise manoeuvres virtually impossible. [1]

What would these nano-robots be made of? The ultimate goal of nanotechnology would be to have a central chip controlling a motor that would move nanotube axles and turn cogs with teeth that can engage with other cogs and so on. However in reality I suspect that the mechanisms will be rather simpler than this. I suspect that the robots will essentially be computer chips with perhaps a motor on the back and sensors that can bind with other molecules causing an electric impulse to travel to the chip, which might in turn trigger the release of a chemical.

I propose that the following would be an extremely useful and effective application of this form of nanotechnology to medicine. Almost all forms of prostate cancer cells contain the same transmembrane proteins. These protein specific antigens could be used by the nano-robots to identify the target cell. This could be done by attaching a molecule to the nano-robot that could bind with the protein, and in so doing change its shape. This shape change could cause a piezoelectric crystal (a crystal that can release electric impulses when its shape is changed) attached to it to send a signal to the central chip. On receiving this signal the chip would either release or unblock enzymes that could cut through the cell membrane, killing the cancerous cell. The advantage of this would be that it would only attack the cancer cells, leaving all other healthy cells untouched. [10]

For all these applications of nanotechnology, the main issue is assembly. Using current technology the only way these nanodevices would be produced is individually by hand (using an STM) or by machines. Either way it would be incredibly expensive and also very slow, especially given the huge number of these devices that would need to be produced.

One suggestion that has been made is to design these devices so that their structures are the most stable arrangement for all of their constituent parts, and simply mix the parts together. [1] They would be moved around by Brownian motion, randomly colliding with other parts and forming weak bonds between them. However, unless they were in the correct place, the parts would break apart again as the forces between them would not be strong enough. When two of the parts collide in the correct way, the bond formed would be strong enough to hold them together permanently. This would be an easy way to produce these nanodevices in a low energy and fairly time efficient way, also possibly allowing the nanodevices to self assemble in situ, i.e. inside the body. However this is self assembly rather than self replication, as the individual components of the nanodevices would still need to be manufactured outside the body.

While enabling these devices to self assemble from pre-made components would be faster and cheaper, many people think that fully self replicating machines would be dangerous because we would be unable to stop them.

The idea and fear of nanodevices being able to self replicate and so multiply out of control destroying the world has long been the subject of science fiction writers and conspiracy theorists, known as the infamous ‘grey goo theory’. It is thought that if nano devices are able to self replicate their populations will grow exponentially, eventually consuming the world. However, I do not think this is a valid concern, since realistically, the component parts necessary to build nanodevices are not naturally occurring, so self replication is unlikely ever to be an option, so all the components will require production by separate machines controlled by humans.

Conclusion

In conclusion, I think that nanotechnology is as yet a newly born area of scientific understanding that has a huge amount to give to society in general but more specifically to medicine and health care.

With the improvements and technological advances that I am certain will come in the future, the face of medicine will be changed completely. These changes will start small, by applying new discoveries and knowledge to current medical problems to improve them, but eventually nanotechnology will be applied in its own right to create entire new areas of health care.

I say this because I think that the scientific understanding necessary to develop nanotechnology in this way is already present, and now it merely needs to be applied effectively, after the mechanical difficulties have been overcome, as I am sure they will.

I believe that the main focus of this nanotechnological revolution will be in cancer treatment and drug delivery. This is because of the success we have encountered in treating most other conditions; cancer is one of the relatively few left for which we have limited treatments.

I do not think that this will be the only area in which nanotechnology will be applied in the future. As we enter further into the 21st century I think that other conditions such as obesity and the conditions associated with it, and old age related diseases will become major concerns as our lifestyles change and the average life expectancy increases. This could include repairing neurons to treat dementia, or helping remove plaques from arteries to prevent atherosclerosis or any of the countless other possible applications of this new and exciting field of science.

References

- Atala, A., Lanza, R., Thomson, J.A. (2010), Principles of Regenerative Medicine, Academic Press [3]

- Bouchelouche, K., Choyke, P., Capala, J. (2010) Prostate Specific Membrane Antigen – A Target for Imaging and Therapy with Radionuclides. Discovery Medicine. [10]

- Cheung, C.L., Kurtz, A., Park, H. Lieber, C.M. Diameter-Controlled Synthesis of Carbon Nanotubes. In The Journal of Physical Chemistry, 106, 2429-2433[4]

- Crook, C.J., Smith, A., Jones, R.A.L., Ryan, J.,(2002) Chemically induced oscillations in a pH responsive hydrogel. In Physical Chemistry Chemical Physics, 4, 1367-1369.[9]

- Jones, R.A.L (2007), Soft Machines: Nanotechnology and Life, Oxford university press [1]

- Endocytosis http://www.biologyreference.com/Dn-Ep/Endocytosis.html [6]

- Intel Atom Processor http://www.intel.com/technology/atom/ [8]

- Amsacrine and side effects http://www.macmillan.org.uk/Cancerinformation/Cancertreatment/Treatmenttypes/Chemotherapy/Individualdrugs/Amsacrine.aspx [7]

- Nanotechnology and medicine http://www.nanotechproject.org/inventories/medicine/ [2]

- Nanotechnology: What it can do for Drug Delivery http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1949907/ [5]