Emerging Technologies

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March 6, 2008

1 Introduction

In the following essay three emerging technologies are outlined in the fields of nanohealing, solar energy and neuron control. Outlines of the technology and research behind them are presented for each, with two being supported and the third being argued against. Each technology is evaluated based on its contributions to society, its positive and negative externalities and its possibility for misuse.

A Nanohealing

In the early 1990s Shguang Zhang and Alexander Rich, biologists at MIT, discovered that a naturally occurring oligopeptide[1] known as EAK16 present in zuotin, a yeast protein, could self-assemble into a membrane of nano-scale fibrous grids or *scaffolds*. These scaffolds were found to form spontaneously under the addition of salt to a solution containing the oligopeptide. Consisting of interwoven filaments between 10 and 20 nanometres in diameter, Zhang and Rich observed EAK16 scaffolds to be extremely stable and robust even under high temperatures, high and low pH levels and protease digestion. This self-assembled nanostructure occurs due to the arrangement of hydrophilic and hydrophobic elements that respectively are attracted to and repelled from water. When present in water the peptides do not however assemble into the scaffold; introduction of hydrated salt ions, such as ionised Lithium, Sodium, Potassium or Caesium initiates the self-assembly process [A1].

EAK16 was systematically re-engineered into RAD16 in which certain amino acid types were substituted for other amino acid types across the

[1] A polymer string of amino acids typically smaller than a string of amino acids forming a protein.

whole peptide. RAD16's altered amino acid sequence results in a similar structure to EAK16 with differences in the structural twists at more dense areas of the fibrous elements in the scaffold [A2]. Both EAK16 and RAD16 were found to support the attachment of various mammalian cells from humans, rats, hamsters, chicken and mice. RAD16 in particular allows cell attachment to occur independently of naturally occurring cell adhesion motifs, known as RGD, that can be found in some, but not all, cells. The cell adhesion property of EAK16 and RAD16 directed research in applying these self-assembling scaffolds for tissue regeneration and tissue transplantation. Another notable property arising from this early work showed that both EAK16 and RAD16 did not elicit anti-body production in mammalian immune systems [A2] therefore an organism's immune system will not reject the peptides. Hence these peptides have the desirable property of a lack of *immunogenicity* that is important for their application in internal medicine.

Since Zhang and Rich's discovery of EAK16's self-assembling behaviour research has continued, in chemistry and biology, in the design of macromolecular materials and nanomaterials. More recently oligopeptides have been applied and tested for aiding tissues regeneration with remarkable results due to the scaffold's cell adhesion property and three-dimensional structure that mimics naturally occurring extra-cellular matrices for tissue repair. Such work lead by Rutledge Ellis-Behnke, also at MIT, uses these oligopeptide scaffolds to promote the regeneration of neurons in mammalian vision systems [A3]. Tissue regeneration at any point within the central nervous system is difficult to achieve due to scar tissue formation, large gaps in tissue and the failure of neurons to start the regrowth and axonal extension procedure. Application of RAD16, and subsequent scaffolds, creates an environment that bridges gaps in tissue giving a structure for cells to attach to and move along between damaged sites hence promoting axonal extension of neurons and preventing formation of scar tissue. The organism's internal chemistry provides the necessary catalysing salt ions to form the scaffold and will eventually break the scaffold down into harmless, natural, and possibly even beneficial amino acid constituents. Ellis-Behnke and his team carried out experiments on hamsters making incisions in the visual areas of their brains. These peptides, in the form of a solution, were then applied to the site of the incision and subsequent changes observed. In 100% of cases, both young and old animals, the scaffold very quickly, within 24 hours, appeared to already be knitting together the site of the injury. Within 30 to 60 days the site of the injury was almost entirely indiscernible with the hamsters regaining an identifiable return in functional vision.

Most recently these nanoscale scaffolds have been used for hemostasis — the staunching of bleeding. Ellis-Behnke and his team stumbled upon using the peptide scaffolds for gaining hemostatic control during previous neural regrowth experiments. Subsequent experiments in hemostatis have been carried out with NHS-1, a solution containing RAD16 peptides, on seven different kinds of tissues in rats. These experiments demonstrated rapid staunching of blood flow within 15 seconds internally and externally [A4]. For example, cutting a high-pressure femoral artery would take 6-minutes to reach natural hemostasis in control experiments whereas hemostasis was reached within 10 seconds in experiments where NHS-1 was applied to the incision.

Ellis-Behnke conjectures that this type of technology could revolutionise surgery and trauma treatment. Surgery commonly requires surgeon's to continually suction blood away from the site of operation, taking time and sometimes requiring blood transfusion for the patient. Application of the peptide solution would provide almost instantaneous hemostasis and, as it is a clear gel, sustains a clean and visible environment to work in. The peptide solution approach is superior to current hemostasis techniques which are typically slow, require lengthy preparation procedures or leave indigestible by-products in the wound. Conversely the NHS-1 peptide solution provides rapid hemostasis, has a long shelf life, has no preparation needed prior to use, is naturally broken down by the body and has regenerative benefits. This technology would be extremely beneficial in situations where patients are in critical conditions, through injury or during surgery. Not only will this be practically useful but if the technology gains success it will further promote research in nanomaterials and nanotechnology, particularly in medicine. One criticism, however, is the large amounts of animal testing that have been, and are currently being carried out. Many of the experiments carried out intentionally cause injury to animals, some of which are left to die for control experiments. It remains for the solution to be tested on humans but testing should and must happen before it can be approved for use. Once approved this technology has enormous potential for helping to save lives, revolutionising treatment, and reducing surgery risks.

B Quantum-Dot Solar Power

In the 1970s a structure known as a quantum well was developed based on very thin, two dimensional structures of semiconductor material which, due to their structure, confine particles to move in only two dimensions. This confinement of particles, particularly electron-pairs (see below), in two dimensions reduces the number of states in which the particles can exist, essentially quantising the states into bands. Quantum wells are typically used in optics for lasers and detectors, made possible by their high optical performance and high levels of fine-tuning based on the well dimensions [B5]. Research into quantum wells lead to research into structures confined to one dimension, a quantum wire, and zero dimension structures, effectively a single point. These zero dimension structures, or quantum dots, are very small, often approximately 50 atoms in diameter. Quantum dots produce a very different behaviour to bulk semiconductors, or quantum wells; the electron-states are discrete with a discrete density of states, that is the states are not continuously dense, but are sparse presenting a behaviour like the discrete sparse states of atom electron bands [B5].

Physically a quantum dot is a nano-scale crystallite of a semiconductor. Its physical properties confine *excitons*, a quasi-particle which can explained as a binding of an electron with its *electron-hole*. An electron-hole denotes the absence of an electron in an energy band around a nucleus where an electron previously existed. The disposition of an electron between bands leaves an electron-hole that is positively charged hence attracts the original negatively charged electron. The exciton is lost when the electron transitions back to its previous state. Whilst the electron and electron-hole are disassociated they may move separately through closely bound atomic structures with a varying radius depending on the amount of separation between neighbouring atoms [B6]. If a photon that has an energy multiple times that of the semiconductor's band gap[1] is incident to a quantum dot then the quantum dot releases several electron-hole pairs. Quantum dots are useful for constructing solar energy cells due to these multiple excitons produced by incident photons. Typically bulk semiconductors used in solar cells exhibit one exciton release per photon absorption where excess photon energy above the band gap is dissipated as heat. The three-dimensional confinement within quantum dots greatly enhances exciton multiplication. For example quantum dots made of Lead Selenide at the scale of 4-6nm have been shown to release 3 excitons [B7] per incident photon. Further work has shown the release of seven excitons in Lead Selenide and Lead Sulfide quantum-dots with photon energies 7.8 times the band gap [B8].

The hypothesis is that if these excitons can be captured before the electron-pair closes then a much higher charge can be drawn hence solar cells can be made at a higher efficiency than current "bulk" semiconductor solar cells. Previous techniques of bulk semiconductor solar cells are known to be theoretically capped at 32% efficiency due to loss of the photon energy as heat to the surrounding substrate. Thermodynamic calculations for quantum dots sets the theoretical limit at 42% efficiency for a quantum yield of 200%, that

[1] The energy difference between the covalent band and conduction band.

is the release of twice as many excitons, or 43% with a quantum yield of 300%, therefore the increased efficiency is gained in the release of two excitons. Reaching the 32% efficiency for current solar technologies is already very difficult to achieve in practice. Quantum dots therefore offer a new, more efficient way to produce solar cells. However current difficulties lie in capturing the multiple excitons produced before they disappear. The typical life time of multiple excitons is less than 100ps whereas single excitons typically have a lifetime greater than 6000ps [B9].

In support of this technology consider the current situation of world energy usage and its impact on the Earth. The population of humans and their power consumption increased dramatically during the 20^{th} century. The levels of CO_2 in the atmosphere have been estimated at increasing from roughly 275 parts per million (ppm), to 370 ppm with current climate models predicting an increase to 550 ppm during the 21^{st} century [B10]. It has been hypothesised that currently experienced warming and subsequent warming of the global temperature will be as much as 3-4°C by the end of next century representing a climate change occurring much rapidly than warming experienced from natural causes [B11]. Effects such as the depletion of coral reef barriers, disintegration of the West Antarctic Ice Sheet, which would cause sea level to rise by 4-6 metres under complete disintegration, and the halting of large-scale ocean circulations are amongst possible effects of an increase in the Earth's global temperature by as little as 3°C [B12]. Proposed atmospheric targets for CO_2 levels are estimated at 450 ppm to stall these negative effects caused by warming, but lower targets are preferable.

Current energy consumption is roughly 12-13 TW, 85% of which is provided by the burning of fossil fuels. Significant evidence gives weight to the argument that the continued burning of fossil fuels is causing the effect known as global warming by increasing CO_2 concentrations in the atmosphere, trapping radiant heat within the atmosphere. Moreover fossil fuels are sourced from a finite amount of resources distributed under the Earth's surface.

Thus research is being carried out to develop energy sources that are renewable and which do not further impact the environment. The Sun provides an abundant source of continuous energy, roughly 100,000TW, far greater than our needs. However the sun's energy is difficult to harness efficiently. Current photovoltaic solar technology can provide some of this renewable energy but is currently limited by its efficiencies and cost. At the present rate of 13TW the current needs could be met by covering 0.1% of the Earth's surface with photovoltaic cells working at 10% efficiency [B13]. As only 29.2% of the Earth's surface is land this would require 0.45% of the Earth's land to be covered with photovoltaic cells, ignoring supporting infrastructures. This is equivalent to roughly a square photovoltaic grid of 67m by 67m per square kilometre of the Earth's land surface, a staggering feat. Not only is this difficult to achieve physically, but financially. Currently the most efficient solar energy sources provide energy at roughly \$0.25-0.65/kWh contrasted with \$0.05/kWh for standard fossil fuelled electricity [B13].

Quantum dot solar cells could help alleviate these problems. In terms of cost QD solar cells deliver electricity at \$0.02-0.04/W contrasted to current photovoltaic cells at \$3.50/W [B14]. Furthermore their tiny size allows them to be applied to a flexible substrate, better for mapping to environments, with increasing success in chemical synthesis of quantum dots via polymers. If quantum dot solar cells could be provided at 40% efficiency the land surface requirement to meet the total current Earth power consumption would drop to roughly 0.11%. Clearly further effort needs to be made in reducing consumption and developing other technologies for providing the Earth's power as completely supplying all power via solar energy plants on land is still implausible. Promising research using solar technology has suggested creating orbiting solar arrays or solar arrays on the moon that transmit power through targeted microwaves back to a collector source [B10]. The work with quantum dots is a step in right direction but needs further research to improve efficiency and make it practical. So far it provides some very promising claims which should be taken notice of in our current situation of a desperate need to reform our energy patterns.

C Neuron Control

For a long time neuroscience has strived to develop methods for exercising finer control in understanding the function of neurons in the brain. Two main approaches employed in the last 30 years for stimulating and observing the brain have been photostimulation and electrodes. Photostimulation, which uses light to stimulate neurons, is more precise than the use of electrodes, which involves a physical device providing an action potential. A particularly useful technique in neuroscience is the targeting of functional groups, or classes, of neurons. However classes of neurons are often sparsely distributed throughout tissue, interleaved with other neuron classes, not aggregated in to mutually exclusive physical groups. The application of photostimulation does not have fine enough control as it stimulates neurons indiscriminately in the affected area. Additionally fine control in the use of photostimulation is difficult to achieve without considerable restraining of the test subject as the exact position is crucial. These difficulties have motivated research in finer control and observation of individual neurons and classes of neurons to aid neuroscience research. Much development has occurred within the last ten years in a new technique in which neurons are genetically engineered to contain a "switch" triggered by light.

In the early 21^{st} century Zemelman, Lee, Ng and Miesenböck demonstrated an extremely precise technique for targeting all neurons in a specific functional class, even those embedded sparsely in tissue [C15] [C16]. Not only does this technique discriminate neuron types but it does so for any physical configuration of neurons without the need for a completely stationary subject.

Neuroscientists previously hypothesised that different classes of neurons had genetic markers which could be used to identify the class of the neuron, even if there was no functional characteristic that could be seen to differentiate the group from other similar neurons [C15]. Genetic markers can be used to select neuron types to genetically encode extra proteins for emitting light, known as *indicators*. Zemelman and Miesenböck rejected this idea as a practical observation technique as the application of these indicators has uncovered very little new scientific knowledge. Instead they proposed genetically encoding classes of neurons with a protein that is sensitive to light which can then be illuminated to provide stimulation and triggering. Photoreceptors in the vision of invertebrates presents a simple, suitable behaviour for developing neurons with specific light sensitivity. Experimentation with different invertebrate photoreceptor proteins encoded into xenopus oocytes — female germ cells in frogs — uncovered a configuration of three proteins that could provide appropriate photosensitivity to light in the region of 400nm-600nm [C16]. The DNA encodings for these proteins were introduced into *in vitro* neurons via calcium precipitate transfection, a method of dissolving DNA that can then be introduced into cells modifying their mRNA — active copy DNA — assuming all the necessary structures and promoters are in place. Further experimentation in fruit flies [C17] used a similar technique with a different protein, found to be more optimal for neuron control in this case, responding to long wave ultra-violet light at 355nm. Experiments were successful, using light stimulus to turn off parts of the flies brain, removing the ability to perform characteristic movements for escaping such as wing opening, flapping and jumping.

Boyden, Zhang, Bamberg, Nagel and Deisseroth [C18] developed these concepts further using a naturally occurring algal protein, Channelrhodopsin-2, which exhibits similar photostimular behaviours to previously used proteins but responds to stimulus much more rapidly. Previous work typically involved neuron control over time periods of seconds to minutes whereas Deisseroth's new approach allows individual spikes and peaks in neuron action potentials to be controlled at the timescale of milliseconds. The finer temporal control in this technique allows a much better understanding of behaviours which occur by "temporal activity patterns" in neurons. High frequency stimulation with different patterns of spikes can thus be stimulated in these neurons to elicit different behaviours as opposed to just single, lengthy exposures with previous techniques.

Intentions may be good for this technology, using it to better understand and treat mental disorders and depression, however there are significant plausible ethical objections to its use. None of the research papers hint at any ethical considerations in any of the research showing gross disregard in light of the ethical issues of neural intervention. Neuroethics, the study of ethics in neuroscience, can be categorised into four areas, of which one is the area of neuroscience of the self, agency and responsibility. This area focuses on the biology that underlies a humans personality, behaviour and decision making [C19]. Our behaviour and personality are ultimately functions of our brain which, if directly controllable, could be modified undermining the notions of self and agency. This technology's ability to turn-off parts of the brain is effectively equivalent to a temporary lobotomy, in which a piece of a patient's brain is removed. Any direct stimulation of the brain has long since be recognised under the header of psychosurgery [C20] therefore any research in this area should be subject to the same ethical considerations. Some have in the past been as extreme to imply that all forms of lobotomy and psychosurgery should be made illegal as their potential for misuse by a totalitarian power are too great [C21]. While those views may be extreme, the techniques being explored in this research do have this potential for abuse and can be made worse if neural photostimulators form a basis of transgenic animals or humans — genetically modified beings — who have these neural "switches" implanted from birth. Currently the technology is not being carefully considered ethically and has far reaching moral consequences. Further study of the ethics and responsibilities must be set in place.

2 Concluding remarks

In the preceding three overviews of emerging technologies an important commonality can be seen: nanoscale science. Each of these technologies hinges on the ability to develop and manipulate structures at a scale of 1 - 100 nanometres. Unique behaviours and interactions at this size, such as those in quantum dots, can be seen that are not present in larger structures and in collections of nanostructures unique behaviours and interactions can be seen at the macro level in nanomaterials technology. Nanotechnology is, and will continue to be, a huge factor in science, technology and society for the foreseeable future, but with all power must come responsibility.

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