NANOTECHNOLOGY
And its applications in neurological sciences

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Abstract

Since the discovery of Nanotechnology, it has become an increasingly promising area of research which has the potential to revolutionise modern medicine. Current research of nanomedicine focuses on its uses as drug delivery devices, through the utilisation of buckminsterfullerene. As well as other carbon based Nano-structures, and their potential to build Nanorobots in aid of cell repair. But this paper will especially focus on its applications to aid the ever developing field of Neuroscience and Neuro-engineering; through the employment of Neuroelectric interfaces and look to offer possible future applications for these visionary technologies.

Introduction

Nanotechnology is an innovative new technology on the frontline of modern scientific research. Focusing on the manipulation of matter on a scale of $10^{-9}$, it allows us to create functional structures through the “bottom-up” approach; where these systems are built from single atoms or molecules assembled chemically. Or the “top-down” approach may be used where these nanostructures are created from splitting down larger systems to its base elements. Nanotechnology is taken where the entity’s smallest functional structure of at least one of its dimension on the nano-scale (normally ranging from 1 ~ 100 billionth of a meter).

When utilising the “top-down” approach (example shown by Figure 1), one of the challenges faced is the fact that entities on a nanoscale have very different physical and chemical properties to those on a macro or even micro scale. For such small objects, gravity becomes significantly less important; however forces such as van der Waals and surface tension have much greater impact on the structures. Once a larger object is split down to its simplest elements, the electronic assets of solids are altered; these quantum materials have completely different physical behaviour to their larger alternatives; it is these phenomenon which create much of the enthalpment for the development of Nanomaterials. As the scale of an article is reduced, its surface area to volume ratio increases; this changes its chemical interactions with other structures, therefore making even inert materials such as gold efficient catalysts for chemical reactions. Down at this scale some insulators become conductors due to the quantum size effect and some substances can also be turned transparent.

The “bottom-up” approach employs a very different technique of manipulating single molecules to create a bigger and more useful system (example shown by Figure 2). Current research has enabled scientists to influence small molecules to form specific shapes but in the near future, small Nanoscale machines may be built which have structures similar to machines on the macro scale and have specific functions. On this scale, molecules have the tendency to organise themselves into small structures. By modifying the organization of these molecules, scientists may be able to persuade them to join in a particular order forming a useful composition; one way of performing this is through the employment of the Watson-crick base pairing rules.

Since the idea of nanotechnology was first envisioned in 1959 by the Nobel Prize physicist Richard Feynman, his speech “There’s Plenty of Room at the Bottom”, suggests the use of one set of specific instruments to manoeuvre another smaller set of instruments and so on, until the smallest set is able to direct subjects on the nanoscale (i.e. molecules and even single atoms). Although at the time this hypothesis was commonly seen as theoretically plausible, the first breakthrough in fulfilling this vision came after the first studies of cluster science and the development of the first scanning tunnelling microscope.

The creation of the fullerenes led by that of the buckminsterfullerene - C$_{60}$ - opened many new possibilities for application of nanotechnology, especially in the field of medicine. For example the round, symmetrical carbon structure unlocked new ways of drug delivery, in which their bioavailability is enhanced.

Another of nanotechnology’s pioneering applications to medicine is its potential to treat a wide range of neurological ailments through the use of Neuro-electronic interfaces or sometimes referred to as Brain-machine interfaces (BMI), which provides a direct interactive pathway between the brain and external
mechanisms such as a computer. Previous to nanotechnology, main area of focus for this technique is its availability to support or repair of sensory-motor functions of the human brain through invasive, partially invasive and non-invasive methods; these methods are made possible because of the Neuroplasticity of the human brain.

The use of the invasive method involves implantation of the BMI directly into the grey matter of the human brain through neurosurgery. This type of BMI produce the best quality of signal but since it is rested on the brain, over time it causes scar-tissue to be built up around the implant resulting in the reduction or even loss of signal, this is one of many problems which face this form of BMI as the body may take some time to become familiar with these intrusions due to the size and nature of these implants. Successful human trials of this procedure have allowed patients with acquired blindness to regain sight, first of which was conducted on “Jerry”, by the researcher William Dobelle in 1978. Later in 1988, research conducted by a team lead by Philip Kennedy and Roy Bakay was the first to install an implant of this nature which created strong enough signals to stimulate movement in patient who has previously suffered a brain-stem stroke, which lead to the development of the “BrainGate™” chip (shown in figure 3) implant and interface in 2005.

The signal produced by partially invasive BMIs is weaker than those produced by the invasive form, as the implant is placed within the skull of the patient but not in contact with the brain. However this form of Neuro-electronic interfacing is much less likely to cause harm to the brain and even over time very little scar tissue will be formed as there is a much lower risk of damaging the delicate grey matter. The application of this procedure mainly focuses on Electrocorticography, a technique that measures the electrical activity of the brain, employing electrodes within a plastic pad positioned above the cortex. The non-invasive BMIs are similar to partially invasive implants, and have also been successful in controlling the movement of muscle implants, but the signals are of much lower resolution, due to the skull’s ability to reduce the electromagnetic waves produced by neurons, therefore scattering the signal.

Through the research into nanotechnology, a new alternative form of BMI is being revealed. By building a nanoscale structure which is able to detect and control nervous impulses given off by the brain, external computers can be directly linked to the nervous system, allowing signals to be measured, interpreted and a response signal sent back to the brain. This technique will be much less damaging to the brain than the invasive method, but at the same time signals will be of the highest resolution as these may be implanted directed onto the grey matter of the brain.

Discussion

The challenges associated with nanotechnology applications in neuroscience are numerous, but the impact it can have on understanding how the nervous system works, how it fails in disease and how we can intervene at a molecular level is significant. Ultimately, the challenges and opportunities presented by nanotechnology stem from the fact that this technology provides a way to interact with neural cells at the molecular level, which has both positive and negative aspects. The ability to exploit drugs, small molecules, neurotransmitters and neural developmental factors offers the potential to tailor technologies to particular applications. For example, neural developmental factors, such as the cadherin, laminins and bone morphometric protein families, as well as their receptors, can be manipulated in new ways. Nanotechnology offers the capacity to take advantage of the functional specificity of these molecules by incorporating them into engineered materials and devices to have highly targeted effects.

This discussion also suggests the main technical challenges that are encountered when using nanotechnology applications in neuroscience: the need for greater specificity; multiple induced physiological functions; and minimal side effects. Greater specificity of interactions with target cells and tissues will result in more significant and specific physiological effects, which should also reduce undesirable and deleterious side effects that are induced by the technology. Another important challenge is the requirement for technologies that are able to multitask, carrying out a diverse set of specific cellular and physiological functions, such as targeting multiple receptors or ligands. This is particularly important when attempting to address multi-dimensional CNS disorders that are the result of numerous interdependent molecular and biochemical events (for example, secondary injuries following traumatic brain injury or spinal cord injury). At
present, synthetic and engineering processes are not advanced enough to allow nanotechnologies that have been designed to interact with the nervous system to fully meet these criteria. From a biological perspective, the most significant successes of nanotechnology applications in neuroscience will be those that appreciate a detailed understanding of neurobiology and take advantage of the known (and unknown) molecular details. As suggested above, the main challenge is the ability to design and use more sophisticated technologies that are able to carry out highly targeted and specific functions while minimizing nonspecific interactions. To achieve this, the design and engineering aspects of nanotechnology as well as our understanding of the underlying neurobiology are crucial. This, in turn, will require more interaction between neuroscientists and physical scientists such as chemists and materials scientists.

Nanotechnologies designed to interact with CNS cells and processes in vivo must take this complexity into consideration, if only to avoid disrupting it. Failure to do so may result in unforeseen and unacceptable ‘side effects’ in the nervous system and/or other physiological systems. A significant challenge in in vivo applications of nanotechnology is that they are designed to physically interact with neural cells at cellular and sub-cellular levels, but ultimately aim at engaging functional interactions at a systemic level, which usually involves large groups of interacting neurons and glia. At present, there are only a few applications of this type; nonetheless, although technically and conceptually challenging, these types of application could have a significant impact on clinical neuroscience. However, there is still a tremendous amount of work to be done.

Apart from physiological complexity, the second main consideration for in vivo applications of nanotechnology is that they must consider the highly anatomically restrictive nature of the CNS. The structures of the CNS are well protected from mechanical and physical injury, and are immunologically privileged behind the Blood-Brain and blood–retina barrier, which have unique molecular and cellular environments. Nanotechnologies designed for in vivo applications must be efficiently delivered with minimal disruption to these structures before it can carry out its primary function. This will surely present significant technical challenges. Similarly, extreme care must be taken to understand and avoid potential safety pitfalls, including both systemic and local side effects associated with the delivery and primary function of the applied technology — an issue that is unique to in vivo nanotechnology. As mentioned above, investigating the safety of nanotechnologies is an active and important area of research. Despite all these challenges, the applications of nanotechnology both in vivo and ex vivo offer tremendous opportunities for understanding normal physiology and for developing therapies.

Applications of nanotechnology to neuroscience are already having significant effects, which will continue in the foreseeable future. Short-term progress has benefited in vitro and ex vivo studies of neural cells, often supporting or augmenting standard technologies. These advances contribute to both our basic understanding of cellular neurobiology and neurophysiology, and to our understanding and interpretation of neuropathology.

Although the development of nanotechnologies designed to interact with the nervous system in vivo is slow and challenging, they will have significant, direct clinical implications. Nanotechnologies targeted at supporting cellular or pharmacological therapies or facilitating

Direct physiological effects of in vivo will make significant contributions to clinical care and prevention. The reason for the tremendous potential that nanotechnology applications can have in biology and medicine in general and neuroscience in particular stems from the capacity of these technologies to specifically interact with cells at the molecular level.

Of course, the use of Brain-Computer Interfaces has sparked some debate among people especially since one of its future applications is the enhancement of human capabilities and mind control (brain pacemakers are now successful in treating depression). Nonetheless, this technology has not yet attained its full maturity and is therefore still relatively below the social radar. As of today, this technology is seen more to help much in fighting against disability through prosthetics and as a treatment for neurological ailments such as depression.

Many sci-fi scenarios can be related to neural interfaces but in reality researchers are heavily working on the potentials of this exciting idea. What is already reality today is something called Neuroprosthetics, an area of neuroscience that uses artificial micro devices to replace the function of impaired nervous systems or sensory organs. Different biomedical devices implanted in the central nervous system already have been developed to control motor disorders or to translate wilful brain processes into specific actions by the control of external devices. These implants could help increase the independence of people with disabilities by allowing them to control various devices with their thoughts. The potential of nanotechnology application in neuroscience is widely accepted. Especially single-walled carbon nanotubes (SWCNT, as shown in figure 4)
have received great attention because of their unique physical and chemical features, which allow the development of devices with outstanding electrical properties. In a crucial step towards a new generation of future Neuroprosthetics devices, a group of European scientists developed a SWCNT/neuron hybrid system and demonstrated that carbon nanotubes can directly stimulate brain circuit activity.

Examples of existing brain implants include brain pacemakers, to ease the symptoms of such diseases as epilepsy, Parkinson's Disease, Dystonia and recently Depression; retinal implants that consist of an array of electrodes implanted on the back of the retina, a digital camera worn on the user's body, and a transmitter/image processor that converts the image to electrical signals sent to the brain; and most recently, cyberkinetics devices such as the BrainGate™ Neural Interface System that has been used successfully by quadriplegic patients to control a computer with thoughts alone. Thanks to the application of recent advances in nanotechnology to the nervous system, a novel generation of neuro-implantable devices is on the horizon, capable of restoring function loss as a result of neuronal damage or altered circuit function. The field will very soon be mature enough to explore in vivo neural implants in animal models.

Over the past few years, there has been tremendous interest in exploiting nanotechnology materials and devices either in clinical or in basic neurosciences research. However, so far the interactions between carbon nanotubes and cellular physiology have been studied and characterized as an issue of biochemical mechanisms involving molecular transport, cellular adhesion, biocompatibility, etc. These new findings boost scientists' understanding of interfacing the nervous system with conductive nanoparticles, at the very fast time scale of electrical neuronal activity which in mammals determines behaviour, cognition and learning.

An interesting piece of current research is one being performed by Matthew Nagel at John Donoghue's lab at Brown University. He is a quadriplegic and from the top of his head emerges a pedestal plug that is connected to a socket that runs to a computer. Hard-wired into that computer through a technology called BrainGate, Matthew can move the cursor entirely with his brain waves. He has become so adept that he beat a wired reporter in a video game when the reporter came to see the lab.

Also, At Emory University, Drs. Roy Bakay and Phillip Kennedy treat J.R., a 53-year-old man who has locked-in syndrome because of a brain stem stroke. They have implanted J.R.'s brain with glass ampules containing electrodes and coated with neurotropic chemicals taken from his peripheral nerves. His neurons migrate into the ampules and connect themselves to the electrodes. Now this man, who could not communicate with the outside world, is hard-wired to a computer where he can move a cursor to spell out words and select phrases.

In the U.K. in 1998, Kevin Warwick, professor of cybernetics at the University of Reading, England, and as much a showman as a scientist, underwent an operation to surgically implant a silicon chip transponder in his forearm. The chip is connected wirelessly with his office; as he enters, computers fire up, lights turn on, heaters activate. A 100-electrode array implanted in the median nerve of his arm in 2002 allows him to operate a remote prosthetic arm and to feel sensation sent to him by a less complex implant in his wife, Irena.

The integration of information technology into the human nervous system has been a relatively recent and quick development. While prosthetics have a long history, and the use of self-contained or feedback information technology in assist devices (like cochlear implants or pacemakers) is decades old, what is new about the types of developments listed above is that they try to integrate or translate neural processes into external outcomes. Not all brain-computer interface (BCI) technologies are implanted. A number of researchers are trying to explore how to translate brain waves or fMRI signals into real time external responses. Jonathan Wolpaw at Wadsworth Center, New York State Department of Health in Albany, for example, uses electrodes on the surface of the scalp to help those who are paralyzed or have movement disorders to control cursors or other electronic equipment using brain waves alone. Along with BCIs, such as artificial vision technologies, we are for the first time beginning to treat the human brain as "wetware" that we can connect to other information technology systems. The social and ethical implications of such a development are vast. Clearly BCIs have the potential to help those whose injuries or diseases have left them with a functioning central nervous system that cannot control the actions of the peripheral nervous system. In that sense these technologies, particularly if they can be developed to use transcranial impulses robustly and
specifically, can be low-impact ways to give such people an enhanced quality of life and control over their environment.

BCIs also raise some concerns, however. In cases like Matthew Nagel’s (whose BrainGate device has since been removed), the computer that translates his brain waves into signals “learns”; it does increasingly well in understanding what Nagel is trying to do and translating it into action. But this computer is hard-wired into Nagel’s brain; as it learns, its relation to Nagel’s intentions changes. In other words, this extension of Nagel’s brain is itself a developing intelligence of a sort, now integrated into Nagel’s own brain processes.

Imagine a period in the near future where we have developed the interfaces between computer and brain to a degree where the information flows in both directions; the brain sends out information to the computer, and it also receives impulses from the computer, which learns and develops. Perhaps that computer is also connected to the Internet. Now we have the human brain hard-wired into the Internet, itself now a wetware node on that system.

Research is being done on brain prosthetic (example shown in figure 5). Theodore Berger and his colleagues at the University of Southern California have designed a brain chip that could bypass lesions in the hippocampus. The chip “reads” the signals entering the hippocampus, processes them just as the hippocampus would, and relays them to the tissue on the other side of the lesion. The USC researchers have tested the concept on rat brain slices with success.

So not only will BCIs connect us through wires to external information technologies, the information technology itself may be integrated into our neural tissue. For the first time, fundamental neural processes in the central nervous system will be part organic, part synthetic. A whole field of cyborgology has developed to try to understand the social, political and ethical implications of our becoming cyborgs, part organic and part synthetic, human/machine hybrids. Books like "Cyborg Citizen: Politics in the Posthuman Age" argue that the very nature of our relationships with each other, as well as with social institutions, will change as we integrate technologies into our physiology and as we integrate our physiologies into our environments.

Conclusion

We can expect that more and more types of injuries and diseases will be treated with BCIs. It is too early to know what ethical and social issues will emerge from these technologies. Clearly, however, they will pose challenges for privacy, as machines are able to tap into our private brain processes. They will challenge personal autonomy, as experiments with other animals show how the brain can be conditioned or even disrupted with implanted technologies. And they will challenge our conceptions of selfhood, when computers are part of the very functioning of our thought processes. Psychiatry will have to develop new ways of understanding the cyborgian mind. A new breed of medical technologist will have to monitor, repair and fine-tune the complicated devices that are interacting with the human brain, and that may include an unprecedented amount of control over people's "minds." Psychopharmaceuticals are being developed now to try to control cognitive and affective traits, and it is likely that BCIs will be able to have similar effects. We already see the beginning of that process with the use of deep brain stimulation for psychiatric disorders.

Human beings have evolved for over 100,000 years with the brain isolated in the skull, inviolate. It is inviolate no more, with not only BCIs but brain imaging technologies revealing the detail of brain function, or with transcranial magnetic stimulation able to shut off discrete areas of the brain. The ability to access the brain, to understand its inner workings, to connect it to external devices, promises remarkable resources to aid the infirm as well as worrisome opportunities to cause harm. It is important to develop these technologies with a careful eye towards using them responsibly.
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