Australian Government
Department of Defence
Science and Technology

EDTAS
EMERGING DISRUPTIVE TECHNOLOGY
ASSESSMENT SYMPOSIUM

noetic

INSIGHTS PAPER

Human Biotechnologies

INTRODUCTION

Aim

The aim of this Insights Paper is to explore possible Human Biotechnology concepts in the 2040 timeframe in order to inform Emerging Disruptive Technology Assessment Symposium (EDTAS) participants and help engender debate during the symposia.

Scope

This paper does not intend to be definitive, we recognise the breadth of the topic being discussed, as well as the ethical considerations around these technologies.

To aid comprehension, and to support discussion across the two days we have divided the paper into two main technology sections, Human Measurement, and Human Modification, and an explicit ethics section.

The technology areas and broader themes discussed in this paper will form the primary focus of the EDTAS. As well as the initial impacts, part of the foresighting process means examining potential second and third order effects. The symposium will allow DST to do this in an immersive environment, but some points for consideration are raised in this document around each technology area.

Background

The field of Human Biotechnologies is an area of research which has the potential to have significant game changing impacts on society in the coming decades. The ability to monitor in real time, and proactively adapt human physiology has enormous implications. As the human population increases, having the ability to adapt to extreme environments will enable us to expand across new areas of the world, and survive where we couldn't before. Tailored gene therapy will enable the development of enhancements both physically and mentally beyond current human limits, augmented by brain interface synthetic systems or exoskeletons.

Conversely, Human Biotechnologies, perhaps more than any other foreseeable technology, also have the potential to engender mistrust and fear across societies. The idea of changing something as fundamental as the structure of our bodies can invoke a visceral reaction. The challenge will be to ensure that the huge potential of the technologies is communicated properly and managed responsibly. The potential for the harmful effects of the biosciences should also not be discounted. Many of the techniques and processes used to enhance humans, can also be used to cause harm. How society regulates and oversees the use of disruptive biotechnology will have major effects on daily life, on the business of Defence and upon national security.

As the agency responsible for leading the development of Defence technological capabilities, Defence Science and Technology (DST) Group is seeking how to best understand the opportunities, threats and challenges the area presents. The themes for EDTAS are drawn from the Next Generation Technology fund. With an investment of $730 million over the decade to 2026, the Next Gen Tech Fund is a forward-looking program focusing on research in emerging and future technologies for the "future Defence force after next". Innovative technologies and concepts researched under the Next Gen Tech Fund could be further developed and realised into capability through the Defence Innovation Hub.

To do this DST, in concert with Noetic and the University of Adelaide, will hold an Emerging and Disruptive Technologies Assessment Symposium to explore potential Human Biotechnology advances in the next 20-30 years. The EDTAS will consider Human Biotechnology in two symposia, one at the unclassified level for a broad audience of academia, government, Defence and Defence industry, and a second classified event for a predominantly Defence audience. Each symposium will feature a diverse range of expert presentations and facilitated immersive workshops to draw key insights on the subject area. DST will capture the output from these collective engagements in a Big Picture Analysis Report that will help identify key research themes for future study.

Questions:

- What are the opportunities in Human Biotechnologies?

HUMAN MEASUREMENT TECHNOLOGIES

Understanding the human body has been a fundamental tenet of science since ancient times. The current state of technology indicates society is on the threshold of a “new renaissance in science and technology” (Rigaud, 2008). Our understanding from the nanoscale, right up to the level of complex systems such as the brain is more comprehensive than ever before. In the next 20 years, convergence of technology and rapid advances in understanding have the potential to not only improve the ability to treat disease, but also to gain deeper insights into how humans function as beings. This knowledge will underpin many of the potential advances discussed below.

Bioinformatics

The tools and processes of bioinformatics will allow scientists of 2040 to structure research and development along well-defined pathways. The ability to map and record metabolic pathways, or the genetic bases of disease will allow researchers to tailor approaches to monitoring to the specific biology of subjects. Working in concert with machine learning and enhanced statistical modelling, Bioinformatics will provide solutions to problems at the individual level, with implanted monitoring providing real time feedback, and adding to the sum of knowledge that scientists are able to obtain.

Implications of Bioinformatics

The implications of bioinformatics are complex. Bioinformatics will potentially have an effect on how people are selected for different professions. As we increasingly understand the underlying biology, people may be selected based on genetic predispositions and phenotypes rather than explicitly demonstrated abilities. Young people could be screened for specific jobs and functions. While this may allow people to take on roles they would never previously have been able to attain, there is an ethical component to be considered as to how this is enacted.

Genomics

Flowing on from bioinformatics is the interdisciplinary field of genomics. Genomics focusses on the structure, function, evolution and mapping of genomes. The key difference between genomics and genetics is the breadth of approach. Genomics facilitates an understanding of DNA and related molecules, allowing a more comprehensive understanding of specific variations and mutations in genes.

DNA Sequencing

The concept of DNA sequencing has been around since the 1960s. However, the time and cost of sequencing a genome has been prohibitive to all but the most well-equipped laboratories. The most common method of sequencing in the current era is sequencing by synthesis. This process uses the DNA enzyme ‘polymerase’ to generate a new DNA strand from a sample. The sequencing reaction causes the polymerase to incorporate them into new DNA strand individual nucleotides that have been fluorescently tagged. Using a light source this tag can be detected and read. This allows reads of 125 nucleotides in a row. While this is an efficient and effective method, it still takes time, and costs are in the range of thousands dollars. As we move towards 2040, the adoption of new sequencing techniques will reduce both time and cost, presenting a potential future where sequencing is routine and provides a large sample size for insights into broader human health.

One new technology involves the use of nanopores. This process involves threading single DNA strands through the extremely tiny pores in a membrane. The DNA bases are then read one by one as they squeeze through a nanopore, and the bases identified by the differences in their effect on ions and electrical current flowing through a pore.
The use of nanopore sequencing offers the ability to sequence DNA cheaper and faster, with the added benefit of being able to re-sequence the same DNA repeatedly. Several stakeholders identified that having “increased processing power in sequencing and the ability to quickly and cheaply sequence the human genome could be a game changer.”

Implications of Genomics for Medical Science

The vast majority of human ailments have at least some genetic component. Following the successful mapping of the human genome, genetic considerations have grown beyond congenital condition and simple, predictable inheritance patterns such as sickle cell anaemia.

The development of tools to study complex diseases and interactions will continue apace into the 2040 timeframe. Much research is aimed at cancer, diabetes and cardiovascular disease. These diseases have multiple genetic factors, which interact with environmental conditions. Genomics may also present new approaches to psychological health. Behavioural genomics stands to provide deeper information on psychological and cognitive tendencies, providing opportunities to detect and treat mental or psychological disorders in the same manner as physiological conditions.

The disruptive potential within the next 20 years is for genomics and bioinformatics to allow for personally targeted treatment regimes, or even prophylactic treatment to ensure a person never actually becomes unwell. Stakeholders commented however that “Health coverage becomes problematic if underlying conditions are known” making these emerging technologies disruptive in particular for countries without socialised medicine.

Questions

- What are the implications of ubiquitous DNA sequencing?
- Will this lead to the development of a “proactive” medicinal approach vs the current reactive system?

Biochemistry

The study of chemical processes within the human body already feeds directly into the multidisciplinary areas described above. However, biochemistry is concerned with the macro domain, and the interactions of proteins, acids, lipids and carbohydrates. In the realm of monitoring technology there are a number of areas which offer the most potential for disruptive advancement.

Proteomics

Future advances in the large-scale study of proteins, or 'quantitative proteomics' will greatly enhance the ability to carry out deep analysis of cellular systems. All biological systems can be disturbed by a number of processes e.g. differentiation, carcinogenesis, etc.

In order to fully understand the implications of developing quantitative proteomics, enhanced quantification and description of proteome wide changes are crucial. Future approaches are likely to build on a systems approach, to give a holistic view of the human body, complimentary to other 'omics' approaches such as genomics and metabolomics. A good example of this is the Cancer Proteome Atlas which sampled 8,167 tumour samples to provide an expression date for around 200 proteins (Li et al., 2013). The development of similar data sets for other types of cells, tissue and even species will be immensely important as a resource for research.

Human plasma proteome

One of the most disruptive applications of proteomics will be the characterisation of the human plasma proteome. The proteome of plasma is unusually complex, containing "immunoglobulin, cytokines, protein hormones, and secreted proteins indicative of infection on top of resident, haemostatic proteins" (Anderson and Anderson, 2002). Given that blood circulates around the entire body, it contains tissue leakage proteins from many tissues and indications of changes throughout the body. This means that the information contained within the blood is almost a "one stop shop" for physiological monitoring of the entire body.

The challenge will be the depth of the plasma proteome, which encompasses a range of >1010 between albumin at the top end and cytokines and the bottom. The various proteins also turn over at different rates, complicating any attempt at standard measurement and classification. The technology of Plasma Proteome profiling has shown promise in mice but will require much greater research to be of widespread applicability.

Metabolomics

As an adjunct to functional genomics, metabolomics offers tools for deeming the phenotype which results from genetic manipulation i.e. deletion or insertion of a gene. While this is currently used to examine food products, particularly animal feed for correct phenotypes, the 2040 timeframe offers potential for more wide-ranging uses. The opportunity to predict the function of unknown genes, by comparing metabolic disturbances caused by manipulating known genes will enable greater understanding of the human body. There are already model organisms used to test this process, most notably Saccharomyces cerevisiae (baker's yeast) but the application to complex human systems would be game changing.

Implications of Biochemistry

The major impacts of biochemistry over the next 20 years are likely to be that they will be the underpinning knowledge for other areas of research. The ability to gather and analyse data across the entirety of the human system is game changing in and of itself. Being able to apply this knowledge to tailor a person's medical treatment throughout their life, for example, will be the disruptive element. Of course, the major question, is one of cost. While the technology becomes ever cheaper, will it be available to all? Or will it lead to the division of humans into those who can, and those that cannot afford to access the technology?

NanoRobotics

Biological nanorobotics build on the as yet unrealised potential of nanotechnology, combined with data gained from previously discussed areas of research. Merging the concepts of biomimicry, synthetic biology and nanotechnology will be a game changing development in the 2040 timeframe. The ability to develop nanosystems which mimic the body's own cells, to provide real time data will allow us to understand interactions on a level never before realised.

Applications of NanoRobotics

Nanomedicine

Future medical techniques will avoid invasive surgical procedure in favour of target nanosystems deployed via the blood stream. These personalised robots will be synthetic products, mimicking the patient's own DNA, but will be designed specifically to be non-replicating. They would be targeted at the cellular level, to measure the functioning of systems and processes, both in healthy individuals as a monitoring technique, and patients as a means of targeted treatment. This will reduce the side effects of non-targeted treatment methods such as chemotherapy.

Cellular repair

The use of nanorobots to support white blood cells in tissue repair is feasible within the 20 year time frame. The body's first response to injury is to use inflammatory cells and white blood cells to flood the affected area of injury. Nanorobots could attach to these cells, be transported to the injury site and assist with the repair. Aligned with embedded sensing systems, there could even be a preventative application, for example if the body detects increased acceleration the nanobots could arrive to predicted impact sites (Kumar et al., 2014) thus preventing injuries and diseases before they occur.

Nanorobots treatment of diabetes

As glucose is carried through the bloodstream, current measurement systems require invasive methods to acquire blood to sample. "Intrinsically related to the glucose molecules, the protein hSGLT3…. can serve to define the glucose levels for diabetes patients."(Abhilash, 2010). Having established this, nanorobots can be targeted to monitor blood glucose variations based on prescription levels. This data could then by transmitted by Radio Frequency to a patient's personal device.

Human Machine Interface

It has been suggested by leading tech firms that nanotechnology has the ability to blur the boundaries between machines and humans. Ray Kurzweil, director of engineering at Google suggests "In the 2030s we are going to send nanorobots into the brain that will provide full immersion virtual reality from within the nervous system and will connect our neocortex to the cloud. Just like how we can wirelessly expand the power of our smartphones 10,000-fold in the cloud today, we'll be able to expand our neocortex."('Nanobots will live in our brains in the 2030s, says Google boss', n.d.). The potential of this is hugely disruptive. Imagine a world where we're instantly connected to everything around us. Messaging as fast as we can think, never worrying where our children are, and having a wealth of information in an instant.

Implications of Nanotechnology

Intellectual property issues

There have been suggestions that as much as biotechnology has allowed the patenting of genes, that nanotechnology's ability manipulate molecules will lead to the patenting of matter itself (Pearce, 2013). There are also concerns that the sheer volume of patents being registered in the area may stifle technological advancement. ('Stallman's got company: Researcher wants nanotech patent moratorium | Ars Technica', n.d.) For example, two corporations, NEC and IBM, hold the basic patents on carbon nanotubes, one of the current cornerstones of nanotechnology, meaning any company looking to manufacture them require a licence from one of these companies.

Effects on labourers

Ray Kurzweil has speculated in The Singularity is Near that “people who work in unskilled labour jobs for a livelihood may become the first human workers to be displaced by the constant use of nanotechnology” (Kurzweil, 2005). This will mean that those less able to adapt would be the first to lose out in a new more technological age. This may mean that a ‘new industrial revolution’ may occur, and new jobs and training become available. However, we need to prepare now by reassessing educational and training needs for the future.

Questions

- How would these systems be administered?

Bio-Sensing

Biosensors are analytical devices involving a biological sensing element regardless of the media being scanned. The first biosensors were designed by Clark and Lyons (Clark and Lyons, 1962) and measure glucose in biological samples. Sensing technology is now much more sophisticated, drawing on innovation in electrochemistry, nanotech and bioelectronics.

Stakeholders consulted indicated that sensing technology, both wearable and non-wearable will provide the ability to tailor learning and testing to the individual, eliminating the need to separate training and assessment. Add to this the ability to "monitor complex functions and systems" monitoring blood chemical composition or examining the entire body holistically.

Detection

With the development of such sophisticated biotechnology, the inherent advantages also present potential risks. Biological weapons ultimately prove to be one of the most difficult attacks to anticipate and respond to, due to the difficulty in detection and controlling of the biological agent. Initial research has shown the potential for biosensors to perform detection activities for biological warfare agents (Kumar & Bhawana, 2015), which will further enable military and defence industries to monitor security threats of this nature. There are also civilian applications for this technology in the monitoring of water and air supplies for pathogens and overall quality, offering significant advantages for public health organisations in the detection and mitigation of disease.

Clinical Diagnosis and Treatment

Currently, biosensors provide invaluable benefits in biomedicine by providing both diagnosis and treatment advantages. Quantum dot biosensors have the ability to assist in the analysis of the tumour microenvironment, enabling a more targeted application of nanomedicine in cancer treatment (Jain, 2013). Biosensors already enable diabetics to monitor their blood sugar level in conjunction with nanotechnology. By 2040, biosensors could allow for a completely personalised analysis of a person's health profile through wearable technology or biosensors embedded in the body. The detailed data provided by sophisticated biosensors could support the early detection of serious diseases, enabling preventative measures to be undertaken before the disease has a chance to present itself. The detailed data could also provide monitoring activities in athletes through these wearable technology or biosensors, enabling preventative or early treatment of illness or injury.

Human-Machine Interface and 'Telepresence'

Biosensors are not limited to physiological data. The increased sophistication in biosensing technology will allow for the real-time monitoring of complex biological systems, including cognitive and psychological inputs. Over the next 20 years, more accurate and fully embedded biosensors could facilitate the collection of cognitive data which would allow autonomous systems or artificial intelligence (AI) to understand human intention. These developments could make telepresence (remote sensory experience using machine and/or computer interface) a theoretical possibility by 2040, fundamentally changing the way that humans and autonomous machines work together to complete tasks.

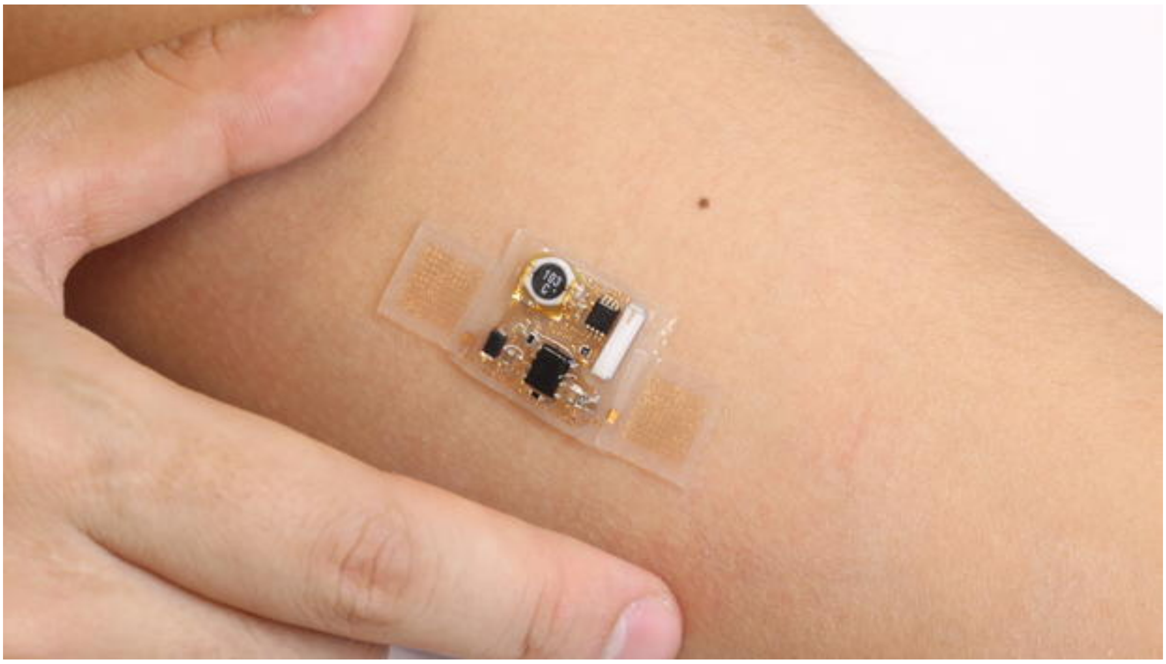
Implications of Biosensors

The ability to sense and monitor biological indicators has significant security advantages but also serious disruptive potential to society. It is possible in coming decades, that the destructive potential of biosensors will be realised to combine virus traits – imagine a combination of highly contagious yet highly resistant diseases presenting a risk to the general public. Biosensing can also provide effective defence against this potential bioterrorism. Biosensing technology and telepresence also have the potential to change the way in which security and law enforcement function.

Biosensors also have the potential to form specialised targeted delivery systems for clinical diagnostic and treatment processes over the next twenty years. This could enable in the future extremely tailored analysis of individual health history and provide a specific breakdown of environmental chemical and biological constituents to identify potential toxicity risks.

Questions

How will the collection of data from biosensors impact on privacy? Who should have access to this data?



Credit: John Rogers, CBS News, 2014.

HUMAN MODIFICATION TECHNOLOGIES

Human modification is not a fundamentally new phenomenon. Drugs, therapies and prosthetics have served as mechanisms to augment the human body and its functions to treat various conditions or improve performance. As we move towards 2040, human modification will extend to tailoring genetic material, cells and organs to support therapeutic functions. Treating disease will become far less intrusive as delivery mechanisms become increasingly integrated with the body's own systems.

By 2040, modification will not only be a means by which to treat the sick but also an opportunity to enhance and improve the wellbeing of the healthy population. The technologies outlined below offer new avenues to enhancing physiological and cognitive performance and raise important questions about the social impact of human biotechnologies.

Metabolic Engineering

Metabolic engineering is an expanded investigation into the pathways that genes and regulatory functions undertake in cells (Stephanopoulos, 2012) and developing tools and systems to enhance or alter cellular biochemistry. Current techniques allow for the manipulation of the entire cell, providing metabolic engineers with considerable control over the expression of genes and their regulatory networks within a cell. As this field develops, metabolic engineering offers promising applications in agriculture and plant development, as well as medical delivery systems. By 2040, metabolic engineering presents a key enabling factor in more effective vaccines, or increased efficiency of cells to respond to medical treatment.

Cellular Development and Augmentation

The potential of metabolic engineering to alter cellular biochemistry and eliciting a specific function of a cell to produce more or less of something opens up the possibility of enhanced immune system development or production of selected hormones to change the physiology of an individual. Currently, metabolic pathway engineering has been used to generate cells with novel biochemical functions for therapeutic use, such as dopamine-replacement therapy (Yarmush and Banta, 2003). In 2040, this may manifest in the form of more motivated workers due to dopamine enhancement; or testosterone augmentation in soldiers, athletes and high-performing physical industries, to enhance athletic aptitude.

Therapeutic Applications

Modelling of metabolic pathways is currently being utilised for understanding the disease state at a cellular and sub-cellular level. This can enable a more specific target for treatment, increasing efficacy and potentially reducing side effects. New manufacturing techniques such as 3D 'bioprinting' will offer increased insight over the next 20 years by allowing complex biological systems and their full range of variations to be examined in three dimensions.

Synthetic Biology

One of the most promising areas for disruptive advancement is the use of personalised genomics to create synthetic biological systems or structures. Within this area, the potential use of genomic data to allow for close measurement of internal systems is immense. The follow-on use of this gathered information, to amend and augment human performance and resilience presents game changing potential.

By 2040, synthetic biology could enhance the function of cells or organs, allowing for the greater production of hormones or compounds such as insulin. There is also the potential for the production of synthetic organs which present entirely new functions, such as an organ that spins silk, or that have self-defence mechanisms inspired by the natural world.

Implications of Metabolic Engineering

Biotechnology advances are leading to improved medications that can target diseases more effectively and precisely. Researchers have begun to reformulate drugs so they may be more safely used in specific conditions.

The more targeted a drug is, the lower its chance of triggering drug resistance, a cautionary concern surrounding the use of broad-spectrum antibiotics. Developments in metabolic engineering offer new approaches to medical procedures and therapeutic treatment by diversifying routes of drug delivery and the variety of vehicles with which drugs can be delivered. Metabolic engineering has the potential to make treatment options more effective and less invasive by replicating and drawing on existing body systems and processes.

Routes of Delivery

Synthetic biology also provides avenues for treatment by altering the function of the body's own cells or organs to deliver drugs with a high degree of accuracy. Each method has advantages and disadvantages, and not all methods can be used for every medication. Improving current delivery methods or designing new ones can enhance the use of existing medications.

Nanotechnology is also opening up new avenues for drug delivery vehicles. Microneedle arrays are one example of a new method to deliver medications through the skin. In these arrays, dozens of microscopic needles, each far thinner than a strand of hair, can be fabricated to contain a medicine. The needles are so small that, although they penetrate the skin, they don't reach nerves in the skin, thus delivering medications painlessly.

The National Institute of Biomedical Imaging and Bioengineering (NIBIB)-funded scientists are developing such a patch with an array of dissolvable microneedles for vaccine delivery. These patches are easy to use and do not require refrigeration or special disposal methods, so they could be used by patients themselves at home. This technology could be especially helpful in low-resource communities that may not have many health care providers or adequate storage facilities for traditional, refrigerated medicines.

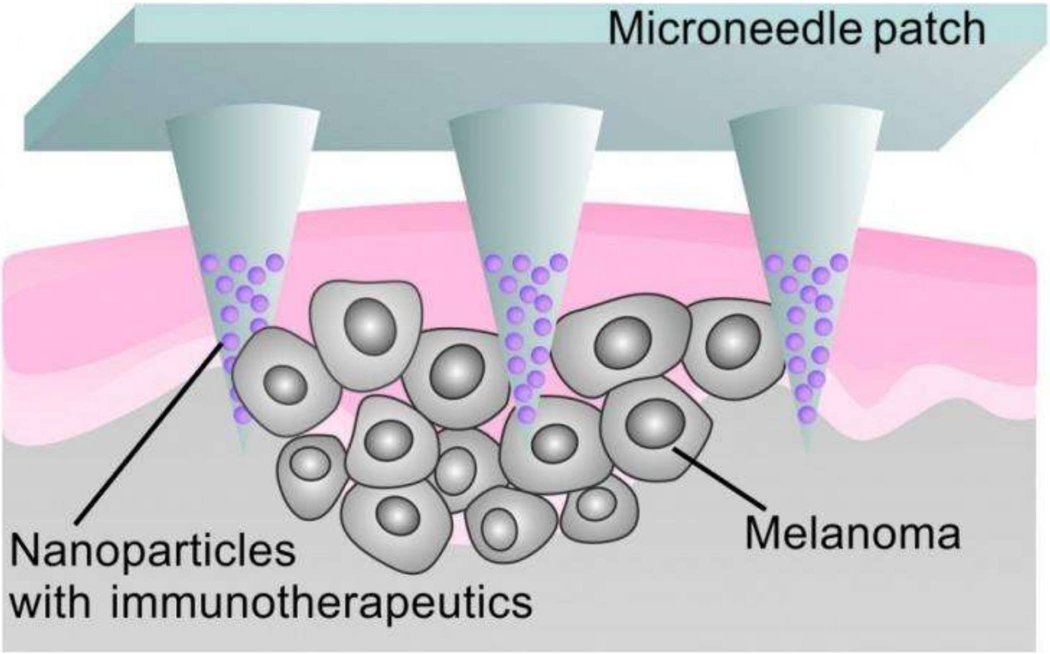
Delivery Vehicles

NIBIB-funded researchers have reported promising results in developing a treatment for glioblastoma, a devastating brain cancer. In rat models of the disease, they have shown that tumours can be penetrated and shrunken when injected with nanoparticles. The nanoparticles target the tumour by delivering an altered gene, or suicide gene, that is programmed for cell death. The nanoparticle method replaces a type of gene therapy using viruses, which can have unpredictable outcomes.

Other NIBIB-funded researchers are developing a system of drug delivery using a type of bacteria that has a two-part navigation system—magnetic and oxygen sensing. They have tested the delivery system in mice, achieving a remarkable success delivering drugs to tumours. The bacteria seek out oxygen-poor zones, which are a feature of tumours. Using a computer-programmed magnetic field to direct the bacteria to tumours, the researchers found that the bacteria were drawn deep into the oxygen starved tumours, away from healthy cells. This process could open the door for directing drug-laden bacteria to tumours deep in the body.

Questions

- How will we manage the differing speeds of advancement between analytical techniques and engineering systems?



Credit: North Carolina State University

Genetic Engineering

The term 'genetic engineering' has gradually broadened to encompass virtually any process involving DNA manipulation. This field is developing rapidly owing to the sharp decrease in the time and expense required to sequence genomes. New tools – most notably Clustered Regulatory Interspaced Short Palindromic Repeats (CRISPR)-Cas9 – provide the ability to edit genes quickly and effectively, reducing development timelines from months or years to a matter of days. Many interviewed stakeholders noted that, over the next 20 years, it is likely that this rapid pace will continue. Genetic engineering techniques and the technology that enables them will become more widespread and more accessible as we move towards 2040.

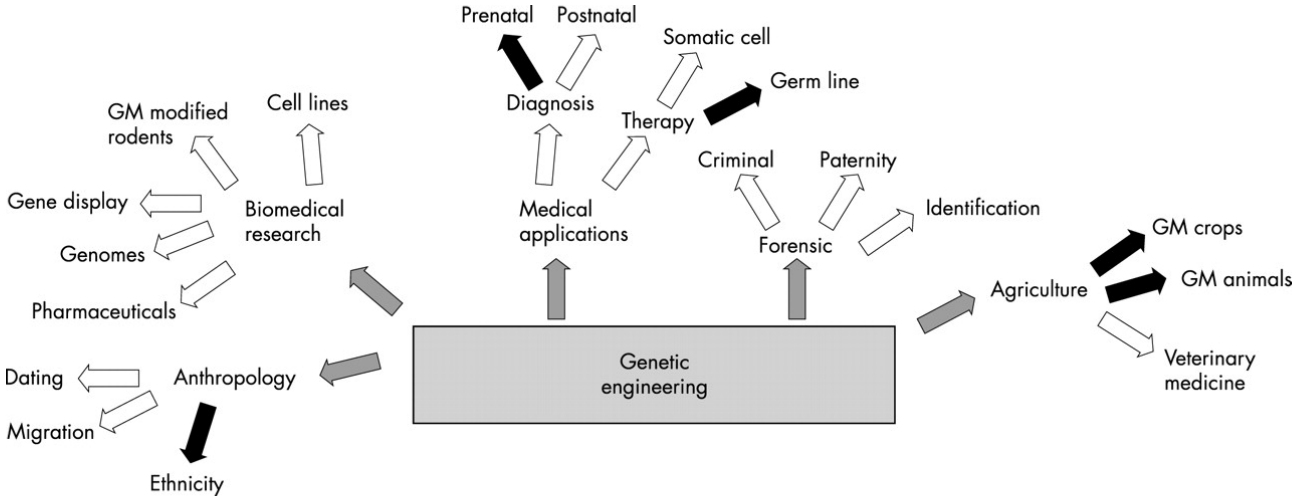


Figure 1: Example applications of genetic engineering and their ethical considerations. White arrows indicate areas of little controversy, black arrows denote more controversial applications (Alexander, 2003)

Tailored Genome Editing

There are two broad varieties of genome editing: somatic and germline gene editing. Somatic gene editing involves transferring or expressing a specific gene in a targeted cell of an adult organism by either in vitro or in vivo mechanisms. Over the next 20 years, the range and complexity of the cells and associated systems that can be targeted by somatic gene editing are likely to expand considerably. Modifying the eye to sense a broader range of light was identified by stakeholders as a likely area of development in the near future. By 2040, it is theoretically possible for somatic editing to take place in complex system such as the human brain.

Germline gene editing is a more controversial field. This form of editing takes place at embryogenesis and the modification affects all cells in the organism by altering the basis of DNA. Unlike somatic editing, modifications introduced as a result of germline gene editing can be passed on to the offspring of the modified individual. This introduces a number of questions surrounding the ethical considerations of germline gene modification and the potential for unforeseen intergenerational consequences.

Diagnosis and Treatment

The ability to quickly and affordably sequence DNA offers unprecedented insights into how pathogens and genetic disorders function and spread. CRISPR technology has proved particularly useful in identifying susceptibility to genetic disorders by uncovering problematic DNA which enable or facilitate the development of disease. Genetic modification allows for the removal of these vulnerable strands of DNA and their replacement with healthy or more resilient strands.

Currently, genetic engineering offers potential solutions to single-gene disorders (such as sickle-cell anaemia). In 2040, this technology could serve as a treatment for complex diseases such as cancer and mental illnesses which have genetic and environmental causes. The likely increased prevalence of genome sequencing over the next 20 years also offers opportunities to personalise treatment options, tailoring treatment options according to the receptiveness of patients' genetic makeup.

Gene Doping

An emerging trend in human biotechnology over the next 20 years is the transition from therapeutic applications to enhancement. Gene doping emphasises the non-therapeutic application of genetic engineering by altering DNA in ways that increase athletic capabilities or improve recovery. Currently this mechanism comes primarily in the form of a recombinant protein that can assist in the expression of particular genes. For example, an athlete's DNA could be engineered to introduce genes which increase production of the hormone Erythropoietin (EPO), resulting in an increased red blood cell count and enhancing the oxygenation of muscles.

Gene Drives

A crucial obstacle to the population scale continuation of genetic modification in organisms is the high rate of attrition as a result of natural selection. Most genetic traits typically have a 50% chance of being inherited, and engineered transgenes are generally eliminated faster unless supported by human intervention. Gene drives provide a way to 'drive' a trait through a population by increasing its likelihood of being inherited using mechanisms such as 'homing' endonucleases which promote the production of self-replicating genes.

A notable application for gene drives has been in the mitigation of malaria. Gene drives have the potential to manage malaria-carrying mosquito populations by engineering changes such as skewing the sex ratio of mosquito populations to favour males, reducing the ability of the overall population to reproduce or spread. The use of gene drives may also apply directly to humans in 2040, as a means to retain or spread modifications introduced through germline gene modification.

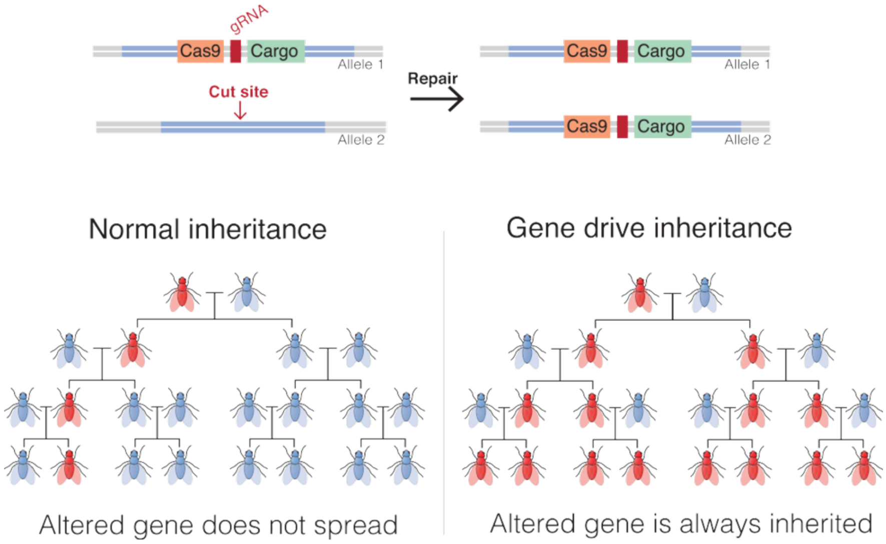


Figure 2: The gene drive phenomenon, where a set of genes is favourably targeted for inheritance, using the CRISPR/Cas9 cutting method.('File:Gene Drive.png - Wikimedia Commons', n.d.)

Implications of Genetic Engineering

The breadth and rapid development of field of genetic modifications makes it difficult to exhaustively imagine the implications of its many applications. While the concept of selective breeding of animals and plants or selecting for desired traits isn't new, the ability to encode the information at a genetic level, and rapidly deploy change is hugely disruptive. From a societal perspective, if we have the technology to eliminate genetic disease, would that be optional? People often fear things that they do not understand, which can complicate the introduction beneficial technologies.

Super sensory function

Genetic engineering reflects the broader domain of human biotechnology in demonstrating a trend from therapeutic applications towards modification for enhancement. There is the theoretical possibility that genetic engineering could promote super sensory function in humans by 2040. Increasing sophistication in introducing new genes or editing existing traits in more complex systems could allow humans to sense phenomena previously impossible without equipment. The human eye could be augmented to see infrared light, and the ear to hear extremely high or low frequencies. This represents not only a change in sensory performance for the modified human, but may also fundamentally alter their interpretation, experience and understanding of the world around them.

‘Designer Babies’

The concept of the ‘designer baby’ is closely linked to increasingly accurate genetic screening. Embryos can be scanned and selected for the presence or absence of specific traits, allowing parents to essentially ‘design’ their offspring. The scope and scale of customisation will likely increase over the next 20 years as somatic and germline gene modification becomes more sophisticated and commonplace. Stakeholders indicated that the ability to alter physiological traits with well-defined genetic foundations – such as appearance and physical strength or resilience – would be developed by 2040. The future is less clear for modifying more complex phenomena such as intelligence, which manifests as a result of genetic and environmental factors.

Bioweapons

It is important to consider the potential for genetic engineering and modification techniques to be used for malicious purposes. The potential for malicious states or non-state actors developing novel biological agents could increase over the next 20 years. Barriers to entry are reduced due to the increased accessibility and affordability of genetic engineering technology. Bacteria and other pathogens can be rapidly sequenced and edited to circumvent known resistances. Interviewed stakeholders noted with concern that the bioweapons of 2040 could be engineered to target the genetic vulnerabilities of specific individuals or groups of people. This would allow the effects of bioweapons to be more easily contained, therefore reducing the risk of deploying a harmful biological agent to a would-be attacker.

Gene drives also factor into the potential future of bioweapons as a delivery system. Highly mobile species with a rapid reproduction rate – such as mosquitoes or flies – could be infected with a malicious gene and released into a target environment. The gene drive would allow the harmful gene to spread rapidly and make identifying the source of an attack extremely difficult. This will place emphasis on not only the need for adequate monitoring, but also on the potential of ‘reversal’ drives – gene drives designed to counteract the impact of another drive.

Questions

- Are we at the risk of a two tier society of those who are augmented and those who are not?

Physiological Enhancement & Augmentation

Whereas genetic engineering offers approaches to modifying the fundamentals of an individual's DNA, physiological enhancement concerns the enhancement of the body to 'beyond normal' performance using tools external to the body's regular function. Drugs, therapies and prostheses have long been used for the augmentation and enhancement of human performance. Moving towards 2040, these approaches are likely to become more sophisticated and give way to new applications which serve both therapeutic and enhancement functions.

Sensory Repair and Enhancement

Neural enhancement, either by wearable or implanted technology, has the potential to be game-changing for augmenting and enhancing human senses over the next 20 years. Interviewed stakeholders noted the game-changing potential of improved implant-brain communication for neural implants currently being enabled by the examination of 3D printed systems. Understanding the full range of variation in healthy and unhealthy system function presents new avenues to the treatment of disease or disorder. By 2040, non-invasive, embedded neural implants have the potential to restore sensory functions lost as a result of disease, injury or birth defects.

The power of implants as a means to enhance human performance is already being explored by the so-called 'biohacker' movement. These groups highlight the potential of neural implants to enhance and expand the range of human senses. Implants may allow for the development of enhanced vision and greater sensitivity to olfactory, gustatory, or haptic information. Theoretically, this may allow for the experience of new senses as a result of combining or altering human sensory abilities. New or enhanced senses as a result of neural augmentation share the potential of genetic engineering to fundamentally alter how humans perceive, understand and interpret the world around them.

Cognitive Enhancement

The potential for enhancement and augmentation extends beyond sensory function. Over the next 20 years, neural augmentation will assist and enhance the function of the brain itself. The United States' defence science organisation, DARPA, is currently undertaking the Restoring Active Memory (RAM) program to develop neuroprosthetics. These augmentations are designed to assist military personnel in overcoming memory deficits as a result of service. There is a therapeutic extension of this work in treating broader problems of confabulation incurred as a result of cognitive degeneration or diseases such as dementia.

The ability of neuroprosthetics to analyse neural signals opens the door to understanding how 'encode' brain function. Encoding with augmentations could support the self-restoration of the brain or the introduction of completely new memories. The ability to implant or alter memories challenges the idea of the 'self' being a product of psychologically continuous experiences and opens questions regarding the nature of personhood.

Cognitive enhancement is also being explored without the use of implants. Developments in the use of psychological exercises, therapies and related drugs has the potential to coalesce into a 'cognitive gym' which would allow participants to expand their cognitive capabilities without necessitating the use of an implant. This treatment is intended to give greater control over cognitive arousal and recovery. Individuals in high-risk roles – such as emergency services personnel – could use the 'cognitive gym' to enhance their focus, awareness and cognitive speed while on duty, before using the same processes to safely recover and avoid cognitive overload and fatigue.

Implications of Physiological Enhancement and Augmentation

> ***"The human of the near future could be nearly unlimited in their cognitive capabilities. How could the man who sees in radio and feels the solar wind relate to the old human?... [T]he new human could very possibly be beyond our current understanding. The first steps in that journey have already been made."***
>
> ***(Barfield and Williams, 2017)***

Cyborg Identity

The combination of technological development and potential for popular uptake by 'biohacker' movements open the possibility for the humans of 2040 to have adopted a wide range of wearable and implanted augmentations. The 'average' human in 20 years may have a variety of beyond-normal sensory and cognitive capabilities compared to the humans of today. These capabilities are likely to shape or alter the way in which people perceive and understand the world around them. Further, the possibility of brain-to-brain communication facilitated by neural implants means that this new experience could be instantly shared between individuals on a thought-to-thought level.

These possibilities are also likely to influence and inform how augmented humans understand themselves. Barfield and Williams introduce the idea of a 'cyborg being' *"as a particular way of life, or set of beliefs, which expresses certain meanings in the context of cyborg technologies"* (Barfield and Williams, 2017). Over the next 20 years, societies could experience a trans-human shift as augmented individuals move beyond the established limitations of their physiology and cognitive function.

Questions

- How do governments generate policy that will foster technology development and uptake in Australia?

ETHICAL AND LEGAL IMPLICATIONS

Ethics

Equity and Social Justice

Advances in Human Biotechnology may allow humans to improve everything from memory to appearance. Unequal access to such advances, however, could stir social tension and result in unfair competition between average and enhanced individuals. As new technologies and options for enhancement are developed, the need arises for social systems that ensure affordable access - and prevent the emergence of an enhanced vs. non-enhanced social divide. Other potential scenarios could result in certain performance enhancing methods, and a lack of transparency in their use, such as doping.

Pioneers operating under relatively loose regulatory requirements could trigger competition that forces other regions or countries to implement related technologies. The uneven distribution and advancement of these technologies may yield increased social inequality, though regional and cultural division could be addressed through global governance. We are entering a trans-human era, and the question of proper guidelines for human enhancement must be addressed.

Legal Implications

Developments in Human Biotechnology are moving rapidly and present challenges to existing regulatory frameworks. Ensuring that legal and regulatory frameworks keep pace with emerging Human Biotechnology will be central to ensuring that Australia is able to fully leverage the advantages of these discoveries while providing necessary protections and restrictions.

There is a perception among interviewed stakeholders that Australia's regulatory frameworks for biotechnology are falling behind comparable countries. This carries the dual risk that Australia could 'fall behind' and lose out on the benefits biotechnology offers and that groups of people may be left vulnerable to loosely regulated technology.

Genetic Non-Discrimination

As DNA sequencing becomes more commonplace, it is important to consider how an individual's genomic data is used. This information provides rich insights into a person's health, vulnerabilities and the receptiveness to treatment options. While this data is highly useful for medical use, it could likewise be leveraged against an individual to deny access to insurance or impose additional costs. Australia's current regulatory framework prohibits insurance providers from requiring applicants to undertake genetic testing as a condition of coverage, but existing knowledge of genetic information must be disclosed to an insurer if already known ('Existing regulatory framework | ALRC', n.d.). This presents a challenge for a future in which DNA sequencing is increasingly ubiquitous.

Work, Health and Safety (WHS) & Duty of Care

A related issue concerns the consideration of scenarios where augmentation may be considered a recommended – or mandatory – requirement for certain jobs or positions. Enhanced physiological and cognitive function could reduce the risk of accidents and injury, improve resilience and aid in recovery. These benefits could see augmentation adopted as part of WHS practice by 2040. In such a world where enhancement and safety go hand-in-hand, maintaining augmentations may constitute a duty of care requirement for industries demanding enhanced workers.

This would not only involve keeping augmentations up-to-date with best practice, but also raises the question of transitioning workers out of the industry. It is not yet clear that all augmentations will be fully reversible by 2040. Enhanced workers may therefore be at an unfair advantage (or disadvantage) competing for jobs in different fields, or may suffer unintended, unforeseen consequences as a result of their augmentations. How we manage the reintegration, reversal or treatment of augmented individuals will emerge as a crucial legal and ethical question over the next 20 years.

Questions

- How will society address the ethical and legal challenges of advanced biotechnology?

Conclusion

This spread of knowledge, while good for the country as a whole, has specific implications for defence and wider government. An awareness of developments must be maintained, and corporate oversight will be hugely important in the next 20 years. Numerous stakeholders and articles consulted pointed towards concerns around people's right to privacy. We are already seeing the effects of these issues with Facebook's reaction to the Cambridge Analaytica scandal, and the potential for disturbance when dealing with something as personal as generic information is huge.

This paper doesn't seek to answer all of the questions it asks. It's role in the EDTAS process is to introduce technology concepts, inform delegates, and stimulate discussion. Numerous stakeholders, both domestic and international were consulted on the issues raised. All supported the notion that Biotechnology is a massively disruptive area of research, and that ethics are a key driver. How defence reacts to these developments out to 2040 will be driven by the outcomes of the EDTAS, and the subsequent Big Picture Report.

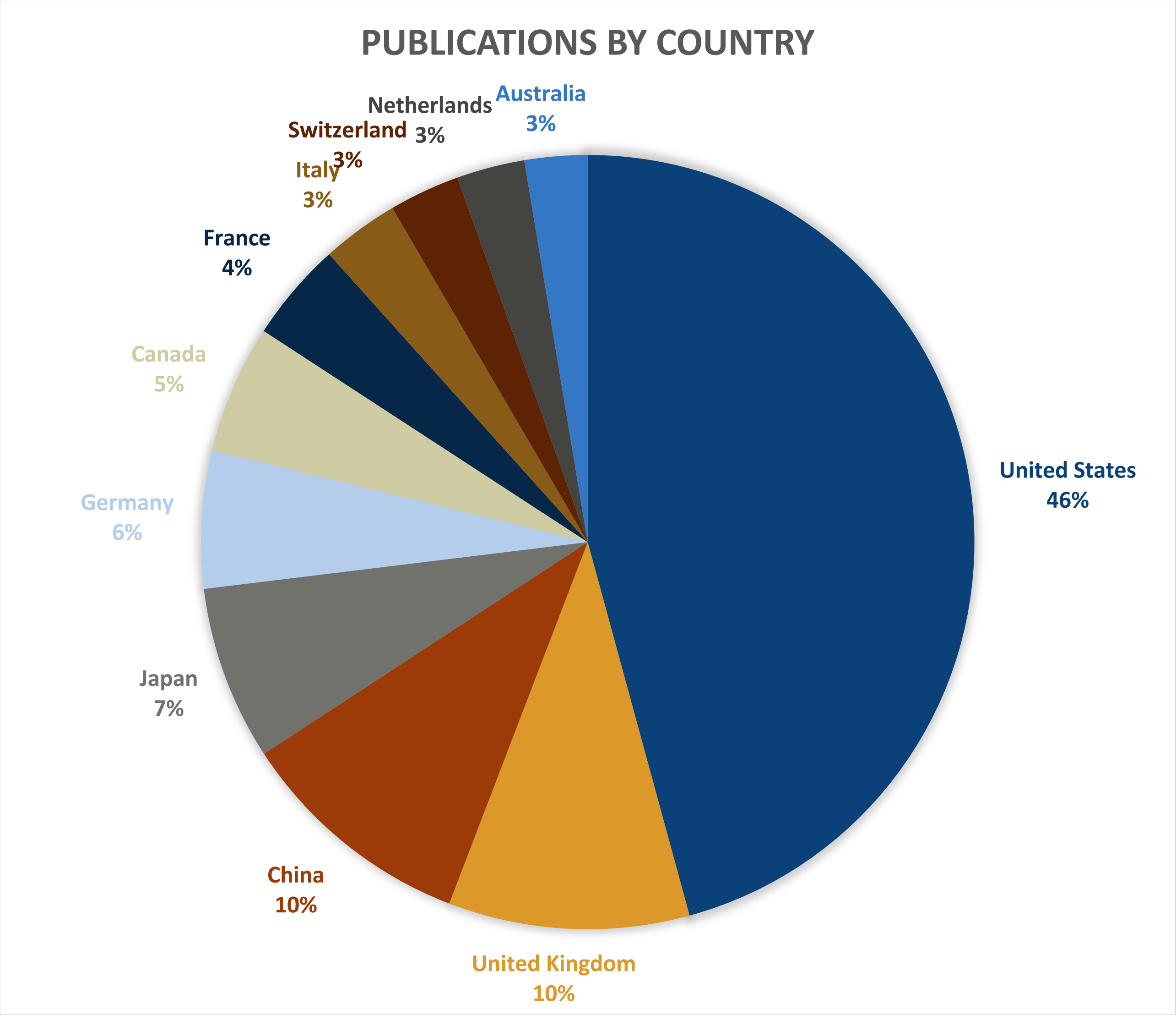
APPENDIX A: SCOPUS DATA

The following graphs represent searches conducted using Scopus, the world largest abstract and citation database of peer reviewed literature. Scopus provides metrics for over 22,600 titles.

The data is presented for both Human Measurement technology and Human Modification technology, along with the search parameters entered to gather the data.

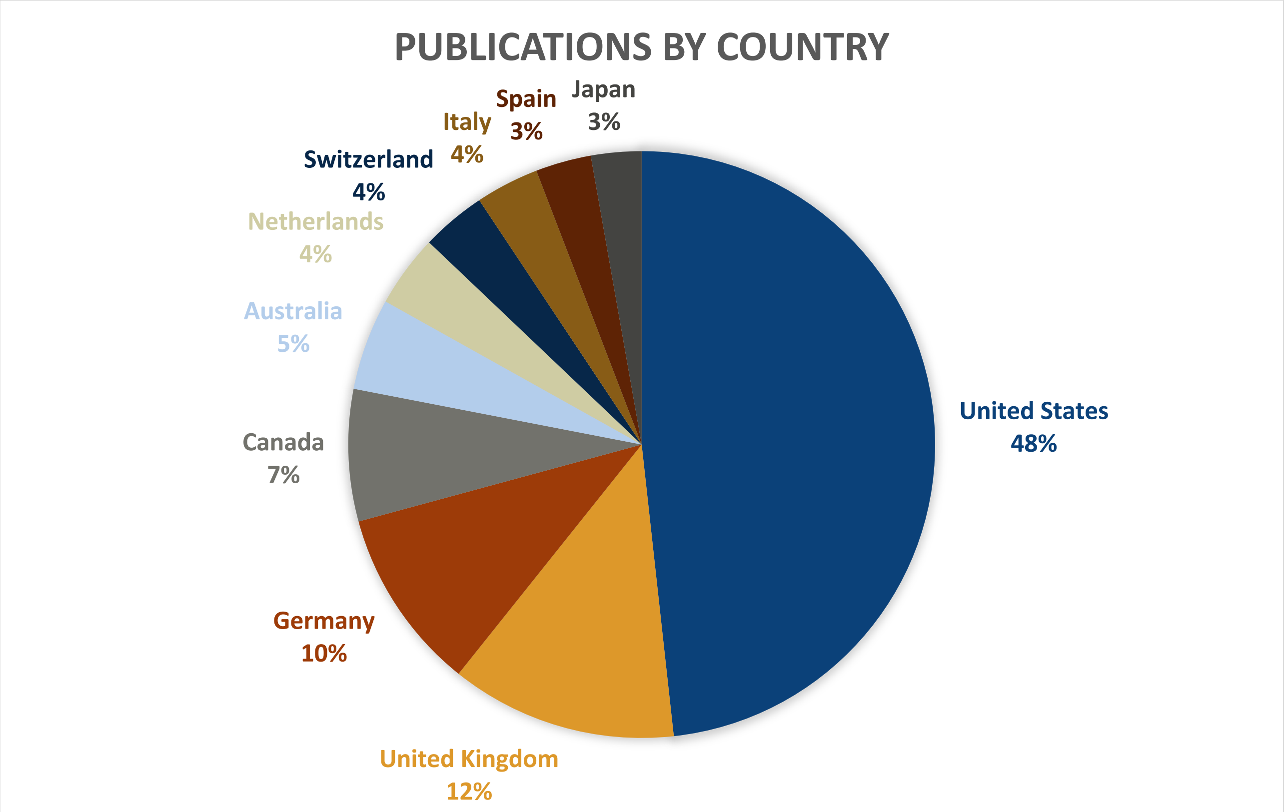
Publications by country – Human Monitoring Technology

Search parameters: *(TITLE-ABS-KEY("cognitive sensing" OR "physical sensing" OR (nano W/1 robotics) OR (human W/3 genomics OR bioinformatics OR biochemistry)))*



Publications by country – Human Measurement technology

Search parameters: *(TITLE-ABS-KEY(cognitive OR physical W/2 enhancement AND human))*



ANNEX A: BIBLIOGRAPHY

Abhilash, M. (2010) Nanorobots. *International Journal of Pharma and Bio Sciences*.

Alexander, D. R. (2003) Uses and abuses of genetic engineering. *Postgraduate medical journal*. [Online] 79 (931), 249–251. [online]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12782769 (Accessed 23 March 2018).

Anderson, N. L. & Anderson, N. G. (2002) The human plasma proteome: history, character, and diagnostic prospects. *Molecular & cellular proteomics : MCP*. 1 (11), 845–867. [online]. Available from: http://www.ncbi.nlm.nih.gov/pubmed/12488461 (Accessed 1 March 2018).

Anon (n.d.) *Engines of Creation - K. Eric Drexler* [online]. Available from: http://e-drexler.com/d/06/00/EOC/EOC_Table_of_Contents.html (Accessed 1 March 2018).

Anon (n.d.) *Existing regulatory framework | ALRC* [online]. Available from: https://www.alrc.gov.au/publications/26-genetic-discrimination-insurance/existing-regulatory-framework (Accessed 23 March 2018).

Anon (n.d.) *File:Gene Drive.png - Wikimedia Commons* [online]. Available from: https://commons.wikimedia.org/w/index.php?curid=62766590 (Accessed 23 March 2018).

Anon (n.d.) *Nanobots will live in our brains in the 2030s, says Google boss* [online]. Available from: https://www.irishtimes.com/business/technology/nanobots-will-live-in-our-brains-in-the-2030s-says-google-boss-1.3259597 (Accessed 2 March 2018).

Anon (n.d.) *Stallman's got company: Researcher wants nanotech patent moratorium | Ars Technica* [online]. Available from: https://arstechnica.com/science/2012/11/stallmans-got-company-researcher-wants-nanotech-patent-moratorium/ (Accessed 2 March 2018).

Ausbiotech.org (2017) *Existing regulatory framework | ALRC* [online]. Available from: https://www.ausbiotech.org/documents/item/389 (Accessed 24 March 2018).

Clark, L. C. & Lyons, C. (1962) ELECTRODE SYSTEMS FOR CONTINUOUS MONITORING IN CARDIOVASCULAR SURGERY. *Annals of the New York Academy of Sciences*. [Online] 102 (1), 29–45. [online]. Available from: http://doi.wiley.com/10.1111/j.1749-6632.1962.tb13623.x (Accessed 2 March 2018).

Feynman, R. P. (1992) There ' s Plenty of Room at the Bottom. *Journal of Microeleciromechanical Systems*. [Online] 1 (1), 60–66.

Kumar, R. et al. (2014) Applications of Nanorobotics. *International Journal of Scientific Research Engineering & Technology*. 3 (8), 2278–2882. [online]. Available from: www.ijsret.org (Accessed 2 March 2018).

Kurzweil, R. (2005) The Singularity Is Near: When Humans Transcend Biology. Book [online]. Available from: http://www.singularity.com/aboutthebook.html (Accessed 2 March 2018). 2011 p.652. [online]. Available from: http://www.singularity.com/aboutthebook.html (Accessed 2 March 2018).

Li, J. et al. (2013) TCPA: a resource for cancer functional proteomics data. *Nature Methods*. [Online] 10 (11), 1046–1047. [online]. Available from: http://www.nature.com/articles/nmeth.2650 (Accessed 1 March 2018).

Pearce, J. M. (2013) Open-source nanotechnology: Solutions to a modern intellectual property tragedy. Nano Today [online]. Available from: https://www.sciencedirect.com/science/article/pii/S1748013213000388?via%3Dihub (Accessed 2 March 2018). 8 (4) p.339–341. [online]. Available from: https://www.sciencedirect.com/science/article/pii/S1748013213000388?via%3Dihub (Accessed 2 March 2018).

Rigaud, N. (2008) *OECD International Futures Project on Biotechnology : Ethical and social debates*. 33 (0), 1–89.