iHuman

Blurring lines between mind and machine

PERSPECTIVE

THE ROYAL SOCIETY

Emerging technologies

As science expands our understanding of the world it can lead to the emergence of new technologies. These can bring huge benefits, but also challenges, as they change society's relationship with the world. Scientists, developers and wider society must ensure that we maximise the benefits from new technologies while minimising these challenges. The Royal Society has established an Emerging Technologies Working Party to examine such developments and create perspectives.

Neural interfaces

Neural interfaces, broadly defined, are devices that interact with the nervous system of an individual. More specifically, the term is frequently used to describe electronic devices that are placed on the outside or inside of the brain or other components of the central and peripheral nervous system, such as nerves and links between nerves and muscles, to record or stimulate activity – or both. Interfaces placed inside the brain or body are known as internal, invasive or implanted technologies, as opposed to external, non-invasive or wearable devices.

The Royal Society expects that neural interface technologies will continue to raise profound ethical, political, social and commercial questions that should be addressed as soon as possible to create mechanisms to approve, regulate or control the technologies as they develop, as well as managing the impact they may have on society.

Supplement materials and references are available online at **royalsociety.org/ihuman-perspective**

iHuman: blurring lines between mind and machine
Issued: September 2019 DES6094
ISBN: 978-1-78252-420-5

This report can be viewed online at
royalsociety.org/ihuman-perspective

Contents

Why neural interfaces matter

MESSAGE FROM THE CO-CHAIRS

From the wheel to the algorithm, humans have innovated by using our brains to create new technologies. Now, we are turning that process inside out – using external technologies to transform our brains.

Our society documents its history in terms of technological milestones: the stone, bronze and iron ages; the industrial revolution that transformed how we use energy and work; and the digital era that has transformed how we communicate and connect. This briefing examines the potential for a new era, that of neural technology – and explores how to deal with the future risks and opportunities.

From the wheel to the algorithm, humans have innovated by using our brains to create new technologies. Now, we are turning that process inside out – using external technologies to transform our brains. It is very new and very different.

With artificial intelligence (AI) spreading fast, much of the technology world's attention is still focused on the digital revolution, including the 'Internet of Things' that is linking physical assets to networks. But neural technology could bring about even more profound change – linking the cognitive power of the human brain to the processing power of machine learning and supercomputing.

As co-chairs, we come to this project as specialists in the relatively new discipline of medical engineering – working at the border between electrical engineering and medicine. We create cochlear implants for children who are born deaf, artificial pancreases for type 1 diabetics, wireless heart monitors and neural stimulators that reduce food cravings to combat obesity. We conduct leading-edge research into implantable devices to restore hearing, sight and movement.

From this front line, we can see how the technologies we work with could mature and expand massively in the coming decades, often overtaking pharmaceuticals in efficacy. Indeed, in many cases, interfaces offer hope where drugs have failed, such as in cases of drug-resistant epilepsy or depression.

At the same time, we are acutely aware of the challenges, particularly when introducing external technologies into the brain; the body's most complex and least understood organ.

Today, we are at the start of that journey. Neural interfaces are like computers in the 1970s; innovation and investment will lead to smaller, more powerful and more usable devices.

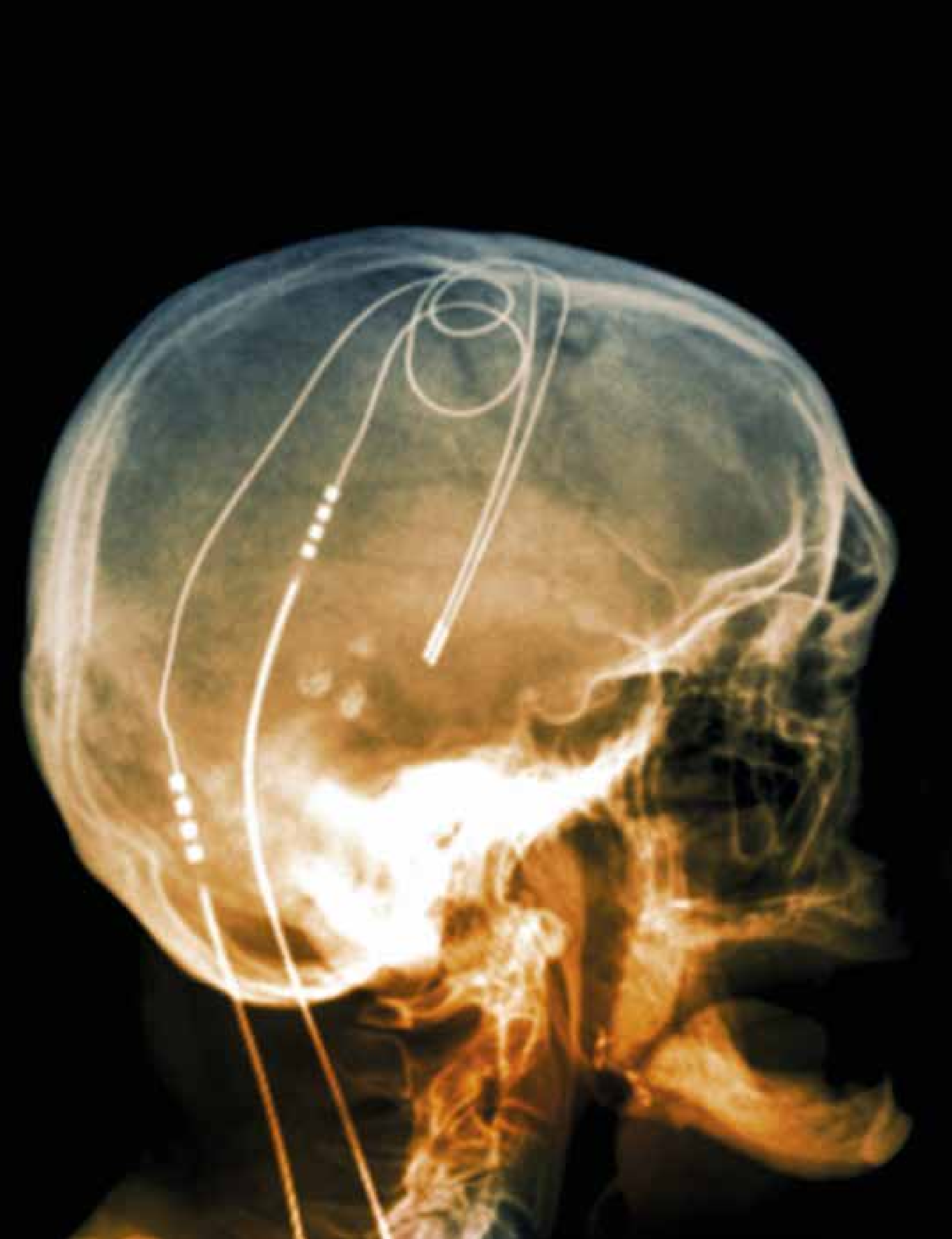
In medicine, the big questions are around how to make life-changing technologies available to more people. Beyond medicine, the questions extend to the ways in which the whole of society may change. Interfaces offer benefits that are as unimaginable today as the smartphone was a few decades ago. Better health. Better memory. Better concentration. Healthier ageing. A more collaborative world. But they also pose new risks: the risk of thoughts or moods being accessed by companies, governments or others; risks to privacy and human rights; and the risk of widening social inequalities. Widespread use of neural interfaces may pose more fundamental issues for society. For example, do they change what it means to be human? Or are they just another example of an ever-expanding toolkit of capabilities?

The opportunities are unprecedented and immense – as are the challenges. We believe that policymakers, business leaders and citizens need to prepare for this new wave of neural technology by building structures and systems needed to realise the opportunities, manage the risks and address the fundamental questions. That is why we have produced this briefing, together with the more detailed papers and other communications that accompany it. The Royal Society also commissioned an independent programme of public dialogues across the UK on the topic that has illustrated that people are interested in the subject and keen to be involved in debating and shaping the policy response.

This Perspective starts by looking at what the long-term destination of this journey could look like, in terms of both benefits and risks. It examines how neural interfaces are already being used today, with some case studies, before reviewing the current state of neuroscience, how the key technologies work and how they have developed. This Perspective then looks ahead to the next frontiers, before tackling issues of ethics and regulation. It concludes with some principles for managing future developments followed by specific calls to action.

Professor Chris Toumazou FRS FREng and Dr Tim Constandinou
Co-chairs, the Royal Society Steering Group on Neural Interface Technologies

Neural interfaces are like computers in the 1970s; innovation and investment will lead to smaller, more powerful and more usable devices.



Summary

Neural interfaces connect the brain or nervous system to equipment, typically digital devices or IT systems. Some act to record physiological activity, such as brain signals or movements, while others stimulate it. Some technologies, known as 'closed-loop' systems, record activity and deliver stimulation in response.

Neural interface technologies have the potential to bring major benefits to society. These include life-changing therapies for people with conditions such as stroke, epilepsy, paralysis or depression. They offer possibilities for enhanced concentration, decision-making and collaboration. They could also contribute to improvements in individual fitness and well-being, as well as enabling safer homes, roads and workplaces, for example by monitoring for fatigue.

Many people worldwide already benefit from medical neural interface technologies. In many cases, their conditions have proved drug-resistant and 'electroceuticals' have achieved what pharmaceuticals could not. Cochlear implants that substitute damaged parts of the ear provide hearing for around 400,000 people. Thousands of people with conditions such as Parkinson's disease, dystonia and essential tremor have been treated with deep brain stimulation[1]. External, wearable interfaces include a range of devices that assist people who have had a stroke in their rehabilitation. People otherwise unable to communicate have been able to spell out words using brain signals alone, providing them with an invaluable means of interaction.

Neural interface technologies have the potential to bring major benefits to society – life-changing therapies for patients with conditions such as stroke, epilepsy, paralysis or depression.

Left:
Coloured X-ray of the head of a patient showing the electrodes (light lines) of a deep brain stimulator (DBS) implanted in the brain to treat the symptoms of Parkinson's disease.
© Zephyr / Science Photo Library.

Opportunities and challenges arise from the distinctive nature of neural interfaces in enabling brain signals, and ultimately thoughts, to be detected or stimulated by external devices.

Beyond medicine, gamers are already using headsets to control on-screen characters, and interfaces are being offered online to students as concentration aids. There have been reports of companies using technology to monitor employees' mood. A number of entrepreneurs and 'Big Tech' companies are investing at scale in applications such as control of a mouse or keyboard using brain signals alone. Such applications may be available in the short to medium term, while very basic thought-transference has been demonstrated in laboratory conditions and could be achievable in some form within decades.

Both opportunities and challenges arise from the distinctive nature of neural interfaces in enabling brain signals, and ultimately thoughts, to be detected or stimulated by external devices. The technologies also raise ethical concerns over issues such as privacy, autonomy, human rights and equality of access. This perspective highlights two separate, but linked challenges. The first is to fulfil the potential of neural interfaces in medicine by advancing innovation, lowering cost and ensuring that safe, effective treatments can be approved efficiently and disseminated to millions who could benefit. The second is to manage the risks associated with wider societal use of neural interfaces in everyday life, as they emerge from specialised markets such as computer gaming and become available to consumers.

Right:
Augmented reality glasses and other wearables may, in the future, be able to detect brain signals, allowing users to control computers and other electronic devices with their mind alone.
© spooh.

Call to action

Given these challenges, the Royal Society makes one central proposal, that the UK should use neural interfaces as a test case for an ambitious, democratised and anticipatory approach to promoting emerging technologies. This joined-up approach would seek to stimulate innovation in the field, while constructing responsible regulation around the technology as it develops.

To achieve this aim, we recommend:

- The UK develop a 'Neural Interface Ecosystem' to accelerate the development of the technologies in the UK and encourage multidisciplinary collaboration across industries.
- An 'early and often' approach to addressing the ethical considerations of the field.
- The UK trial new approaches to technology regulation on neural interface technologies. These could include the use of regulatory 'sandboxes' and new ways of gathering evidence about the efficacy of medical devices.
- The general public be given a clear voice in shaping the future of neural interface regulation. Furthermore, the processes of consultation, regulation and policy choices be designed so that the public's voice has an impact on them. This should include a key role for public consultation in developing regulatory frameworks and public representation on relevant advisory boards.

All technologies create both benefits and risks and this report seeks to set out a course towards maximising the former while minimising the latter. However, the unavoidable point for opinion formers, decision takers, policymakers and the public is that they have the opportunity to shape the future of neural interface technologies. These technologies are being developed now. Investment is accelerating. The impacts will be profound – and if they are to be positive ones, society needs to be engaged early and often.

Visions and challenges of neural interfaces

What opportunities do neural interfaces create? And what risks do they pose? Here, we look at some of the possibilities. Many of these are unproven and uncertain. But all are conceivable as eventual outcomes of technologies that have been developed today, at least at a basic level.

They are outlined here to stimulate thinking among scientists, policymakers, investors and others about potential objectives to pursue and dangers to avoid.

"Innovation in every generation… solves problems, creates wealth and new employment, while at the same time potentially disrupting the status quo of existing wealth and employment, and creating new problems and challenges."

Mark Walport, Government Chief Scientific Adviser, 2013 – 2017[2]

Left:
Some people with paraplegia have been helped to walk again by wireless spinal implants that apply targeted stimulation to their nerves. © Jamani Caillet / EPFL.

VISIONS

What could be gained from neural interface technology?

The neural revolution could be part of driving advances in human well-being that exceed those brought about by the industrial and digital revolutions.

In the medical world, neural interfaces could be transformative. People with paralysis or missing limbs could use brain-controlled prosthetics to bypass damaged limbs, spines or nerves. Surgery could become more effective, with precision robots used to perform increasingly complex tasks. Pain could be alleviated by electrical stimulation; sight and hearing restored or enabled for the first time by sophisticated implants.

Mental health conditions could be treated by using interfaces to target relevant parts of the brain, bringing relief to the hundreds of millions worldwide who have depression[3]. Even Alzheimer's disease, which has proved resistant to conventional therapies, might be halted or reversed[4].

In the broader sphere of health and fitness, people could undergo 'whole brain diagnosis' to identify their unique talents and challenges. Today's 'brain training' computer games, whose impact is debated, might give way to demonstrably effective 'brain cleaning' or 'mind gym' sessions to keep minds sharp and creative. Monitoring of health indicators and neurostimulation could prompt people to exercise, possibly assisted by direct muscle stimulation.

Neural interfaces offer myriad possibilities to enhance everyday life. We could use our minds to open doors, turn on lights, play games, operate equipment or type on computers.

Then there are opportunities to enhance or supercharge the brain itself. Implants, helmets, headbands or other devices could help us remember more, learn faster, make better decisions more quickly and solve problems, free from biases. Training could be transformed by the ability simply to 'download' new skills. Neural devices that help students to concentrate, remember, learn and decide could raise educational achievement levels and widen opportunity. If the technologies were affordable and available to all, then such technologies could support several of the UN Sustainable Development Goals.

Linking human brains to computers using the power of artificial intelligence could enable people to merge the decision-making capacity and emotional intelligence of humans with the big data processing power of computers, creating a new and collaborative form of intelligence. People could become telepathic to some degree, able to converse not only without speaking but without words – through access to each other's thoughts at a conceptual level. This could enable unprecedented collaboration with colleagues and deeper conversations with friends[5].

Not only thoughts, but sensory experiences, could be communicated from brain to brain. Someone on holiday could beam a 'neural postcard' of what they are seeing, hearing or tasting into the mind of a friend back home. Alternatively, people might choose not to undertake some activities physically at all and instead experience them virtually through images, sounds, smells, tastes and sensations fed into the brain – from meals to parachute jumps.

Implants could become body parts, as pacemakers or artificial hips are today. Mood, knowledge and memory could be securely and confidentially backed up or uploaded to a digital cloud. Interfaces attached to animals or birds could enable experiences such as virtual flight.

Mentally and physically enhanced military or police personnel could protect the public by being able to see more effectively in the dark, sense the presence of others and respond rapidly. Firefighters, paramedics and other public protection workers could benefit from enhanced perception and focus, operating as members of an integrated team with access to the same data and imagery as control room staff.

People who work in hazardous environments could optimise their performance by training in immersive simulations, and in the service sector, people who have caring needs could be empowered to live more independently if they were enabled to command robots using brain signals while having their mood monitored remotely. ■

CHALLENGES

Risks raised by neural interface technology

However, just as digital systems that are mainly beneficial also give rise to risks of cybercrime and create other challenges for societies to negotiate, neural interfaces also raise potential risks for individuals and society. Many of these arise from the possibilities of human augmentation and the ultimate potential for access to people's thoughts.

Military and security applications are among those that raise the greatest concerns. The potential to enhance humans mentally as well as physically not only provides countries with welcome protection, but with the means to organise hostile operations remotely. Already, military activities are conducted in which ground or air forces are linked to command centres through speech and vision.

The prospect of cognitive enhancement also raises issues of access and fairness. Today, citizens in many countries can choose to pay for privately supplied health or education. But, should people also be able to pay for enhanced brainpower when others may not be able to afford it? How would state-provided health and education vary between nations?

Access to peoples' thoughts, moods and motivations could lead to abuse of human rights. Companies might ask employees to wear interfaces that reveal their feelings. If thoughts could be accessed, then they might be used by corporations in efforts to market goods and services or by politicians or campaigners seeking recruits to their causes. The prospect of being constantly watched may itself alter people's behaviour and affect their well-being[7]. Health insurers might use access to neural data to refuse cover. While some would welcome advanced lie detectors,

> "When you invent the ship, you also invent the shipwreck; when you invent the plane you also invent the plane crash; and when you invent electricity, you invent electrocution... Every technology carries its own negativity, which is invented at the same time as technical progress."
>
> Paul Virilio[6]

© Laurence Dutton

how should society view the possibility of police or military interrogators gaining clearer access to a subject's mental processes? There is, today, evidence of the potential to hack networked devices of all kinds from computers to kettles[8], – 'The Internet of Hackable Things' as one paper puts it – as well as neural interfaces[9] such as cochlear implants[10].

On a more philosophical level, there are fears that widespread use of neural interfaces could lead to human decisions being directed by what some have called 'neuro-essentialism' – the perception that the brain is the defining essence of a person and that our choices can be reduced to a set of neurobiological processes, leaving no room for individual agency or moral responsibility. Critics say that too great an emphasis on neuroscience overestimates its importance in human functioning compared to qualities such as emotional intelligence[11]. Research has also shown that defining 'fairness' in a mathematically rigorous manner is difficult[12] and that notions of fairness are often strongly dependent on context. In general, increasing reliance on non-human technologies that enhance human abilities could lead to overdependence on them and a consequent attrition of pure human cognitive capacities. ■

Access to peoples' thoughts, moods and motivations could lead to abuse of human rights.

Reality check

Could this actually happen?

This feels like science fiction. What are the actual chances of mind control, mind reading and mind boosting?

These things are a long way off but not impossible in some form. Think how distant and futuristic landing on the moon or the internet would have seemed in 1950, when few UK households even possessed a telephone[13].

Is this something completely new?

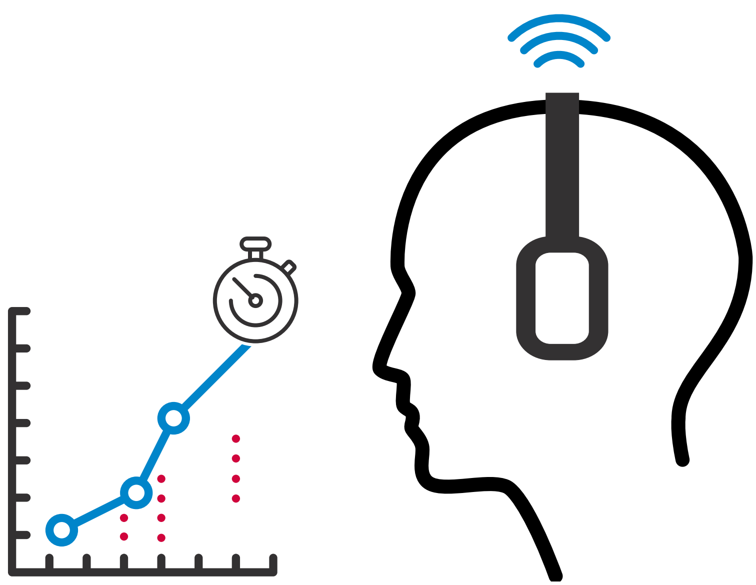
We already influence our minds by other means, including pharmaceuticals or exercise. There is a parallel debate in progress over so-called 'smart drugs' such as Modafinil, which studies have shown to improve cognitive function[14]. Access to the internet gives us a capability that would have been seen as a superpower 30 years ago. The basic building blocks of neural interfaces have also been around for some time. We already have mind-controlled model helicopters, brain-controlled artificial limbs and headsets that can boost concentration and memory. Changes that could transform society do not depend on inventing new technologies but on innovation.

QA

Isn’t it still a very long journey?

Indeed – though it took fewer than 100 years to get from the car to the spaceship. Innovation in digital and other technologies is accelerating and investment is pouring into neural technology as never before. New technologies are being enabled by rapid increases in computing power – which has broadly followed ‘Moore’s Law’ that the processing power of a computer chip doubles every two years.

There is no guarantee that telepathy or supercharged decision-making will come about, but there is equally no guarantee that they will not. Meanwhile, less dramatic but nonetheless game-changing innovations such as typing by brain are much closer to reality. ■



Right:
Illustration showing how a headset could be used to monitor and boost concentration and memory.

Neural interfaces now

Where we are on the journey

In many cases, interface treatments are pursued when conditions have proved resistant to pharmaceuticals.

Neural interfaces are already widely used in medicine, with external devices more prevalent than implanted ones. A few devices have been deployed widely, while many others are being explored in research, trials and demonstrations.

Beyond the medical world, a range of external interfaces have been researched, trialled and in some cases commercialised, causing excitement among gamers and 'brain-hackers'.

Medical applications

Neural interfaces, sometimes called 'electroceuticals', are used to treat a range of medical conditions. Some treatments have been established in medical practice for decades, such as cochlear implants used to help thousands of people with hearing loss; stimulators to aid stroke recovery; and deep brain stimulation (DBS) for essential tremor, Parkinson's disease and dystonia[15]. Other treatments are still being explored in the laboratory, such as transcranial direct current stimulation (tDCS) for depression[16]. Others are in the early stages of medical use, such as DBS used for epilepsy[17] or the 'Mollii Suit' body garment that delivers electrical stimulation to people with muscle spasticity caused by conditions such as stroke or cerebral palsy[18]. Often such new technologies are approved in some countries but not others, such as the 'NeuroPace' system for epilepsy that is available in the USA[19] but not the UK[20]. In many cases, interface treatments are pursued when conditions have proved resistant to pharmaceuticals. For example, around 20 – 30% of epilepsy is estimated to be drug-resistant[21]. Such 'electroceuticals' can prove more effective than drugs as they can be precisely targeted on relevant brain or body parts, avoiding the side effects associated with exposing the entire body to the impact of an ingested chemical medicine.

Left:
A clinical trial of the cortical implant 'BrainGate' demonstrates how a person with paralysis is able to control a robotic arm using just their thoughts. © Brown University.

Implanted technologies

The most extensively used form of internal interface today is the cochlear implant – worn by more than 400,000 people worldwide[22] to enable them to experience hearing despite damage to parts of their cochlea or inner ear. While the restoration of hearing is transformative for people's lives, work to improve the systems continues as sound quality is poorer than 'normal' and the devices are obtrusive. Other sensory implants are at an earlier stage of development. These include retinal implants, approved for use in the USA and Europe in the last decade, that provide people with sight loss with a form of vision[23] and vestibular implants that help with motion detection and balance. While pacemakers are a form of implanted technology, they are not discussed in this report as they are not classed as a neural interface.

DBS is approved in the UK as well as other countries to treat Parkinson's disease, tremor and other conditions[24]. It has not yet been approved for NHS funding in England to treat epilepsy[25]. An estimated 200,000 people with Parkinson's disease worldwide are being treated with DBS[26]. The treatment typically involves two long, thin electrodes being inserted into the deep brain nuclei, linked by a wire under the skin to an implantable pulse generator (IPG) in the chest, delivering constant stimulation. Changes in its settings can be implemented by the user via a wireless external controller. The IPG delivers pulses to brain cells that control movement in people with Parkinson's disease or prevent seizures for people with epilepsy. The latest 'NeuroPace' system licensed for use in the USA[27] is a 'head-only' neurostimulation therapy, similar to DBS. It is also 'responsive' – detecting when a seizure is imminent and delivering a stimulus to prevent it, instead of providing 'always-on' or patient-triggered stimulation[28]. DBS has also been successful in small-scale trials among people with anorexia[29] and obsessive-compulsive disorder[30].

Above:
The Hybrid Assistive Limb (HAL) aids neurorehabilitation by detecting the brain's instructions to move muscles and in response, assisting the wearer to exert more power than they are capable of, slowly building capability to perform the desired motion unassisted.
© Constance Care Robotics Rehabilitation Center.

Vagus nerve stimulators have been used to treat epilepsy, depression and substance abuse, typically when other therapies have failed[31]. They also use an IPG implanted in the chest, from which a spinal electrode is wrapped around the left vagus nerve, which runs from the brainstem to the abdomen. The electrical stimulation causes nerve activation and the release of neurotransmitters such as noradrenaline to change brain networks. Researchers are now looking into the possibility of using vagus nerve stimulation to treat many other conditions including pain, anxiety, addiction or autoimmune disorders.

Interfaces have also been used to treat people who have suffered damage to parts of the nervous system with the result that the electrical signals it uses to communicate with itself and the muscles connected to it have become too weak to be effective. For example, newly demonstrated spinal implants have enabled people to walk again by boosting signals sent down the spinal cord from the brain[32]. People with paralysis have also been treated with interfaces in efforts to restore physical movement, bladder voiding, and communication. Chronic pain has also been treated by stimulating the part of the spinal cord that carries pain signals[33].

A cortical implant – surgically implanted onto the motor cortex of the brain – called 'BrainGate' has enabled immobile people to use brain signals alone to move cursors[34], type on an electronic keyboard[35] and grasp using a robotic hand[36]. These people can also be helped through external interfaces such as an electroencephalography (EEG) headset that enables them to type by mentally selecting a desired letter from a sequence on a screen[37].

External technologies

One of the most mature external interface technologies is Functional Electrical Stimulation (FES), originally developed in the 1960s to help people recover motor function. The most common application is the 'drop-foot stimulator' used by people who have difficulty lifting their foot when walking, such as those who have had strokes or have multiple sclerosis[38]. The device applies electrical stimulation through the skin to the nerves that activate the muscles that lift the foot.

External devices have also been used to treat people who have sustained damage to the nervous system, for example providing an alternative to implants for people who cannot walk due to spinal injury. These treatments work by priming the system to respond to brain signals rather than driving an immediate motor response as with FES. Electrodes attached to the skin near the spinal cord can upregulate electrical activity so that the threshold for sending nerve signals is reached, messages are passed and an injured person can begin to activate their muscles. Recent research has shown how people with paralysis can begin to walk using such technologies. People with paralysis have also used 'exoskeletons', or wearable robots, such as the Hybrid Assistive Limb (HAL) designed by Cyberdyne, that detect the brain's instructions to move leg muscles via the skin and convey them to artificial limbs attached to the person's legs, bypassing the injured spine[39].

Transcutaneous Electrical Nerve Stimulation (TENS) is used to treat pain, for example in the back, joints and in childbirth, by lightly stimulating nerves over a long period so that the sensory cortex becomes less responsive to actual painful stimuli.

External interfaces are also used in medical diagnosis, including electromyograms (EMG) that are used to help identify conditions from carpal tunnel syndrome to muscular dystrophy by detecting abnormal muscle activity, including fatigue and spasticity[40].

One technology set to emerge from trials into everyday medical use is the use of 'gamification' to treat chronic pain and other conditions. Using a 'neurofeedback' approach, EEG headsets are used to read the brain signature of someone with chronic pain and graphically represent it, for example, as a car taking part in a race. The person can then attempt to change their brain signature to make the car go faster, and when that occurs, pain is reduced because the system is programmed to accelerate the car when their efforts succeed in lowering the particular brainwaves that are active during pain and amplifying other non-pain-related brainwaves.

Research applications

A wide range of interface technologies is used in neuroscience research. For example, brain imaging is carried out using external techniques such as Positron Emission Tomography (PET), Magnetic Resonance Imaging (MRI) and EEG[41]. Some research on memory has been done using internal devices, typically with volunteers who are using implants to control drug-resistant epilepsy. One study, for example, showed how individual 'concept' neurons fired in response to particular images – such as one subject's 'Jennifer Aniston' neuron[42] – while another demonstrated proof of concept for a 'neural prosthesis' to help restore memory[43]. 'Neuromorphic' systems and chips are designed to emulate the operation of the brain's neurons, synapses and networks. As well as providing insights into how the brain works, this offers a novel method of computing, based on the brain, with improved energy efficiency as well as potential for applications such as speech and image recognition[44].

A cortical implant called 'BrainGate' has enabled immobile patients to use brain signals alone to move cursors, type on an electronic keyboard and grasp using a robotic hand.

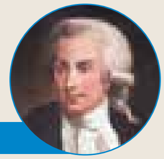
Timeline

Ancient Egypt

Electric catfish used to treat arthritis[45]

First century AD

Electric rays used by Romans to treat headaches[46]

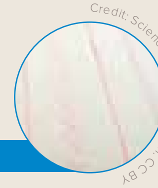


1780s

Luigi Galvani of Bologna shows that muscle and nerve cells possess electrical force responsible for muscle contractions and nerve conduction[47]

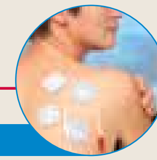
1875

Dr Richard Caton of Liverpool, UK, uses galvanometer to observe electrical impulses from the surfaces of living rabbit and monkey brains[48]



1912

Ukrainian physiologist Vladimir Pravdich-Neminsky publishes the first animal electroencephalography (EEG)[49]



1919

The Electreat, a TENS device, is patented by Charles Willie Kent and manufactured in Peoria, Illinois, USA[50]

1973

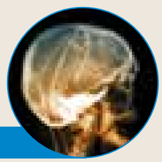
Professor Jacques Vidal of the University of California at Los Angeles coins the term 'brain-computer interface' and sets out the aims of the Brain-Computer Interface project to analyse EEG signals[62]

1974

Medtronic patent TENs for pain control [63]

1988

EEG signals are used to control a mobile robot[64]



1997

The US Food and Drug Administration approves DBS for treatment of essential tremor and Parkinson's disease (followed by approval for dystonia in 2003 and epilepsy in 2018)[65]

1998

Researchers at Emory University in Atlanta report installation of a brain implant that stimulates movement in a person with 'locked-in syndrome'[66]

2005

Tetraplegic Matt Nagle becomes the first person to control an artificial hand using a brain-computer interface (BCI) as part of Cyberkinetics's BrainGate project[67]

2013

BrainGate patient demonstrates control of a robot prosthetic limb[68]

2013

FDA approves Argus II retinal implant system developed by Second Sight[70]

2013

FDA approves NeuroPace RNS system of responsive deep brain stimulation (DBS)[69]

1924

German physiologist and psychiatrist Hans Berger records the first human EEG[51]

1928

Australian Mark Lidwell uses external cardiac pacemaker to save a child's life[52]

1935

Frederic Gibbs, Hallowell Davis and William Lennox of Harvard Medical School report on the use of EEG to demonstrate epilepsy[53]

1952

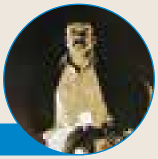
Spanish neuroscientist José M Delgado begins implanting radio-equipped electrode arrays in animals and humans[55]

1957

André Djourno and Charles Eyriès perform the first direct electrical stimulation of the human auditory system[56]

1963

Natalia Petrovna Bekhtereva, neuroscientist at the Institute of Experimental Medicine and the Academy of Medical Sciences in Leningrad, publishes a paper on the use of multiple electrodes implanted in sub-cortical structures for the treatment of hyperkinetic disorders[57]



1965

Alvin Lucier uses EEG to compose music in *Music for the Solo Performer* [59]

1965

Gordon Moore writes seminal paper on annual doubling in the number of components per integrated circuit[58]

1969

American otologist William House installs first cochlear implant that is not rejected by patient's system[60]

1969

Researcher Eberhard Fetz at the University of Washington in Seattle shows that a monkey can control the needle of a meter using only its mind[61]

2016

Entrepreneur Bryan Johnson launches Kernel[73] 'to develop technologies to radically improve and expand human cognition'[74]

2016

Neuralink founded by Elon Musk and others[71] to develop 'ultra-high bandwidth brain-machine interfaces to connect humans and computers'[72]

2017

US Defense Advanced Research Projects Agency (DARPA) launches programme to make neural implants that can record high-fidelity signals from one million neurons[76]

2017

Facebook reveals that it is working on wearable interfaces to enable people to type using brain signals alone[75]

2018

Researchers at University of California, Berkeley create world's smallest, most efficient implanted 'neural dust' wireless nerve stimulator [77]

EEG headsets have also been used to control model helicopters and drones using brain signals alone.

Non-medical applications

Outside medicine, external interfaces are increasingly being used to play games, control equipment and attempt enhancements of memory, concentration and physical performance. However, this study has not found any cases of internal devices used for non-medical purposes other than research. A programme of public dialogues commissioned by the Royal Society to engage with people across the UK found that most participants would welcome the use of neural interfaces to enhance experiences in relation to entertainment and creativity.

The gaming world is particularly significant in pioneering control of games using brain signals or impulses from muscles and nerves, typically using EEG headsets with multiple electrodes[78]. The gaming company Valve is exploring the use of brain-computer interfaces to create adaptive gameplay able to respond to the emotions or ability of the player, which could be achieved by placing EEG sensors in virtual reality (VR) headsets[79]. EEG headsets have also been used to control model helicopters and drones using brain signals alone[80]. Other gamers interact with immersive environments using VR headsets and even full body suits such as the Rez Infinite Synesthesia Suit[81].

Headsets using tDCS – which delivers constant current – are widely marketed as aids to working memory for under £100, with instructions on building them at home also available online[82]. One website asks: 'What if you could improve your memory, perform better at work or at school, or even learn new information up to twice as fast?'[83]. Working memory has been improved in older people for almost an hour using a similar technique – high density transcranial alternating current stimulation (HD-tACS)[84]. Experiments in the US military have suggested tDCS could sharpen mental skills of air crews or drone operators. It is worth noting that while such applications of interfaces are novel, there is a long history of 'study drugs' among students[85] and stimulants used to boost alertness in the military[86]. There have also been reports that tDCS can enhance physical as well as mental performance. For example, 20 minutes of exposure to tDCS was found in some studies to improve the peak performance of cyclists[87]. Other researchers have issued warnings about the unknown factors in tDCS, such as the possibility of unintended damage to parts of the brain not being stimulated and variable impacts on different people[88]. Others have suggested that the apparent effects of do-it-yourself tDCS may amount to a 'placebo response' in people resulting from an expectation of benefit[89].

More far-reaching military and civilian applications are being explored by organisations such as the US's Defense Advanced Research Projects Agency (DARPA). For example, the Next-Generation Nonsurgical Neurotechnology (N3) programme aims to develop 'high-performance, bi-directional brain-machine interfaces' for applications such as control of unmanned aerial vehicles, cyber defence or 'teaming with computer systems… during complex military missions'[90]. DARPA's Neural Engineering System Design (NESD) programme focuses on increasing the capacity of neural interfaces to engage more than one million neurons in parallel enabling 'rich two-way communication with the brain'[91].

Other forms of 'active clothing' may improve safety by tracking brain signals and movements to detect fatigue levels, and intervening if necessary[92]. Automotive companies have already used EEG and related equipment to analyse physiological signals, alongside monitoring of vehicle movements and driver behaviour such as yawning or blinking[93].

In the business world, 'neuromarketing' exercises include using EEG systems to show brain activity as a person makes judgements about brands. The information gathered helps companies to target advertising to elicit brain signals associated with positive feelings towards their products[94]. The Neuromarketing Science & Business Association has been formed to establish principles that address ethical concerns, such as revealing data-collection techniques to research participants[95].

Neural interactive art has been created, such as Christoph De Boeck's Staalhemel, or Steel Sky, which maps users' brainwaves onto steel squares suspended from the ceiling. When users are in a relaxed state, accompanied by the prevalence of alpha waves, the steel is mainly silent. When users are more mentally active, the brain's beta rhythms act to move the squares and fill the room with the sounds of crashing steel[96].

External interfaces are being developed to support behavioural change, for example by making DNA-based recommendations for improving diets[97] and thereby training the body's automatic decision-making system to appreciate the resulting increase in energy. While not strictly 'neural' interfaces, devices such as bracelets to monitor heart rates and step counters are booming and are set to evolve[98].

The programme of public dialogues found many participants believed neural interfaces were acceptable when they enabled people to recover something that had been lost due to an injury or a medical condition. By contrast, the public questioned whether neural interfaces should be used to enhance functions such as memory or concentration among healthy people[99]. ■

Above:
Electroencephalography (EEG) headsets are used to record brain signals and are one most widely deployed external interfaces. They have a long history of use in medicine and research but are also of particular interest to the gaming world. © gorodenkoff.

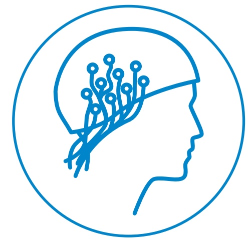
NON-INVASIVE TECHNOLOGIES

Recording technologies · Stimulating technologies · Recording and stimulating technologies

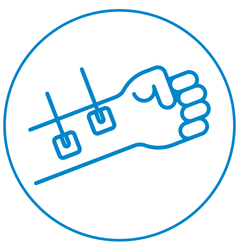
EEG
Electroencephalography

MEG
Magnetoencephalography

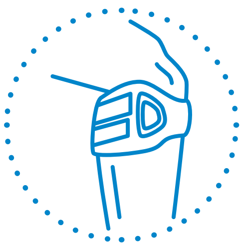
fMRI
Functional magnetic resonance imaging



fNIRS
Functional near-infrared spectroscopy

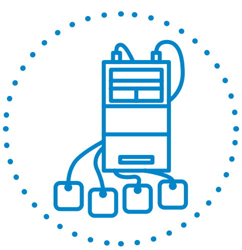


MMG
Mechanomyography



FES
Functional electrical stimulation

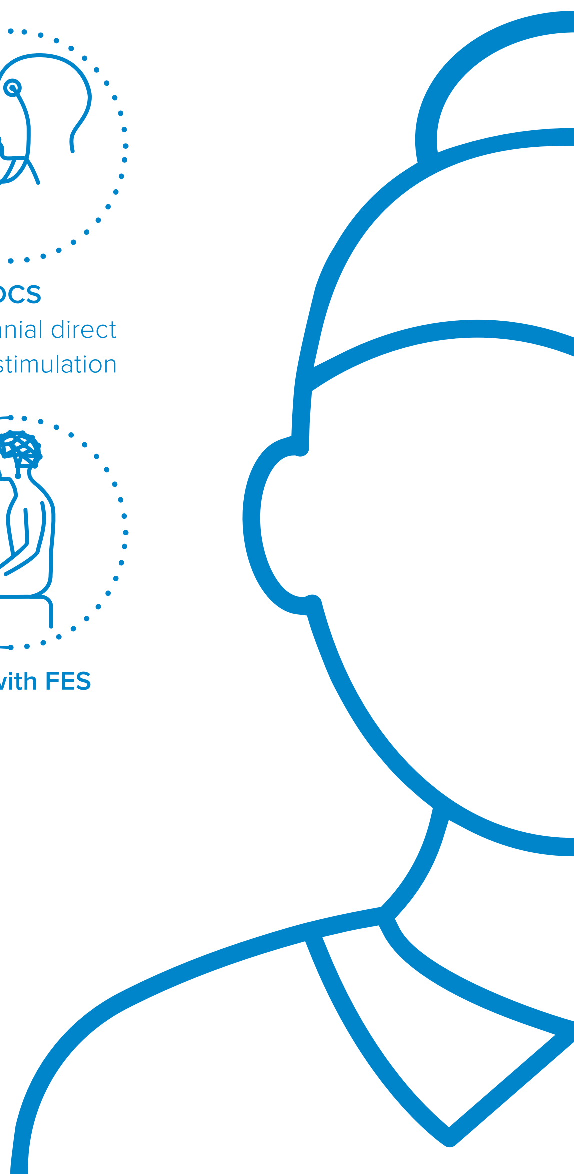
tDCS
Transcranial direct current stimulation



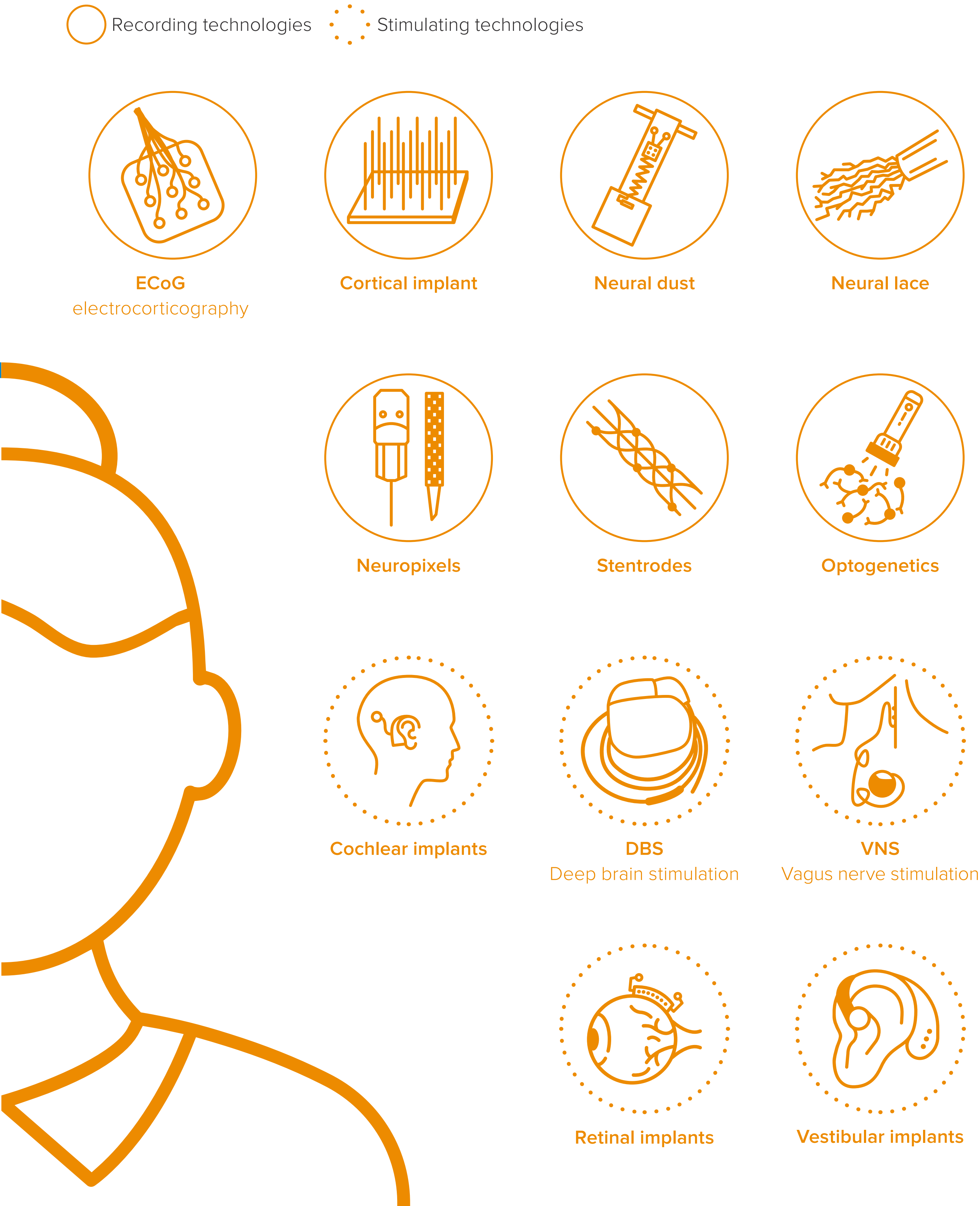
TENS
Transcutaneous electrical nerve stimulation

TMS
Transcranial magnetic stimulation

EEG with FES



INVASIVE TECHNOLOGIES



Invasive technologies

RECORDING TECHNOLOGIES

ECoG – electrocorticography
ECoG uses an array of electrodes placed directly on the exposed surface of the brain to record electrical activity from the cerebral cortex, typically in preparation for epilepsy surgery. ECoG was developed to treat people with severe epilepsy, identifying regions of the brain that generated seizures for removal. ECoG has generally been used as a short-term intervention, but specialists are conducting tests to determine whether systems could be implanted and used for long-term recording and stimulation[100].

Cortical implant
Cortical implants are interfaces such as the 'BrainGate' system, inserted directly into the brain's cortex, which transmit signals to a device located on the outside of the head that sends them on to external objects. They can also be used to stimulate activity. Cortical implants are currently limited to laboratory research, where they have been trialled to restore sight or hearing, improve cognitive functions and enable people who are paralysed to move cursors or objects using brain activity[101].

Neural dust
Neural dust consists of wireless, battery-free miniature implants fitted with sensors and stimulators and powered by ultrasound. The technology was developed by scientists at the University of California, Berkeley who are now developing it through a start-up called iota Biosciences which has attracted $15 million of funding[102]. Current prototypes are around three millimetres long, and researchers are trying to bring the size to submillimetre levels[103]. In experiments with rats, researchers found that neural dust implanted in the leg could record and transmit electrical data[104].

Neural lace
Neural lace (a term coined by novelist Ian M Banks in 2000) consists of arrays of tiny electrodes, placed on polymer wires or threads, which can be injected into the brain. Neuralink has announced the development of arrays of threads each much thinner than a hair, with as many as 3,072 electrodes per array distributed across 96 threads. It has also built a neurosurgical robot– yet to be trialled on humans – capable of inserting six threads together carrying 192 electrodes into a brain in one minute, avoiding blood vessels[105].

Neuropixels
Neuropixels probes are a new type of multi-electrode array that can simultaneously record the activity of hundreds of neurons. The use nearly 1,000 electrical sensors positioned along a probe thinner than a human hair to access many regions of a brain simultaneously[106]. Two Neuropixels probes have already been shown to record simultaneously from over 500 neurons in five regions of a mouse brain[107]. Neuropixels have been developed through an international collaboration largely funded by medical charities by a group of research teams[108].

Stentrodes
Stents are medical 'scaffolds' initially designed to hold open blood vessels, for example to prevent blockages that lead to heart attacks. Stentrodes are stents with electrodes on their outer sides that are injected via catheters into blood vessesls in the brain in an outpatient prodcedure. The electrodes are pushed against the blood vessel wall, from where they record brain activity[109]. Multiple applications are possible, from treatment of neurological conditions[110] to mind control of a wheelchair[111, 112].

Optogenetics
Optogenetics offers a new way to stimulate neurons, using light rather than electrical current. In optogenetic treatments, cells are injected with harmless viruses containing microscopic opsin proteins that can be activated by light. Optogenetics offers an unprecedented level of precision as individual cells or circuits can be targeted with exact timing[113]. Following successful animal trials, small-scale human trials have begun in the USA[114].

STIMULATING TECHNOLOGIES

Cochlear implants
A cochlear implant (CI) is a surgically implanted device that provides a sense of sound to people with severe to profound hearing loss. The implant has an outside component fitted with microphones that detect sounds and convert them to electrical signals that are transmitted to an internal component which stimulates hearing cells in the cochlear nerve.

DBS – Deep brain stimulation
DBS is carried out by inserting electrodes into deep regions of the brain. The electrodes are typically connected to a battery-powered implantable pulse generator (IPG), implanted just below the clavicle or in the abdomen, which stimulates or blocks signals as needed. DBS has been approved in the UK for people with Parkinson's disease, dystonia and tremor, and is being tested for people with Tourette's syndrome and obsessive-compulsive disorder. Worldwide usage has included chronic pain, treatment-resistant depression and drug-resistant epilepsy[115].

VNS – Vagus nerve stimulation
In VNS, leads delivering electrical current are wrapped around the left vagus nerve that runs from the brainstem to the abdomen and are connected to an implantable pulse generator (IPG) under the collarbone in an outpatient procedure. Pulses activate neurons and release neurotransmitters such as noradrenaline, leading to changes in brain networks. Dosage levels can be adjusted from outside the body using a magnetic wand. VNS has been applied most widely in the treatment of drug-resistant epilepsy, but it has also been used to treat depression[116] and substance abuse[117].

Retinal implants
Retinal implants are arrays of microelectrodes (25 – 100) that are surgically attached on or beneath the surface of the retina. They generate signals from incoming light that bypass damaged photoreceptors and stimulate the retina's remaining cells, typically providing partial restoration of vision. Retinal implants have been used to treat people who have lost their sight due to retinitis pigmentosa or macular degeneration[118].

Vestibular implants
Vestibular implants are used to artificially restore vestibular function – which supports balance – in people with bilateral vestibular loss[119]. They consist of motion sensors; an electronic processor that transforms that data into electrical signals; and electrodes implanted near the vestibular nerve branches that transmit the signals to the brain.

Non-invasive technologies

RECORDING TECHNOLOGIES

EEG (Electroencephalography)
Multiple electrodes are placed on the head, typically using a web or cap, which picks up electrical signals created when neurons, or brain cells, send messages to each other. EEG is often used to record brain signals as the equipment is very portable. EEG is used to diagnose conditions that produce distinctive patterns, such as epilepsy, sleep disorders and coma. Gamers have used EEG to control movement using brain signals.

MEG (Magnetoencephalography)
MEG records brain activity by picking up magnetic fields produced by electric currents. MEG has historically required the patient to remain still with the head encased in a bulky scanner, but new 'wearable' helmet devices have now been trialled[120]. MEG produces more accurate recordings than EEG.

fMRI (Functional magnetic resonance imaging)
fMRI provides high resolution images by measuring changes in blood flow in the brain, requiring the patient to lie inside a large expensive scanner. fMRI has provided insights into memory, language, pain, learning and emotion. Outside medicine, fMRI has been used as a lie detector[121] as well as for 'neuro-marketing', for example indicating differences in brain activity when people knowingly drank Coca-Cola as opposed to unlabelled 'coke'[122].

fNIRS (Functional near-infrared spectroscopy)
fNIRS is a relatively new technology that detects neural activity by measuring blood flow patterns revealed by changes in near-infrared light. Unlike fMRI, fNIRS can be worn while a patient is standing or moving and is less sensitive to the user's head movements. Studies indicate that fNIRS could have benefits in diagnosing brain injury[123] and that using fMRI and fNIRS in combination could help investigations of brain function[124].

MMG (Mechanomyography)
MMG detects muscle movement via microphone-type sensors embedded into a wearable garment. Feedback is provided to people with movement disorders to encourage rehabilitation. Experts believe such systems hold great promise, not just for therapy, but also for understanding the causes of loss of function and the mechanisms of recovery[125].

STIMULATING TECHNOLOGIES

FES – Functional electrical stimulation
FES devices directly deliver electrical pulses to nerves to stimulate movement in muscles that have become paralysed or weakened. A typical control box is around the size of a pack of cards, with a battery and electrodes. Many FES treatments are widely used by people with movement disorders.

tDCS – Transcranial direct current stimulation
tDCS delivers constant and direct low current impulses using electrodes placed on the head. Medically, tDCS is used to treat conditions such as depression and pain, as well as to stimulate movement. Recently, there has been a surge in interest in using tDCS to enhance cognitive processes and movement in people without health conditions[126]. Trials of tDCS have suggested it helps the brain form connections but no evidence yet exists from large-scale systematic research[127].

TENS – Transcutaneous electrical nerve stimulation
TENS uses electrodes to stimulate nerves and reduce pain signals going to the spinal cord and brain. TENS can help reduce pain caused by a wide range of conditions including: arthritis; period pain; pelvic pain caused by endometriosis; knee pain; neck pain; back pain; sports injuries and labour.

TMS – Transcranial magnetic stimulation
TMS uses a coil close to the scalp to produce a changing magnetic field. It can be used to activate or disrupt activity in the brain, which can help scientists understand the role of these areas. TMS has also been shown to be effective in treating drug-resistant depression[128]. In the UK, NICE have approved the safety of the treatment option[129] and it has been available to people privately at a typical cost of £150 per session[130]. It is now the focus of a two-year, £2 million study of 420 participants to assess future potential[131].

RECORDING AND STIMULATING TECHNOLOGIES

EEG with FES
Some research has been done whereby people's brain signals and movements have been picked up using EEG and wearable technology, with FES delivered in response. For example, this combination can be used to record a person recovering from a stroke's arm movement, deliver stimulation to improve it, then reduce stimulation as their typical ability recovers.

On, off and **aha**

How neural interfaces work

Mind-to-mind communication as per the 'mindmelds' of Star Trek remains the stuff of science fiction for now, but the fundamentals have been demonstrated in the laboratory.

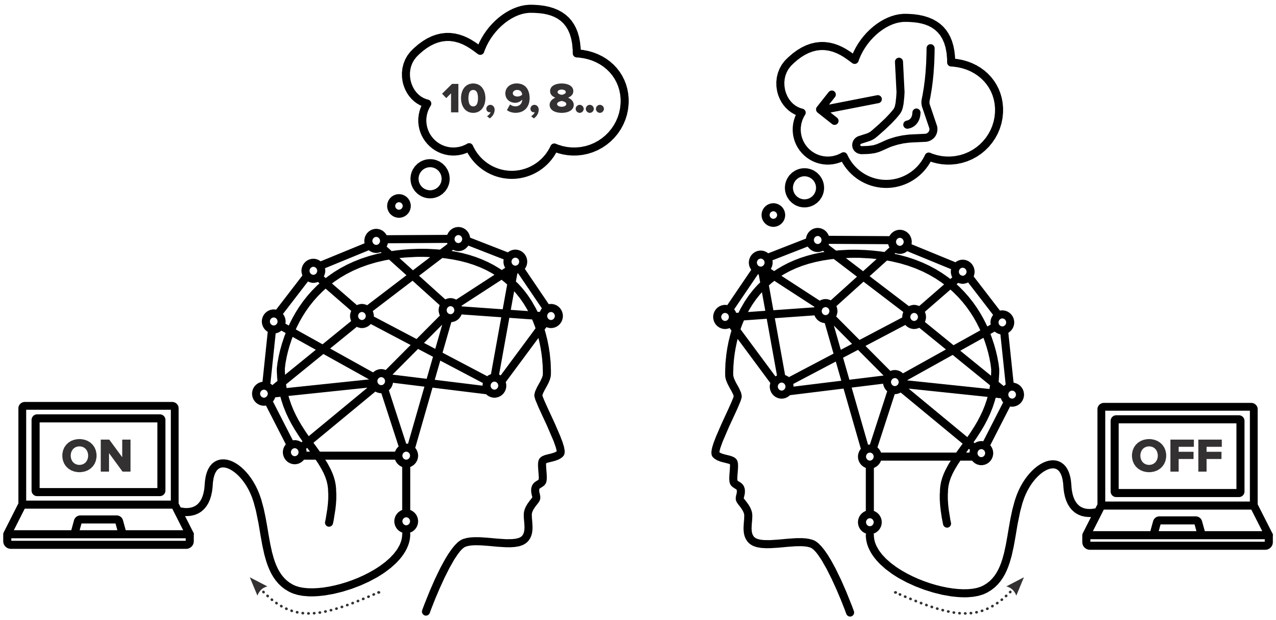
While life-changing applications are some way off, many of the basic building blocks for communication between brain and machine have been established in the laboratory.

On and off

One essential process for interfaces to work is the ability to create a simple on and off signal using thought alone that can be captured by a device such as an EEG headset. One way to achieve this is for the subject to count downwards from ten to one, creating one type of signal. The person then thinks about moving their foot – a completely different activity – and a different type of signal is produced. If the subject can repeat those two contrasting patterns at will, then the computer can sort them into two categories or 'boxes' – on and off, or left and right, or yes and no – opening the way to binary communication.

Brain-controlled movement

Alternatively, more sophisticated interfaces can be deployed that directly read the brain's intention to move a limb or finger. 'BrainGate' is a system that has enabled people with 'locked-in syndrome' to control physical objects. It uses an array of 100 silicon hair-thin electrodes implanted over the hand motor cortex of the brain – the part controlling hand movements – to send signals to external objects via a recording device[132]. Participants have progressed from moving a 2D cursor to typing and grasping using 3D virtual arms[133]. External wearable technologies have been used to control the same activities, such as armbands fitted with sensors developed by CTRL-Labs[134].



Aha

An alternative to the on-off pattern is to detect the characteristic brain signals generated when people spot something they are looking for or see a mistake. Applications of this 'aha' effect include spelling out words by thinking about the letters required when they appear on a screen[135].

Basic thought transference

Mind-to-mind communication as per the 'mind-melds' of *Star Trek* remains the stuff of science fiction for now, but the fundamentals have been demonstrated in the laboratory, progressing from the transfer of an impulse to press a lever from one rat to another[136], to two humans sending instructions on making simple computer game moves to a third by concentrating on LED lights marked "yes" and "no"[137]. ■

Stroke treatment

How neural interfaces support rehabilitation

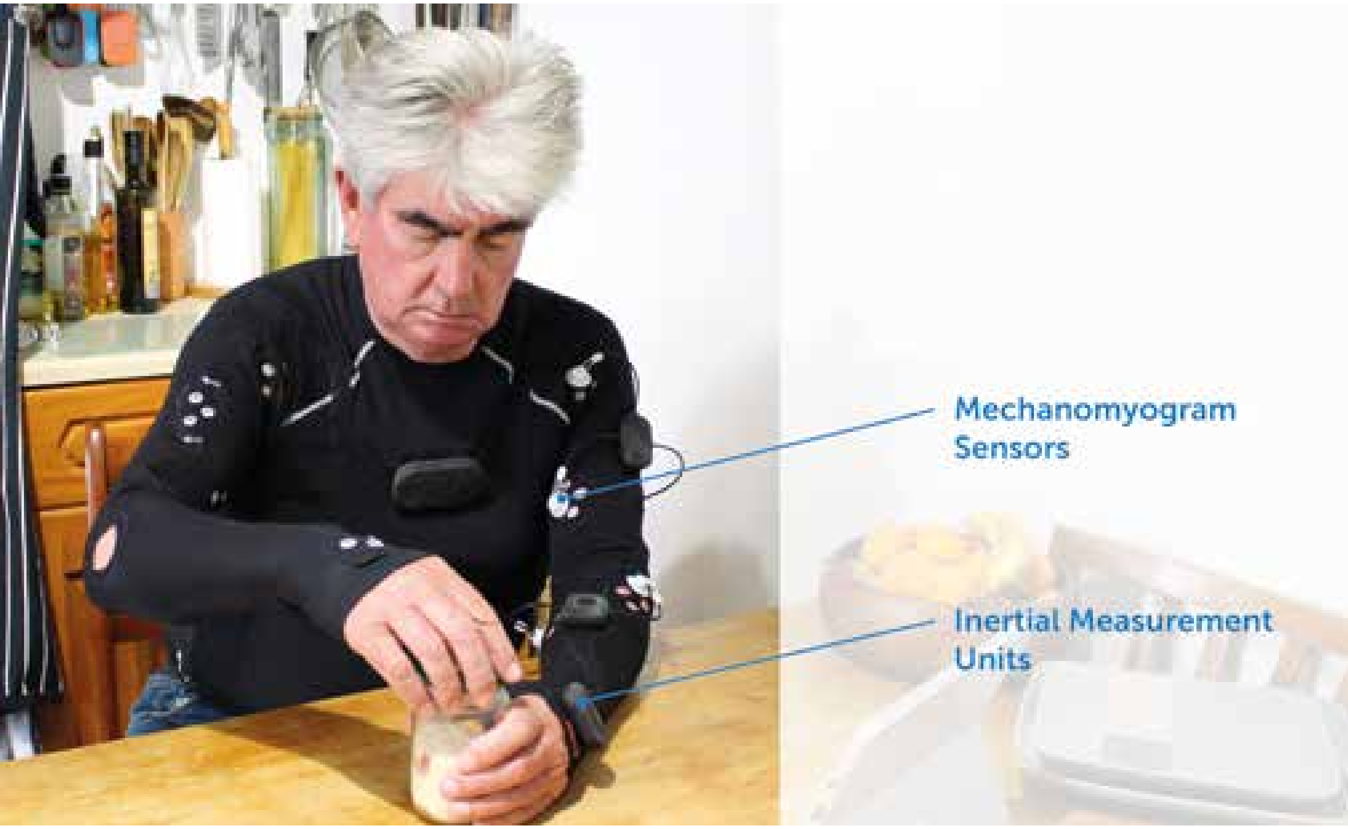
Among the most widely used external neural interfaces are those used to help people who have had a stroke. Strokes, which affect around 150,000 people in Britain annually[138], occur when the blood supply to part of the brain is cut off. Loss of brain cells and connections often affect parts of the brain that control movement, vision, speech or feeling. Full or partial recovery is possible if those affected can restore and retrain new neural pathways. This depends on prompting the surviving neurons to fire and create connections – a process known as 'neuroplasticity'.

"You're not thinking about your arm's limitations. You're learning to control a dolphin."

Neurologist, John Krakauer[142]

Historically, people have undertaken physiotherapy and occupational therapy, stimulating neurons through repetitive exercises. Interface technology augments these therapies in several ways. First, interfaces can apply direct functional electrical stimulation (FES) to nerves, using equipment such as the 'dropped foot stimulator' that people wear on their legs to strengthen weak movements. Electrical impulses are timed to activate muscles to lift the foot during walking.

Other 'wearable' technologies are used to document and motivate people in their rehabilitation. For example, the M-MARK long-sleeved T-shirt uses microphone-like sensors to detect arm muscle activity and movement sensors to detect movements, capturing the data on a tablet. People can review the data to monitor improvement and the system suggests new exercises as they progress[139]. Clinicians are now starting to combine recording and stimulation technologies, for example, reading brain signals with



Electroencephalography (EEG) headsets and limb movements using wearables. Systems can now deliver FES in response to demand, reducing the level of stimulation as typical function recovers[140].

In another project, people undergoing rehabilitation play a video game wearing a sleeve that both records and stimulates the arm, detecting the person's efforts to play the game with sensors and then using stimulators to help the person repeat the movement more successfully[141]. Another video therapy involves using a robotic sling to control an animated dolphin, with the target only being achieved when the user makes the movements required for recovery. Clinicians point out that even the apparently simplest muscle movement involves many neural computations and people often find it easier to focus on the task of moving the computer figure, with the required arm movement occurring as a kind of side effect. Neurologist John Krakauer said: 'You're not thinking about your arm's limitations. You're learning to control a dolphin'[142]. ■

Above:
The M-Mark long sleeved t-shirt is a wearable neural interface that can aid stroke rehabilitation. © Maddison Product Design.

Cochlear implants

- **11,000,000** people in the UK have some hearing loss
- **8,000,000** people with hearing loss are aged 60 and over
- **6,700,000** people could benefit from hearing aids
- **2,000,000** people use hearing aids
- **900,000** people are severely or profoundly deaf
- **12,000** people in the UK use cochlear implants[147]

The world's most widely used implant

The world's most widely used internal neural interface is the cochlear implant, with more than 400,000 people using them to provide or restore hearing[143]. Cochlear implants help people who have partial or profound deafness as a result of damage to the inner ear, or cochlea.

The cochlea enables people to hear by converting vibrations received from the outer and middle areas of the ear into electrical signals that pass along the auditory nerve to the auditory cortex where they are decoded into the sounds we hear. The cochlea has a spiral shape like a shell. Through it runs the basilar membrane which turns vibrations into electrical pulses using around 15,000–20,000 tiny hair cells[144] which detect a sound's volume, pitch, frequency, tone and direction.

Cochlear implants act as substitutes for the cochlea. They include an external component that uses a miniature microphone to pick up sounds and an internal part that does the work of the cochlea and basilar membrane by converting the sounds into signals and passing them to the auditory nerve. The internal system includes a speech

Left:
Cochlear implants are surgically implanted devices that provide a sense of sound for people with severe to profound hearing loss.
© brittak.

processor, data transmitter, receiver and an array of electrodes arranged along the path of the basilar membrane.

As well as being life-transforming for thousands, cochlear implants also illustrate some of the challenges faced by interface technologies today. First, they are expensive, typically costing at least £40,000[145] including assessment, device, surgery and post-operative care. Second, they are obtrusive, requiring a bulky component attached to the outside of the head. Third, while they have changed people's lives for the better, the devices are still a long way from replacing the full typical function of the ear. Even the most advanced implants cannot recreate the full richness of the signals created by the cochlea with its thousands of hair cells. To a person with typical hearing, the implant's sound quality appears limited, although for some people with hearing loss, the technology makes the vital difference between complete silence and hearing something. Even so, some people reject implants on the grounds that deafness is a cultural identity rather than a disability and sign language provides them with a full and natural means of communication[146]. ■

The cochlea converts vibrations received from the outer and middle areas of the ear into electrical signals that pass along the auditory nerve to the auditory cortex where they are decoded into the sounds we hear. Cochlear implants act as substitutes for the cochlea.

Brain games

Interface-controlled games

Brain signals are picked up and analysed by software that determines how the character will move.

Boston area company Neurable has created a brain-controlled game called *Awakening* whose central character is a child with telekinetic powers. The character is set the task of escaping from a laboratory by using mind power to pick up toys such as a balloon dog and rainbow rings[148].

Players wear a headband studded with electrodes that connects to a virtual reality headset. Their brain signals are picked up and analysed by software that determines how the character will move. Players are then able to train their brains to produce the right signals to pick up the toys[149].

Some researchers believe that the investment and momentum generated in the gaming world will enable such technologies to advance with benefits for different applications among people with severe disabilities[150].

Neurable is also working with Trimble, specialists in positioning technologies such as GPS, to provide training and safety services for the transportation, architecture, engineering and construction industries[151]. ■

Right:
Neurable's non-invasive device can detect the brain signals of its users. It is compatible with HTC Vive virtual reality headsets and can be used for both gaming and simulation training. © Neurable.


VIVE
neurable

Powering up the brain

Enhanced multitasking

Over the last two decades, evidence has accumulated on the capacity of neural interfaces such as those using transcranial direct current stimulation (tDCS) to enhance performance in cognitive areas such as working memory[152] and attention[153] as well as in physical activity such as cycling[154].

tDCS involves the use of a headset and electrodes that are typically contained in sponge bags with saline solution used to conduct electricity from the electrodes to the scalp[155]. Adverse effects are rare – users have reported mild tingling sensations and occasionally headaches or fatigue[156].

One study showed how tDCS improved the ability of US Air Force personnel to 'multitask'. The participants, all stationed at the Wright-Patterson Air Force Base in Ohio, USA, were asked to monitor and respond to four independent tasks on one computer screen. Their tasks were to: keep dial markers centred in a 'system monitoring' box; change the communications channel frequencies as requested by an audible prompt; keep a target centred in a 'targeting' box; and keep fluids moving in a 'resource management' box by turning tanks on and off. The ten participants who received active tDCS stimulation from the headsets, provided by Wales-based company Magstim, performed about 30% better than those who did not[157].

While such evidence has grown, other scientists have urged consideration of the potential risks of tDCS, including the possibility that it may improve the ability to perform one task but damage the ability to perform another, and the variability of effect between participants[158]. ■

Right: Transcranial direct current stimulation (tDCS) is administered while performing a multitasking cognitive test. © U.S. Air Force photo by J M Eddins Jr.

The ten participants who received active tDCS stimulation from the headsets performed about **30% better** than those who did not.

wiring Spaghetti

The technological challenges of taking brains online

The nature of the brain

While technologies have been created to interpret brain signals and stimulate parts of the nervous system, researchers face formidable obstacles in moving from these basic building blocks to larger and more complex applications.

The brain is a uniquely intricate and sensitive environment into which to introduce external technology. Physically, it consists of a mass of soft material resembling a mesh of spaghetti floating in a sea of cerebrospinal fluid, with each person's brain itself being different. Inserting pieces of metal or other human-made materials into the brain creates risks of damage, infection or 'foreign body response' – an immune system reaction that creates a wall around the implant and reduces its functionality.

While scientists have investigated and classified the brain's regions and activities, there remain huge unknowns. Some experts believe that interface technology cannot make major progress unless more of the brain's secrets are unlocked, while others contend that if the technologies work, then full understanding is unnecessary.

> "Our brains are way, way more complex than any computer we know how to make. They're way more creative. The input's pretty good, but the output is constrained by our tongues and jaws moving and us typing... If we could communicate at the speed of thought, we could augment our creativity and intelligence."
>
> Mary Lou Jepsen, CEO, Openwater[159, 160]

However, there is wider consensus that the key to more effective interfaces is to be able to 'read out of and write into the brain' more effectively, particularly in engaging larger numbers of neurons. Current implants tend to engage precisely with small populations of neurons while external devices, such as headsets, use more of a 'scattergun' approach – recording or stimulating more neurons, but more randomly. Both often require bulky equipment and wires. These challenges have led specialists to define a range of priorities for more advanced interfaces. ■

> A major challenge is to create materials that can be easily fitted and will be accepted by the brain or other body parts over the long term.

Left:
Section of of an image reconstructing the physical connections between different regions in an adult human brain. © Katja Heuer and Roberto Toro.

BANDWIDTH

A top priority for many researchers is more bandwidth – the capacity to record or stimulate much larger volumes of brain signals than are available today – moving from hundreds to millions. Today's interfaces are comparable to traditional telephone lines, capable of carrying only a simple voice signal. Specialists are seeking to develop the equivalent of broadband channels that can convey large quantities of brain activity to a machine or vice versa. Elon Musk's company Neuralink for instance, claim to have developed a high-bandwidth brain-machine interface with thousands of channels, delivered by multiple microelectrodes positioned on polymer threads[161].

CONNECTIVITY

Both implants and external devices also need high levels of network connectivity, with wireless links if users are to move freely.

PLATFORMS

Some investors' ventures, for example Kernel, are working on the basis that the initial objective is not to create a particular application, but to develop platforms upon which multiple applications – mainly unforeseen today – can be built, comparable to Windows for computers, or iOS and Android for mobile phones.

MINIATURISATION

Widespread use of implant technology depends on creating submillimetre semiconductors – smaller than a grain of rice – that could be fitted during an outpatient procedure. While external devices can be larger, performance will be magnified if numbers of electrodes on a helmet, headset or armband can be multiplied.

PROCESSORS

To understand what the brain is doing accurately, a new generation of powerful 'neural processors' is needed, building on current digital signal processors (DSPs) that convert analogue signals to binary code as used in audio or image capture.

PORTABILITY AND ROBUSTNESS

More advanced interfaces will need to work for long periods outside laboratory conditions. For implants, this means ensuring devices do not require external equipment such as wires. Potential advances include wearable versions of powerful technologies such as magnetoencephalography (MEG), which currently requires people to lie still inside scanners[162].

POWER

Providing electricity efficiently and wirelessly to internal interfaces has been a major issue for researchers but one that is starting to be overcome by using tiny rechargeable units powered by inductive coupling. External interfaces will also require more advanced power sources as they become more portable.

COMMODITISATION

To enjoy similar scale economies to the IT industry, the interface community needs to develop standardised components and production line manufacturing – of the kind that fabrication centres or 'fabs' provide for computer chips.

BIOCOMPATIBILITY

Implants require complex surgery and still run risks of infection or foreign body response by the body. A major challenge is to create materials that can be easily fitted and will be accepted by the brain or other body parts over the long term.

Implantability?

Some innovators are focused on implantable, or injectable, technology to achieve sufficient bandwidth for highly ambitious applications such as telepathy. Neuralink, for example, has developed a neurosurgery robot likened to a 'sewing machine' designed to implant flexible polymer threads, each one fifth of the the thickness of a human hair and containing 32 tiny electrodes, into precise locations in the brain at a rate of six per minute[163].

Others, such as Facebok and CTRL-Labs[164] believe external devices can achieve applications such as 'typing by brain' by picking up the brain's intentions 'downstream' and that the public may not wish to explore implantable devices.

Right:
CTRL Labs' CTRL-kit is a brain-computer interface that users can wear on their wrist. It detects users' intention to move, allowing them to control a range of computers or electronic devices. © CTRL Labs

Merging our intelligence?

© DKosig

NI and AI

Today, AI is an important technological tool that allows many neural interfaces to function. Several interfaces use AI to convert neural signals into digital data using algorithms, for example to interpret the brain's instructions to move a prosthetic arm[165] or to decode the neural commands being sent by the brain to the arm when typing[166].

In the future however, a much more complex relationship between AI and neural interfaces could emerge. While some concerns have been raised over the disruptive potential of AI, several technology experts believe beneficial impacts could arise from linking human and artificial intelligence via neural interfaces. As stated in an article published in *Journal of the Royal Society Interface*: "Brains are flexible, imprecise, error-prone and slow; computers are inflexible, precise, deterministic and fast"[165]. Polina Anikeeva, Associate Professor in Brain and Cognitive Sciences at MIT, observes that transistors used in computers can perform billions of operations per second but are typically only connected to three neighbours, while the brain's neurons can perform only around 1,000 operations per second, but communicate with 6,000 neighbours at once[168]. Collaboration between these two powerful units is currently limited by the slowness of interfaces such as the keyboard or mouse.

Creating interfaces that allow us to link the sophistication of human thought with the processing power of AI – whether implanted or external – could open the way to game-changing applications: prostheses that feel like a natural part of the body, enhanced decision-making, or even whole new sensory experiences. However, the prospect also raises a number of ethical issues concerning our autonomy, privacy and perception of 'normality'. ■

Creating interfaces that allow us to link the sophistication of human thought with the processing power of AI could open the way to game-changing applications.

Neuroscience

What do we know, what don't we know and what are neuroscientists now focused on?

The brain is the most complex organ in the human body, and consequently remains one of science's greatest mysteries. Neuroscientists have made major progress in mapping the structure and function of different areas of the brain. But many unanswered questions remain.

What we know

- The brain is composed of around 86 billion neurons[169], comparable to the number of stars in the Milky Way[170], each of which can make connections with thousands of others via links called synapses.
- Neurons drive cognitive activity such as learning and decision-making, as well as controlling movement and balance, by receiving, processing and transmitting information – or 'firing'.
- Different brain regions drive different activities, for example the occipital lobes at the back of the brain are responsible for vision, while the frontal lobes handle movement and decision-making.

What we don't know

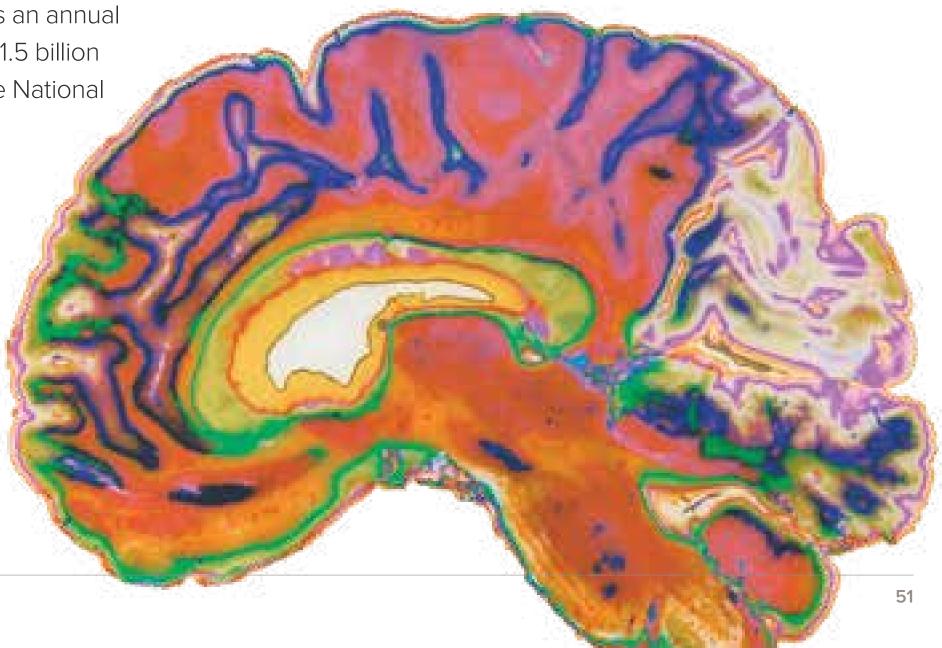
- Unlike the genetic DNA code, discovered in the 20th century, scientists have yet to break the 'neural code' – the language with which neurons communicate to drive cognition, emotion, perception and action.
- The brain's propensity to form connections, known as 'neuroplasticity', is also only partly understood.
- The underlying causes of many neurological and psychiatric conditions remain largely unknown.
- While many interfaces have been shown to be effective, specialists do not always understand how they work – their so-called 'mechanism of action'.
- While single neurons have been studied for decades, researchers recognise that much brain function depends on computing by networks or circuits of neurons, composed of neurons from different parts of the brain, about which less is known[170].

“Trying to introduce the study of the brain to students, I said: ‘If understanding everything you need to know about the brain was a mile, how far have we walked?’ I got answers like ‘three-quarters of a mile’, ‘half a mile’, ‘a quarter of a mile’. And I said: ‘I think about three inches.’”

Jeff Lichtman, Professor of Molecular and Cellular Biology, Harvard University[172]

What neuroscientists are now focused on

- The last few years have seen a surge of investment into major research programmes, many targeted on more detailed mapping of the brain and improved understanding of neuronal circuits.
- The US BRAIN (Brain Research through Advancing Innovative Neurotechnologies) initiative is focused on mapping the circuits of the brain, measuring their patterns of electrical and chemical activity and understanding how their interplay creates humans’ unique cognitive and behavioural capabilities. It has an annual budget of $300 million with $1.5 billion committed cumulatively to the National Institutes of Health alone[173].
- Europe’s Human Brain Project is a 10-year programme launched in 2013 with an expected budget of around €1 billion and a network of around 500 researchers[174]. It aims to use computing and large-scale data analytics to develop a more coherent atlas of the brain, run simulations of brain activity and enhance understanding of the mechanisms behind its workings[175].
- Other countries undertaking brain research programmes include Australia, Canada, China, Japan and South Korea[176]. ■



Investment in interfaces

In its 2018 report, *The Market for Neurotechnology: 2018 – 2022*, Neurotech reports projected that the overall worldwide market for neurotechnology products – defined as "the application of electronics and engineering to the human nervous system" – would be $8.4 billion in 2018, rising to $13.3 billion in 2022[177]. The 2018 figure represents less than 1% of estimated total 2018 global spending on research and development of around $2 trillion[178] or less than 5% of all estimated life science research and development spending.

The overall scale of governments' investments in neural interfaces is largely unknown although some agencies provide budget documents. For example, the US's Defense Advanced Research Projects Agency (DARPA) runs a series of relevant projects including a biomedical technology programme with a planned 2019 budget of around $100 million[179].

The scale of private sector investment is becoming clearer, for example with the Crunchbase database listing around 400 start-ups, companies and organisations[180] and the US 'Angel List' of start-up companies listing around 250 neuroscience start-ups with an average valuation of $4 million[181]. Four examples suggest significant interest. Entrepreneur Bryan Johnson has said that he has invested $100 million in Kernel, 'a neuroscience company focused on developing technologies to understand and treat neurological diseases and radically improving our cognition'[181]. Meanwhile around $158 million has reportedly been invested in Neuralink, founded by entrepreneur Elon Musk[183], to develop 'ultra-high bandwidth brain-machine interfaces to connect humans and computers'[184]. Galvani Bioelectronics, formed by global healthcare company GSK, and leading technology company Verily Life Sciences – part of Google's parent company, Alphabet – is planning to invest £540 million over seven years[185] to develop 'tiny implantable devices to change precise electrical signals in nerves to treat a range of debilitating chronic diseases'[186]. Finally, Facebook is helping to fund research into 'speech decoders' that attempt to decipher intentional speech by analysing participants' brain activity in real time[187]. The company's goal for this work is to create augmented reality (AR) glasses that could act as a brain-machine interface to enable typing from thought or other applications including communicating with others[188].

What makes an innovation investible?

Six criteria mark out innovations that succeed in making the leap across the chasm between early adopters and the general population

Clinical or consumer necessity

The interface should provide a solution that is not adequately met by existing therapies or products and has benefits which overcome any fears – such as the fear of surgery.

Scientific validity

A scientific basis for the interface helps with regulatory approvals, where needed, and optimising the design of the system in practice.

Workflow viability

The interface must be suited to practical, everyday use. For example, the challenge of placing EEG electrodes on the scalp has arguably limited the adoption of wearable technology – both for medical applications as well as games.

Technological maturity

Any interface requires robust designs that can safely interact with the body and improve the systems within which it operates. Durability for a decade might be required from an implant, for example, while a gaming headset needs to be comfortable and easy to use.

Deployment cost

Over their life cycles, technologies need to cover substantial costs, including securing intellectual property, satisfying regulatory constraints, meeting quality controls and funding distribution.

Economic viability

Interfaces need to deliver the value required by users or investors. Healthcare providers measure net economic value of treatments. Consumers need to be prepared to pay for access. And investors need to be found – often governments or foundations – who will support early stage innovation when traditional investors are wary of long-term commitment.

Investors in interfaces face distinctive challenges. In seeking government funding they represent a new, specialist, multidisciplinary field without established bodies or research institutes such as those of engineering or medicine. Start-ups and private sector companies face the problem of reconciling high-level long-term ambitions with the need for short-term cash flow. Often the strategy adopted is to create therapeutic products as a first step towards non-medical technologies with wider application. Neuralink, for example, plans to seek approval to test its product on people with paralysis by the end of 2020[189], while the longer-term aspiration includes such goals as 'direct conceptual communication' with another person[190]. ■

UK strengths

The UK and neural interface technology

The UK has a unique set of strengths that mean it is well positioned to become a world leader in neural interfaces.

Academic excellence in relevant disciplines, from neuroscience to electrical engineering.

Supportive regulation – with an internationally renowned regulatory system that is taking a new approach to accelerate responsible innovation in emerging technology.

The NHS – providing a unified national platform for research, innovation and commercialisation.

Competitive advantage provided by a dynamic life sciences sector and thriving creative industries, of which gaming is a big part.

Taken together, these factors provide a clear technological pathway for the development of neural interfaces in the UK that builds on existing strengths. Looking forward, investment in neural interfaces could be an important avenue for the UK to explore as it considers how to meet its commitment to devote 2.4% of GDP to research and development by 2027.

Specific UK strengths include:

- **Academic strength**
  The UK ranks highly in the international science and research community, being home to four of the top 10 universities in the world[191]. It has notable strengths in neuroscience and behaviour; University College London's neuroscience and behavioural research is the most cited in Europe and second most cited in the world[192]. A ranking of electrical engineering included three UK universities in its top ten alongside five from the US and one each from China and Singapore[193].

- **Life science leadership**
  The UK is a global hub for life sciences, with more than 5,600 life sciences businesses with a presence in the UK, generating turnover of £73.8 billion and employing over 248,000 people as of 2018[194]. The sector is a crucial part of the economy, having generated almost 9% of all value in manufacturing in recent years[195]. Most of this value has historically been created by pharmaceuticals, but with many drug-resistant conditions and patent expirations, there is an opportunity to explore how and where interfaces may be able to step in to meet unmet medical needs and generate value for the UK.

- **Creative industries and gaming**
  The creative industries represent one of the fastest growing parts of the UK economy, contributing over £100 billion of value in 2017[196]. The UK consumer gaming market alone is worth £5.7 billion[197], with games sales comprising over half the UK's entertainment market, more than music and video combined. Britain also has the largest games development sector in Europe[198], with over 2,000 companies working in the field[199].

- **The NHS**
  Britain's centralised health service provides a consistent platform for research and innovation, offering access to large, diverse and longitudinal datasets as well as a national-scale market into which successful new technologies can be launched[200].

- **Ethics**
  The UK is home to organisations such as The Centre for Data Ethics and Innovation, The Ada Lovelace Institute, The Alan Turing Institute and Doteveryone. It is a global leader in exploring and driving the ethical use of AI and emerging technologies.

- **Regulation**
  The UK's regulatory practices are internationally renowned, scoring the highest overall of all countries assessed by the Organisation for Economic Co-operation and Development (OECD)[201]. The UK is seeking to build on this position of strength by taking a new approach to the regulation of emerging technologies designed – as a June 2019 White Paper states: "to give businesses confidence to innovate and invest in the UK and give citizens confidence in our protections"[202].

To become a world leader in neural interfaces, the UK needs:

- **A collaborative 'ecosystem'**
  Developing neural interfaces demands a convergence of high-level skills from a range of specialists including neuroengineers, electrical engineers, neurologists, psychologists, research leaders, gaming professionals, designers and policy and regulation experts. The UK has a track record in bringing together multidisciplinary teams such as those coordinated by UK Research and Innovation (UKRI) to tackle areas such as mental health and antimicrobial resistance. It could benefit significantly from building a similar neural interface 'ecosystem'. This might extend to joint initiatives between different types of funders, such as research councils, Innovate UK and charities.

- **A common platform**
  This kind of 'ecosystem' activity could create common platforms in infrastructure, good practice and experience on which successive innovators could build, averting the need for each start-up venture to 'reinvent the wheel'. This could overcome challenges faced under the current model whereby companies may need to invest hundreds of millions to make limited progress in development and trials among very small numbers of participants. A more collaborative community could identify and pursue common technical priorities such as reducing costs, increasing ease of use and improving performance. It could also take on regulatory and project management challenges, such as navigating NHS approvals, taking technologies from prototypes to clinical trials and meeting regulatory and legislative requirements.

- **Long-term start-ups**
  Many start-up technology companies are focused on apps or other short-term plays. Start-ups with the longer-term vision and plans required for neural interface work require support of the kind that might arise from a more coordinated ecosystem.

- **Academic-medical links**
  More efforts could be made to encourage clinicians in training and practice to engage in research, such as via a combined MD-PhD programme.

- **Commercialisation pathways**
  Researchers with promising technologies often have to find their own bespoke routes towards the market, and could benefit from more streamlined and established processes to support them from basic research through medical innovation, regulatory approval and commercialisation. ■

Why UK-based scientists are involved

"This topic really captures the imagination. The potential impact is huge! The high barriers for business and the long-term outlook needed make it a good opportunity for university research. In the short term, goals are attainable as core technologies can be deployed as effective new research tools for neuroscience, also enabling preclinical testing. Once experimental efficacy and safety data is available, we can move to first-in-human trials and clinical translation and commercialisation."

Dr Tim Constandinou, Reader in Neural Microsystems, Department of Electrical and Electronic Engineering, and Deputy Director of the Centre for Bio-inspired Technology, Imperial College London.

"I believe it is the future. Sooner or later, this will be a disruptive technology significantly improving different aspects of our quality of life through opening a new communication pathway between humans and the environment as well as from human to human."

Dr Mahnaz Arvaneh, Lecturer, Department of Automatic Control and Systems Engineering, University of Sheffield.

"I am very interested in how the human brain works. It is a unique system in that it has an objective reality in the same sense as any inanimate matter but also is involved in generating subjective reality. Neurotechnologies allow me to probe that system and at the same time to work on solutions to societal problems where neurotechnologies hold the greatest promise."

Professor Slawomir J Nasuto, Deputy Research Division Leader, Biomedical Sciences and Biomedical Engineering Division, School of Biomedical Sciences, University of Reading.

The **next** frontiers

What's probable by 2040?

Over the next two decades, specialists expect current medical interface treatments to evolve and expand, while new applications could extend their use to millions. Beyond medicine, interfaces are expected to become widely used for gaming, fitness and well-being.

Today's medical implants are expected to become more effective and more widely deployed, exhibiting sought-after advances such as greater miniaturisation and connectivity. Cochlear implants, for example, are likely to reach many more users as they become less bulky and provide higher-quality sound perception.

Deep brain stimulation (DBS) is expected to evolve into an 'intelligent' automated, or semi-automated platform, with stimulation occurring responsively in 'head-only' devices.

Researchers linked to the Chan Zuckerberg Initiative have reported successful trials of an interface known as a 'Wireless Artifact-free Neuromodulation Device' (WAND). In a paper in the scientific journal Nature, the researchers explain how the device was implanted in a monkey to record, stimulate, and modify its brain activity in real time, including sensing an expected movement and stopping it immediately[203]. This could enable more responsive 'closed-loop' therapies, for example for Parkinson's disease, whereby stimulation is delivered when required.

Similarly, external interfaces for people who have had a stroke are expected to develop from simple stimulators into sophisticated systems that blend recording and stimulation. Spinal implants and external devices to restore movement and bodily functions in people who are paralysed are expected to improve significantly and provide a mainstream rehabilitative option. Spinal implants have recently been demonstrated to restore movement among people with chronic Parkinson's disease[204].

Both implants and external devices are expected to treat an increasingly broad range of conditions, particularly those resistant to drugs. For example, depression, which affects around 300 million globally, might be treated using either implants, such as DBS, or external stimulation platforms, such as transcranial direct current stimulation (tDCS)[205].

Interfaces to support fitness are likely to progress from wearable monitors to adaptive clothing, such as tennis shirts that encourage the most effective serves. Consumer-facing neural interfaces are expected to become more practical and appealing and could take the form of a 'hearable' device tucked away in the ear[206].

High bandwidth medical implants with thousands of microelectrodes are expected to be trialled soon[207]. Others are focused on what increasingly powerful external devices can achieve as the lines between the capacities of invasive and non-invasive interfaces will become blurred. External devices are already showing promise in producing very focused and deep stimulation. Therapies that currently require DBS could be successfully targeted by non-invasive approaches. For example, an image-guided, ultrasound technique is already used to target tissue in the thalamus and treat essential tremor[208]. Researchers have also developed a non-invasive interface that enables a patient to control a robotic arm via EEG signals instead of a cortical implant[209].

Such developments would also be likely to open up avenues for more non-medical applications of neural interfaces, as public acceptance of non-invasive devices may be higher than invasive ones.

Those who have trouble sleeping may see today's simple monitoring devices that help people understand their sleep patterns[210] replaced by devices that act more directly to calm the racing mind[211] and potentially by implants or external devices that act on the brain to promote sleep[212].

Some of the most striking new applications are set to extend beyond medicine and affect millions. Hands-free control of computers, typing or entering data using the brain alone using a 'mental mouse' represents a game-changing development that is nonetheless seen as probable.

Hands-free control of computers, typing or entering data using the brain alone using a 'mental mouse' represents a game-changing development that is nonetheless seen as probable.

What's possible beyond 2040?

Mass-market technologies often begin with the creation of enabling 'platforms', such as the internet or mobile phone, which then facilitate myriad unanticipated applications. The 'mental mouse' could provide such a platform.

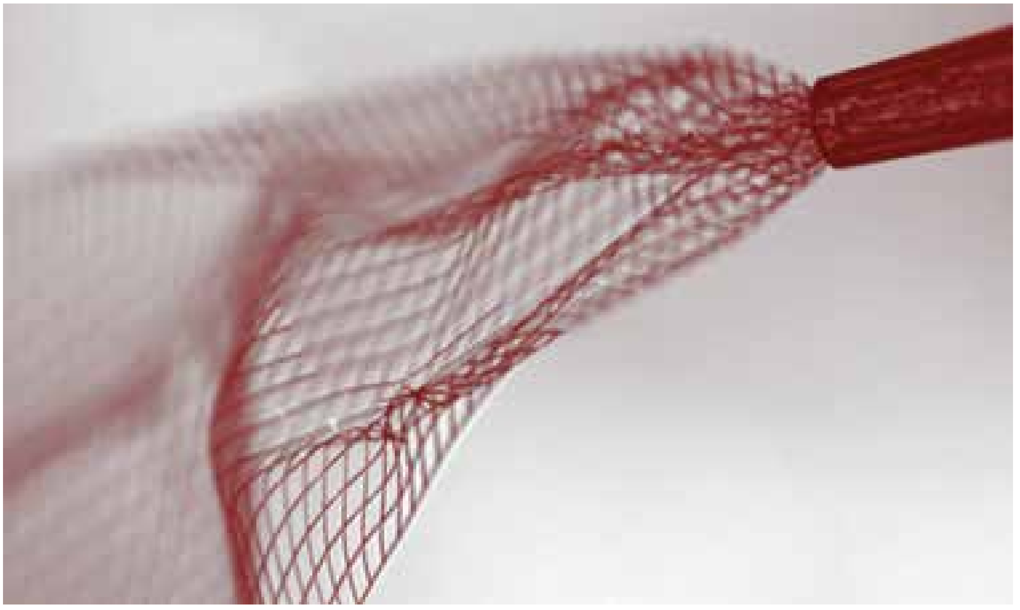
In looking beyond what is expected to what might be 'possible', innovators stress that they expect many unforeseen applications to emerge.

Mass-market technologies often begin with the creation of enabling 'platforms', such as the internet or mobile phone, which then facilitate myriad unanticipated applications. The 'mental mouse' could provide such a platform, as could more powerful external headsets[213], or if developed scalably, neural dust or neural lace[214]. Facebook, Neuralink and Kernel are among those reportedly pursuing such possibilities, as well as others such as NURO, whose operating system NUOS is designed to enable people who are unable to speak or move to select options on a tablet to communicate using neurological signals alone[215].

In general, companies such as Neuralink are likely to seek ever-higher levels of multi-channel implant connectivity as they pursue the ambitious goal of linking human brains and artificial intelligence[216, 217].

In medicine, mental health conditions of many kinds that have defied conventional treatment could be treated using interfaces[218]. Clinicians are also hoping to apply them to the more complex condition of Alzheimer's disease which affects around 850,000 people in the UK and an estimated 47 million globally[219]. Early trials using deep-brain stimulation (DBS)[220] focused on the fornix, part of the brain's memory formation circuit, but some experts believe that multiple brain regions responsible for memory may need to be engaged to deliver significant results[221]. Other research has identified the neural biomarkers associated with physiological properties such as heart rate, blood pressure or glucose levels, potentially offering a new platform for 'neuroceuticals' to treat conditions by targeting relevant neural signals[222]. While applications such as these may well be welcomed as much-needed advances, the next 20 years are also likely to see other developments that could raise questions over autonomy, agency and privacy as well as impacts on social interaction and communities. For example, interfaces supporting dietary behaviour could progress from consumer-friendly applications like DNA-customised shopping to direct stimulation or inhibition of the brain to influence mood and appetite. Anorexia has already been treated experimentally by placing electrodes inside the brain to stimulate regions that control mood and anxiety[223].

The ability to read mood from brain signals is already reportedly being used by Chinese companies to monitor employees for signs of anger, anxiety or depression, via devices fitted to safety helmets and caps[224]. According to media reports, companies involved say they are using the data to help workers, but critics say the technology invades privacy. Also, there is concern among the public, from a data-collection perspective, that there may be more at stake with neural interfaces in the future than with other technologies today.



Left:
Ultra-fine neural mesh described as 'syringe-injectable electronics' which may offer wireless brain-computer connectivity in the future. © Lieber Research Group, Harvard University.

The prospect of thought transfer raises opportunities and challenges. Researchers have already demonstrated very simple examples of brain-to-brain communication, including an experiment in which two people managed to transfer an instruction in a computer game to a third person using brain signals generated by focusing on LED lights marked 'yes' and 'no'[225].

Efforts to enhance memory, learning, decision-making and attention may also provide new solutions. Today's basic, cheap headsets are likely to be supplanted by more advanced enhancement technologies, possibly including platforms such as multiple micro-implants[226]. Animal tests have already shown ways to create memories[227], control motion by human thought[228] or embed learning[229].

Interface technology will also inevitably be studied for potential military applications, such as augmenting decision-making, physique and motivation. In research, sharks[230], beetles[231] and pigeons[232] have been implanted with devices that can control their movements. Other technologies could provide personnel with infrared sensing capabilities to detect other people in darkness – or enable their actions to be stimulated by a remote controller. The US's Defense Advanced Research Projects Agency (DARPA) has set out an aspiration to create a non-invasive neural interface for possibilities such as "immersive training, new forms of interaction with AI systems, improved situational awareness and intelligence analysis, and distributed task management"[233]. ■

Drivers

What could make the possible actual?

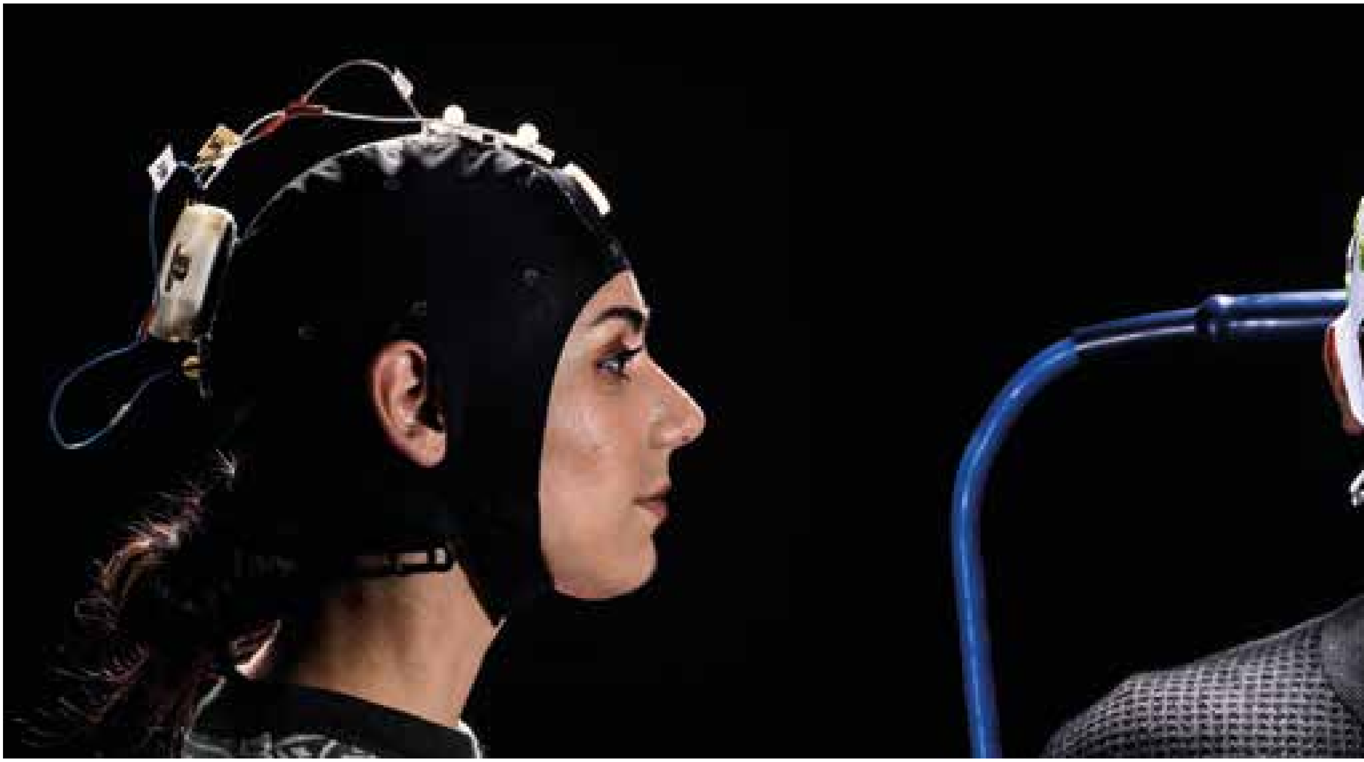
Below: University of Washington researchers created a method for two people to communicate the correct move to a third person playing a Tetris-like game using only their minds. © Mark Stone/University of Washington.

Breakthroughs in technology

Interfaces are attracting increased attention, investment and research effort, with many routes being explored to improve performance, lower costs or develop new technological approaches. Investment in neural interfaces currently represents a small but growing proportion of medical research. Further uplifts driven by government policy or private sector capital might increase the chances of advances.

Wide deployment of existing technologies

While technologies exist to control physical objects or computer cursors by brain power alone, they are currently restricted to a small population of enthusiasts and early adopters. If devices such as Electroencephalography (EEG) headsets became much more common, for example becoming popular gifts, this might drive popular interest in – and investment in – next-generation technologies.

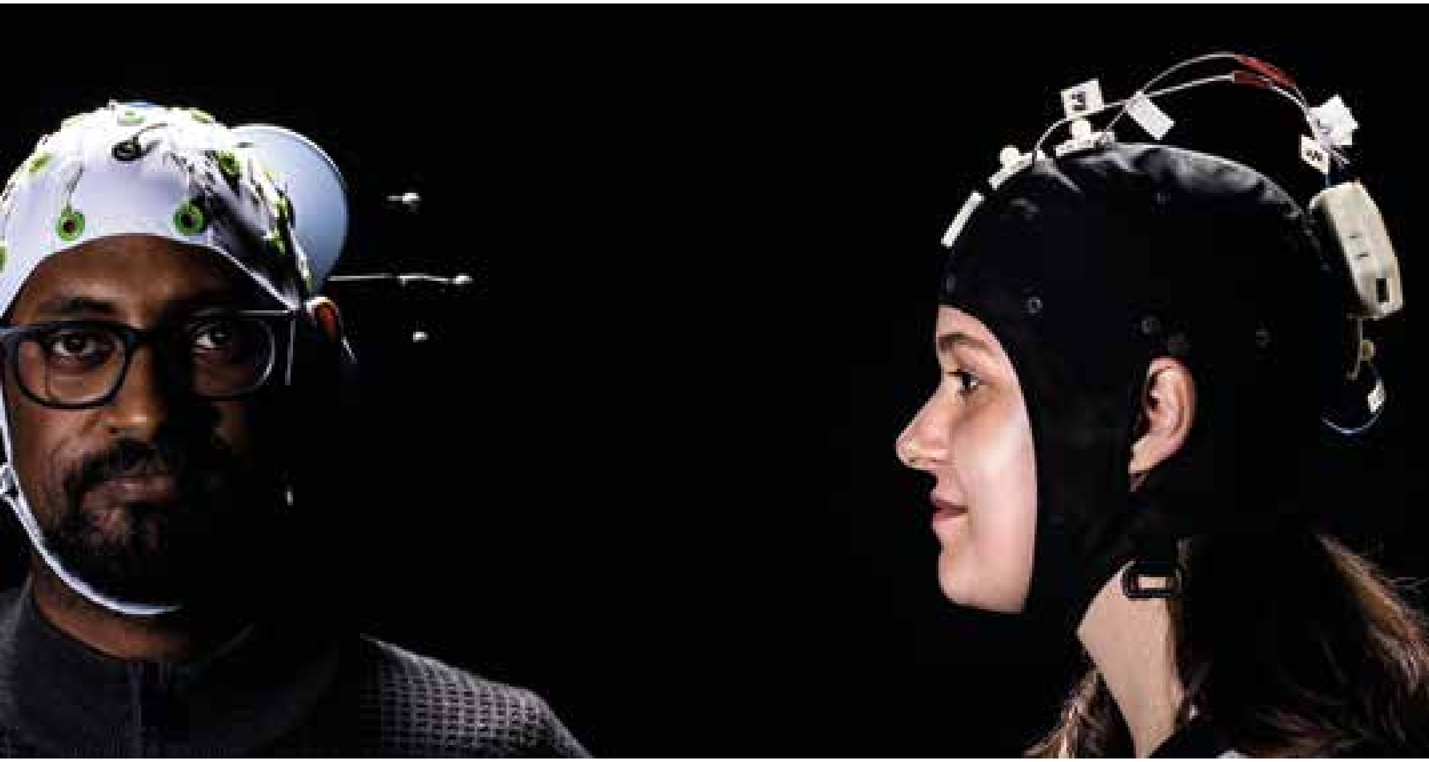


Big impacts from incremental advances

Although applications such as thought-sharing via implanted interfaces may require decades of research and investment, other dramatic advances such as ‘typing by the brain’ are much closer to being achieved. Wide deployment of such technologies could also change the investment climate and accelerate development of more complex devices.

Focusing of demand

If demand were to grow from particular groups of users, such as people who have had strokes or students demanding cognitive aids, greater market momentum might be generated, prompting more investment and deployment. ■



Mental health

How interface technology can help

Neural interface therapies represent new hope for millions who have mental health conditions that drugs and therapy have failed to treat. However, their use is generally in its infancy and the field requires support to reach its potential – reflected in this Perspective's 'A Call to Action'.

One in four people will be affected by mental or neurological conditions at some point in their lives according to the World Health Organization[234]. Yet around one-third of cases of depression, the most common mental health condition and the leading cause of disability worldwide[235], are regarded as treatment-resistant[236]. Drugs can prove ineffective because they affect the entire body, whereas interfaces can be precisely targeted on relevant areas of the brain. Mental health medications can have a range of side-effects from weight gain to decreased libido. Interfaces can also have side-effects but such effects vary between people and individuals may find the adverse impacts of devices less severe than those of drugs.

In the past few years, several interface technologies have been trialled or deployed with small numbers of participants, showing encouraging results. Deep brain stimulation (DBS) has been found to be safe and effective[237] as a treatment for depression in some trials where electrodes have been placed on regions such as the nucleus accumbens that are responsible for motivation and mood[238]. Transcranial magnetic stimulation (TMS) for depression, typically stimulating the left frontal cortex[239], has also been found to be safe and effective by the National Institute for Health and Care Excellence (NICE)[240], with some people reporting life-changing experiences[241]. TMS has also shown promise in improving social abilities among people with autism[242]. However, equipment costs and expertise required mean that TMS is not available across the NHS[243], although the National Institute for Health Research is now funding a wider trial within NHS Trusts[244].

Vagus nerve stimulation is even less advanced, with NICE judging evidence on safety and efficacy 'inadequate in quantity and quality' as yet[245], despite some early anecdotal evidence of benefits[246]. External interfaces such as transcranial direct current stimulation (tDCS) have also shown promising signs. Electroconvulsive therapy (ECT) differs from others in that it has been used for many decades, induces a seizure and retains associations of barbarism from film depictions of 20th century use without anaesthetic. However, today, used with general anaesthetic and muscle relaxants, many people with severe depression have reported significant benefits[247]. ■

Left:
Transcranial Magnetic Stimulation. Keith Bedford/Boston Globe © Getty Images.

The **ethics** of **neurotechnology**

Ethical questions raised by neural interfaces

What kinds of ethical issues do neural interfaces raise?

> If we use neural interfaces to do something, is it us as humans doing it? Or is it the technology?

Some of the most prominent are: how, if at all, should use of the technologies be limited; what 'normality' means; how can privacy be protected and which specific concerns, for example around surveillance, might be felt strongly by certain social groups; whether neural interfaces may contribute to widening inequalities; and what it means to be human. People close to the technology are urging governments to address such concerns 'early and often'. One example cited as good practice is the way that the Human Genome Project was accompanied from its inception by programmes to consider ethical, legal and social implications[248]. Another is the process that led to the Human Fertilisation and Embryology Authority (HFEA) being set up as a dedicated body to regulate an area of high impact and great sensitivity[249]. More recently, scientific institutions have championed the concept of 'responsible innovation', described by the UK's Engineering and Physical Sciences Research Council (EPSRC), as "a process that seeks to promote creativity and opportunities for science and innovation that are socially desirable and in the public interest", recognising that innovation can raise questions and dilemmas[250]. Drivers for such a process relating to interfaces include the creation of a group known as the Morningside Group that brings together scientists, engineers and others from industry, academia and international projects to propose priorities for government and international regulation[251].

QA

How do the technologies affect what it means to be human?

They pose questions about human autonomy or ‘agency’. If we use neural interfaces to do something, is it us as humans doing it? Or is it the technology? In one sense, interfaces can increase our own agency by enabling individuals to improve performance in their work or leisure activities, but at the same time they cast doubt on the idea of the ‘self’ as a decision-maker. If implantable ‘smart’ technologies are making decisions within our bodies, do we as humans retain our own autonomy?

Should there be limitations on the use of neural interfaces?

If neural interfaces can be voluntarily used to influence behaviour by individuals, then should these be prescribed by states? For example, should technologies that seek to help people eat more healthily be used by governments to reduce their public health bill? Then, should that power be extended for use in wider contexts, for example as sanctions in criminal justice? Conversely, in terms of proscribing applications rather than prescribing them, should there be ‘red lines’ beyond which interfaces are banned? And who would decide where such lines would be drawn?

How might interfaces change our perception of 'normality'?

The concept of 'normal' itself is not universal, nor is 'normality' universally desired.

In the medical field, clinicians have demonstrated the use of interface therapies to help people restore what is seen as 'normal', 'typical' or 'average' ability or function. However, the concept of 'normal' itself is not universal, nor is 'normality' universally desired. For example, some people who are deaf challenge whether they need treatment when sign language provides them with a rich, expressive communication and implants can be a shock to the brain[252]. Another set of questions is raised by the use of interfaces to make people 'better than well' – enhancing capabilities beyond the average. Should this be seen as promoting human flourishing, creating a new standard of 'wellness' – or as enhancement? Should a distinction be made between enhancement for personal fulfilment rather than personal or competitive advantage? In sport, many forms of chemical enhancement are against the rules; so should neural enhancement be allowed to confer advantages – either in sport or in other forms of competition – from job applications to exam grades or pub quizzes?

What are the key privacy issues associated with interfaces?

Interfaces present the opportunity to harvest vast amounts of physical and neural biodata. In these circumstances, how can privacy be preserved and use of personal data controlled? How can 'Big Brother' style mental surveillance be avoided along with the psychological harm caused by the knowledge of being under surveillance? Or are there arguments that it should be allowed for those who are a risk to society? The Morningside Group recommends making opting-out of neural data-sharing the default choice[253] – as does our 'A Call to Action'.

Who should control access to neural interfaces and the data that they harvest? How should governments respond to the power of 'Big Tech'?

Today, neural interfaces are being developed in different parts of the public and private sectors. While some research is publicly funded in universities and institutes, much of the momentum is being generated among well-funded start-ups founded by already successful entrepreneurs. 'Big Tech' companies are also entering the field, such as Facebook with its programme to explore typing by brain and Alphabet in its support of CTRL-Labs and Galvani[254]. The involvement of tech giants enables researchers to explore a wider range of options than they might otherwise. 'We want people to do the thing that's crazy, the thing that other people wouldn't try'[255] says Joe DeRisi, co-president of the $50 million CZ Biohub[256] which funds research as part of the Chan Zuckerberg Initiative that has awarded around $1.5 billion in grants and venture investments since 2015[257].

However, if such research leads to intellectual property and product development, these large businesses may acquire similar market power in interfaces and the data they gather as they possess now with regard to social media platforms. Indeed, such power would be multiplied if, for example, mood data from neural technologies was cross referenced with other personal data held and sold by 'Big Tech'. Governments, regulators and the public need to ask if they believe such a level of control is acceptable, given the way that public trust in 'Big Tech' regarding privacy and access to data handling has fallen[258], along with public concern about continuous neural interface data tracking and loss of control over data. If such power is not seen as acceptable, what measures might be put in place to promote beneficial behaviour among large companies, as well as to constrain market power and enable a wider range of large and small players to participate?

How might interfaces exacerbate inequality?

If cognitive enhancement confers a long-term advantage to users who can afford it, this increases inequity within generations; if those users are then better able to afford enhancement for their children, disadvantage is multiplied across generations.

Today, interfaces are available to relatively small groups of people, including enthusiasts who seek out headsets; those who can afford expensive therapies; and those chosen for trials of experimental treatments. As interfaces become more widely available, inequality could be worsened as access becomes more dependent on affordability. If cognitive enhancement confers a long-term advantage to users who can afford it, this increases inequity within generations; if those users are then better able to afford enhancement for their children, disadvantage is multiplied across generations. Should policymakers step in to prevent this? Or should they accept the process on the basis that earlier innovations such as cars or mobile phones were initially adopted by a wealthy few but ultimately became available on a mass-market scale? Or, should they look at ways to increase access for all?

How might bias be an issue for neural interfaces?

Scientists and technologists need to be aware of risks of bias occurring in research and development related to neural technologies and associated scientific disciplines. For example, studies have identified and corroborated concerns that findings of psychological research have at times been unrepresentative as a result of relying on participants who are described by researchers as Western, educated, and from industrialised, rich and democratic countries (WEIRD)[259]. Research has also supported concerns that unrepresentative participant selection can result in biased outcomes outside medical trials[260]. For example, female crash test dummies were often smaller versions of male dummies that failed to replicate women's different muscle mass and vertebrae spacing, resulting in higher injury risk for women[261]. More recently, 'algorithmic bias' has been found in artificial intelligence systems such as a system which correctly identified the gender of 99% of white men but only 35% of dark-skinned women[262]. There have also been reports of wearable heart rate monitors working less well on darker skin[263, 264]. In terms of neural interfaces, inequality arising from unequal access could be exacerbated by bias if systems were designed based on uneven data – for example collecting more data from men than women[265]. Conversely, the likelihood of algorithmic bias can be reduced by ensuring interfaces are developed by – and tested on – diverse and inclusive groups. ■

Sharing thoughts

Are neural interfaces currently capable of 'mind reading'?

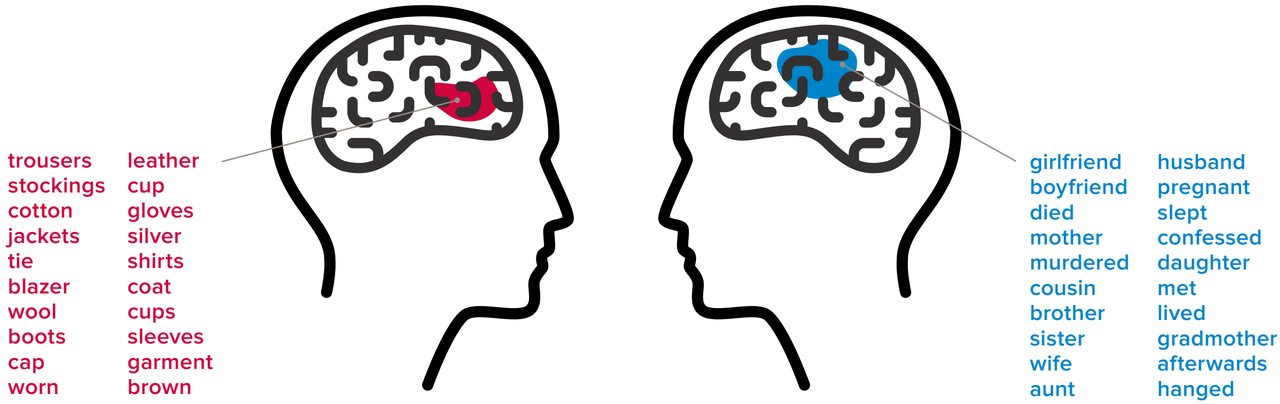
Neural interfaces are still at the stage of detecting and transferring very simple signals... They remain a long way from meeting a richer definition of 'mind reading' as deciphering someone's more complex cognitive processes and inner thoughts.

Already, we are seeing examples of developments in neural interfaces being referred to in the press as 'mind reading'. But do the technologies merit such a description? And how close are we to being able to read or transfer people's thoughts or feelings?

Many of the technologies described in this Perspective could be classed as 'mind reading' according to a very broad definition that includes the capacity to detect any impulse or simple signal from the brain using external hardware and software.

For example, in an experiment described as 'mind reading' by the media, researchers at Columbia University were able to detect brain signals of participants listening to numbers being spoken and then reproduce the sounds of the spoken numbers from the brain activity using a vocoder that converts digital data to sound[266]. Researchers at the University of California, San Francisco have created equipment that converts neural activity into speech by decoding the instructions the brain sends to the tongue, lips, jaw and throat[267]. In a parallel experiment, researchers at Kyoto University detected the brain activity of a participant looking at a picture, typically an animal, and then converted the signals into an image that contained many of the shape and colour characteristics of the original picture[268]. Similarly, researchers at University of California, Berkeley have been able to decode detailed semantic information about a movie that participants were watching based solely on measurements of their brain activity[269] (see illustration above, right).

Other studies have gone beyond decoding signals by transferring signals between participants. In one experiment two people wearing electroencephalography (EEG) caps focused on either a 'yes' or 'no' LED light in order to tell a third player who received their signals whether or not to



rotate a block in a game of Tetris[270]. This followed earlier work in which a signal from the brain of a rat in the USA that had been trained to press a lever to receive water was transferred to the brain of another rat in Brazil that then pressed an identical lever[271].

However, it is important to be clear that these projects, and the whole field of neural interfaces, are still at the stage of detecting and transferring very simple signals, individual yes/no choices or words. They remain a long way from meeting a richer definition of 'mind reading' as deciphering someone's more complex cognitive processes and inner thoughts.

'Mood reading' not mind reading

What neural interfaces are currently capable of doing is detecting how we respond emotionally to stimuli, or 'mood reading'. This capacity has been demonstrated in the laboratory[272] using simple technologies such as EEG and applied in contexts such as 'neuromarketing', which companies use to detect favourable or unfavourable responses to advertisements among consumers[273]. Although less technically complex than decoding cognitive processes, 'mood reading' is comparable in terms of breaching privacy and represents an urgent issue because it is possible today.

It is evident that attempts to improve data privacy will grow in importance in years to come. The Royal Society report *Privacy Enhancing Technologies in data analysis*[274] highlighted a need for further research into these technologies and measures to encourage adoption. A programme of public dialogues commissioned by the Royal Society found participants specifically raised concerns about neural data gathered from the use of neural interfaces. This issue is covered further in the recommendations made in our 'A Call to Action' ■

The regulation of neurotechnology

What should be allowed?

"Debates about risk are often highly technical while, at the same time, being as much about values and choices, about who benefits and who pays... When governance goes wrong, we can miss out on major potential benefits, or suffer needlessly."

Mark Walport, Government Chief Scientific Adviser, 2013 – 2017[275]

What kinds of regulation do neural interfaces require?

The main concern of regulators is safety, although they also make judgments on areas of efficacy and cost-effectiveness. Rapid advances in neural interface technology raise issues in three broad areas. The first is whether there is sufficient regulation of non-medical devices. The second is that of striking the right balance between support and scrutiny as manufacturers seek to bring potentially life-saving medical technologies to patients. Finally, there is a need to address the larger long-term ethical issues set out in the preceding section, including concerns over privacy, access to data, autonomy, unequal access and bias.

What kinds of regulation exist currently for neural interfaces in the UK?

To be placed on the market, medical devices must be approved to carry a clinical 'CE mark' by one of four notified bodies. This mark shows that the devices adhere to requirements set out in the EU's Medical Devices Regulation (MDR) including clinical evaluation, which may involve results of trials. Non-medical interfaces have historically faced much lighter regulation, having been able to gain a CE mark through 'self-certification'. The MDR has now been extended to cover non-medical devices used for brain stimulation, such as transcranial magnetic stimulation (tDCS) headsets to enhance concentration. However, electroencephalography (EEG) headsets used for gaming and other non-medical devices remain outside the MDR's scope and it will still be possible – and legal – to make a tDCS headset at home following online instructions. Beyond safety, the National Institute for Health and Care Excellence (NICE) in the UK assesses medical technologies for efficacy and cost-effectiveness, recommending whether devices should be available on the NHS and if so whether their use should be mandatory to ensure equitable access.

How might governments or regulators update regulation of medical devices?

In medicine, neural interfaces are often not suited to the standard format for clinical evaluation known as 'randomised controlled trials' (RCTs), as their outcomes cannot be defined as clearly as for drugs, and conditions that interfaces are used to treat, such as strokes, vary from person to person. Consequently, many interface specialists advocate extending the use of alternatives to RCTs.

These include use of 'real-world data' such as clinical outcomes and patients' experiences, as well as 'longitudinal trials' which have no control group but instead focus on repeated observations of the same cohort of patients to see how their conditions respond to treatment over time.

QA

What options do governments have to address longer-term ethical issues?

An overarching principle might be to strive for 'responsible innovation' that recognises ethical issues and provides space to consider them. One option is to follow the Human Genome Project's process and set up a programme to to monitor and make recommendations on the ethical, legal and social aspects of the technologies as they evolve[276]. Another is to start with a bespoke public inquiry that takes evidence from experts and interested parties and recommends further steps, such as legislation or institutions – a precedent for this approach being the establishment of the Human Fertilisation and Embryology Authority (HFEA).

There is currently an appetite within the UK for exploring new approaches to technology regulation, which the Royal Society believes should be trialled on neural interface technologies. Whatever route is taken, many experts highlight the importance of being proactive in engaging the public early and often so that people learn about the issues in an informed and balanced way that provides context for media coverage which may be less dispassionate. This approach has been strongly supported by people from across Britain who have taken part in the programme of independent public dialogue commissioned by the Royal Society to complement this perspective. ■

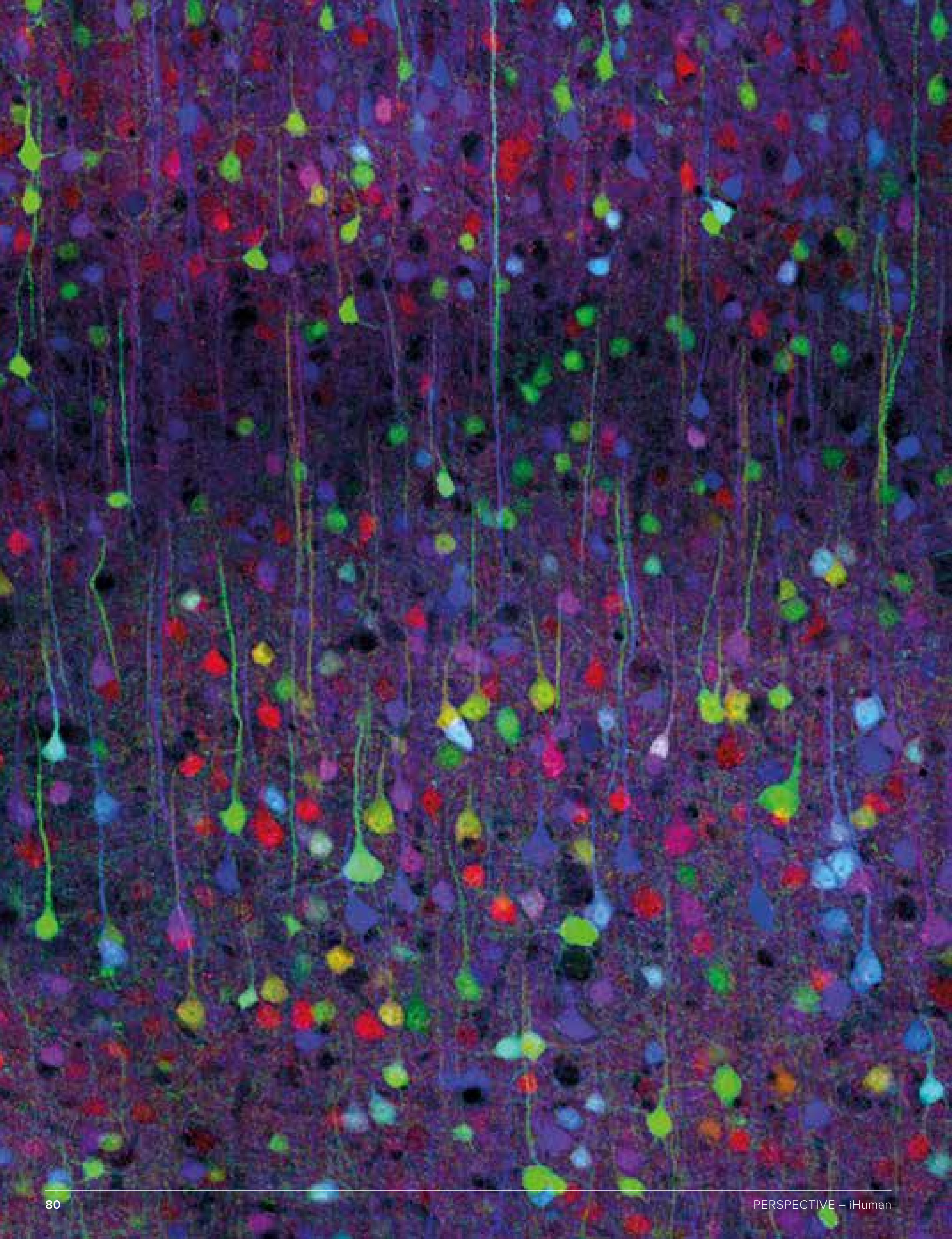
There is currently an appetite within the UK for exploring new approaches to technology regulation, which the Royal Society believes should be trialled on neural interface technologies.


60

Mollii Suit

The Mollii Suit illustrates some of the issues presented by innovative medical interface therapies. It is a wetsuit-like stimulation garment designed at Sweden's Karolinska Institute for use by people with conditions such as cerebral palsy and stroke. Costing approximately £4,000 and certified as safe with an EU CE mark[277], it delivers low-frequency electro-stimulation that prompts the body's neurological reflexes[278]. Users have praised the product[279], boosting sales to over 1,000 worldwide[280] on the basis of anecdotal evidence. However, the only formal clinical evidence thus far includes one peer-reviewed publication, a pilot trial of 27 people and a National Institute for Health and Care Excellence (NICE) briefing paper. NICE points to 'uncertainties around the technology' and lack of evidence from randomised controlled trials as reasons for currently not recommending funding through the NHS[281]. Hence the suit remains available only in the private sector, to those who can afford it.

Left:
The Mollii Suit.
© Inerventions AB Sweden.

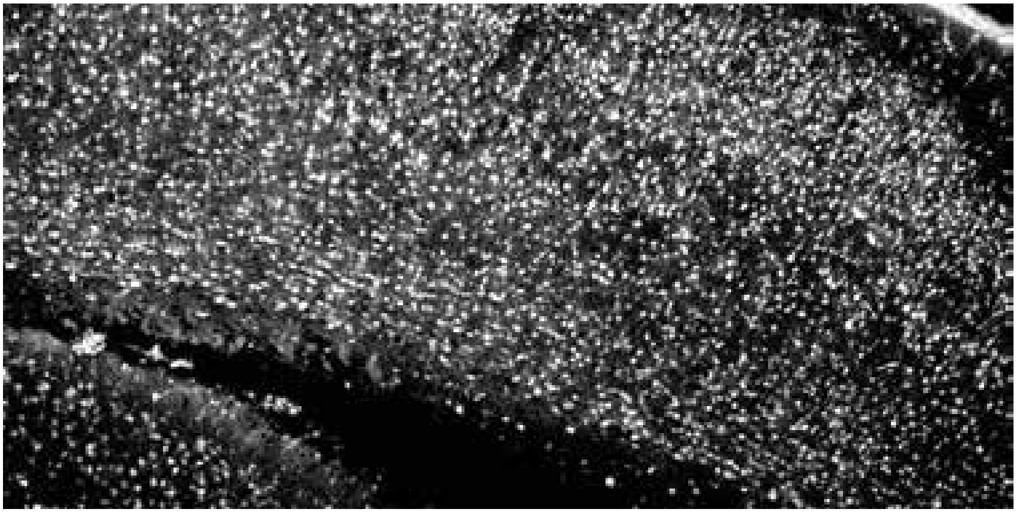


Neural interfaces and the future of emerging technology regulation

How capable are traditional regulatory frameworks of dealing with the ever-changing and rapidly accelerating technology landscape?

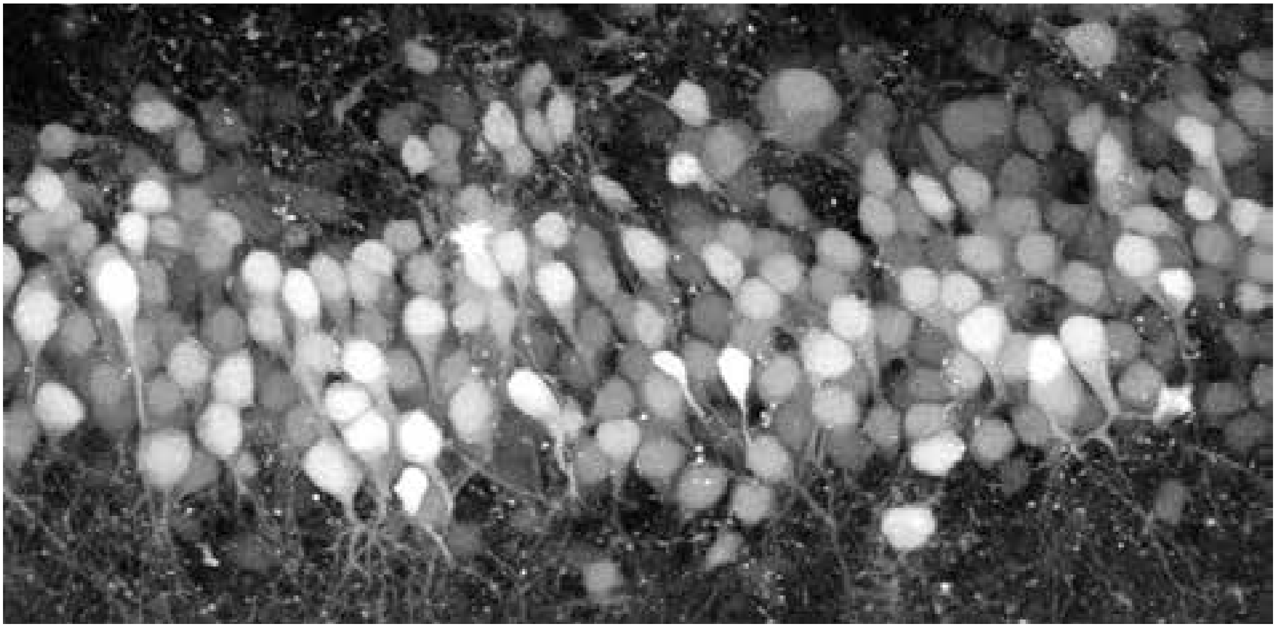
Throughout the development of this report, clinicians have asserted that people are unable to access the best medical innovations quickly enough due to regulatory restrictions. At the same time, neural interfaces are being used by 'brain-hackers' with little regulatory constraint, despite limited understanding of the safety and efficacy of the devices.

The UK is internationally renowned for its regulatory system for science and technology. However, there is growing interest in the UK in taking a more proactive, anticipatory approach to regulating new technologies (as shown by work carried out by Ministerial Working Group for Future Regulation[282], Nesta[283], Wellcome[284] and Department for Business, Energy and Industrial Strategy[285]). The UK has announced a partnership with the World Economic Forum, which will '… push forward a modern "agile" regulatory approach that fosters innovation while protecting customers'[286].



Far Left:
'The Brainbow' is a method of illuminating and tracing the axons and dendrites connecting neurons to each other. Featured image shows the cerebral cortex of a mouse produced by Livet *et al.*, *Nature*, 2007 by Tamily Weissman.

Left:
Image of a 'cortical slice' © YusteLab Columbia University.



Neural interfaces offer the ideal suite of technologies for the UK to explore and shape new forms of technology regulation.

Above:
A close-up image of a slice of the hippocampus, an area of the brain associated with memory. © YusteLab Columbia University.

As set out in our 'A Call to Action', we believe that neural interfaces offer the ideal suite of technologies for the UK to explore and shape new forms of technology regulation.

Neural interfaces encompass a broad and interdisciplinary field. As well as having huge, transformative potential for medical use, the technology is already of great interest to gaming and the creative industries more broadly, as well as consumer robotics and well-being.

Using neural interfaces as a test case for new approaches to technology regulation would allow the UK to become a centre of innovation in neural interfaces. The UK currently lags behind the USA in the development of neural interfaces and the US Food and Drug Administration recently issued draft regulatory guidance that seeks to further accelerate medical applications of the technologies and investment in the field[287]. Taking an anticipatory approach would aim to bridge this gap, ensuring that start-ups and specialists both relocate to, and are developed in, the UK. At the same time, it would allow the UK to drive forward the responsible and ethical use of neural interfaces, covering both medical applications and interfaces that fall outside the scope of medical regulation.

Positive steps are being taken in regard to many aspects of this agenda. For example, NICE has published a new Evidence Standards Framework for Digital Health Technologies[288]. The Department of Health & Social Care has issued a Code of Conduct for data-driven health and care technology, which includes, for example, making security of data integral to system design and being transparent about how algorithms work[289]. The section 'A Call to Action' that follows suggests ways to build on such work through a co-ordinated national effort to realise the potential of neural interface technologies while managing the associated risks. ■

A call **to action**

principles and practices

These recommendations all fall under one central proposal that the UK should use neural interfaces as a test case for a new democratised and anticipatory approach to promoting emerging technologies. Below we set out a set of principles that could be applied internationally, along with recommendations for specific practices to implement those principles in the UK. This joined-up approach would seek to stimulate innovation in the field, while constructing responsible regulation around the technology as it develops.

To achieve this aim, we recommend:

- The UK develop a 'Neural Interface Ecosystem' to accelerate the development of the technologies in the UK and encourage multidisciplinary collaboration across industries.
- An 'early and often' approach to addressing the ethical considerations of the field.
- The UK trial new approaches to technology regulation on neural interface technologies. These could include the use of regulatory 'sandboxes' – in which innovators can test products in a controlled environment with limited regulation – and new ways of gathering evidence about the efficacy of medical devices.
- The general public be given a clear voice in shaping the future of neural interface regulation. Furthermore, the processes of consultation, regulation and policy choices be designed so that the public's voice has an impact on them. This should include a key role for public consultation in developing regulatory frameworks and public representation on relevant advisory boards.

Neural Interface ecosystem
in the UK

PRINCIPLES

Action to create a ‘neural interface ecosystem’ to accelerate the development of the technologies in the UK. This ecosystem would be underpinned by progress in digital technologies which will drive progression in neural interface applications. Such an ecosystem would bring together scientists, clinicians, game developers, sensor development communities, artists, policymakers, investors, funders, regulators, members of the public and others in a collaborative network which promotes cross-fertilisation across industries.

The ecosystem should develop consensus standards to accelerate the commercialisation and scale up and to build trust with investors, regulators and consumers.

The ecosystem should actively encourage inclusivity and diversity in both those developing neural interfaces and those the devices are being tested upon. Doing so would help address issues of bias and mitigate against the potential of neural interfaces to drive inequality.

PRACTICES

- The Department for Business, Energy & Industrial Strategy (BEIS) should consider making neural interfaces a Grand Challenge.
- Innovate UK should consider funding a 'UK Centre for Neural Interfaces', to be run with a similar remit to that of 'Immerse UK' for virtual reality. A specific goal might be to support collaboration between the medical and gaming communities. It is suggested that at least 10% of board members overseeing the centre should be members of the general public.
- UKRI is encouraged to support members of the ecosystem to develop ways of treating mental health conditions with neural interfaces; these are currently under-represented in medical applications of the technology.
- The British Standards Institute (BSI) should consider having an active role in engaging with the ecosystem to help create internationally-recognised standards for the emerging field. One early focus could be the safety of interfaces not covered by medical device regulation.
- In annual reports, the 'UK Centre for Neural Interfaces' (see above) should assess the state of diversity and inclusion in the emerging field.
- The ecosystem should develop specific industry-led standards that ensure diversity in participants who trial neural interfaces.
- The ecosystem should encourage and facilitate auditing to assess the diversity of training datasets that neural interfaces are built upon. This would aim to ensure that the technology works equally as well for users regardless of their gender, ethnicity or socio-economic status.

Ethics

Towards an 'early and often' approach

PRINCIPLES

Constructing appropriate ethical guidelines for neural interfaces will take time, experimentation and public consultation, with key issues being brought up early and often throughout.

The proposals put forward by the Morningside Group could act as a 'sticking plaster', temporarily safeguarding against many of the worst-case uses of neural interfaces while such guidelines are developed.

A national investigation on ethical issues raised by neural interfaces is required. It should encompass a programme of public, industry, and academic engagement, and funding calls which prioritise exploring the ethics of neural interfaces. The overall aim of the approach should be to recommend standards and safeguards for future development of the field and to guide regulatory choice and policymaking.

International frameworks should be able to define the direction of the field rather than so-called 'Big Tech' (Google, Amazon, Facebook, Apple, Microsoft).

As these technologies develop, protecting the privacy of users should be a key priority for the field of neural interfaces.

A programme of public dialogues commissioned by The Royal Society found participants raised concerns about everything being tracked in today's society and losing control over their data, particularly to companies. They expressed a desire for transparency about who is gathering the data and for what purpose, as well as about the pros and cons of the applications.

These recommendations aim to avoid a situation whereby technology companies freely cross-reference neural data gathered from interfaces, such as data about someone's emotional mood, with other personal data held and sold, such as that about social media use.

PRACTICES

- Urgent consideration by government of the proposals of the Morningside Group, who bring together scientists, engineers and others from industry, academia and international projects to propose priorities for government and international regulation of neurotechnologies. These include making opting out of neural data-sharing the default choice; defining prohibited actions similar to the Convention for the Protection of All Persons from Enforced Disappearance; stringent regulation of military technology; and steps to counter bias in neural devices[290].

- The UK government might commission Sciencewise to carry out public dialogue to inform government decision-making on the future development and regulation of neural interfaces.
- The Department for Digital, Culture, Media & Sport (DCMS) and The Centre for Data Ethics and Innovation could launch a consultation on the ethics of neural interfaces, engaging the public, academia, business and regulators seeking to promote best practice and address gaps in the regulatory landscape.
- UKRI should consider developing a funding call to explore the ethics of neural interfaces.

- Insights from the proposed public consultation could be used by The Centre for Data Ethics and Innovation to inform the construction of an International Regulatory Framework for Neural Interfaces.

- Technology companies driving innovation in neural interfaces, especially those from 'Big Tech', should develop open codes of conduct concerning how to protect the privacy of users, particularly in relation to what happens to the neural data that the technologies produce. The Royal Society recommends these include:
  - The default choice for users of neural interfaces being 'opting out' of sharing their neural data. In the UK, this could be considered by the National Data Guardian for Health and Social Care.
  - The full functionality of neural interfaces should not be withheld from users who do opt out of neural data-sharing.
  - Measures should exist to ensure that when users do opt in to neural data-sharing, they are doing so on the basis of transparency about what the data is being used for and who will have access to it, as well as what safeguards are in place.

Trialling new approaches
to technology regulation on neural interfaces

PRINCIPLES

Neural interfaces offer the ideal suite of technologies for the UK to explore and shape new forms of technology regulation.

Regulators should be enabled to experiment in their approach to neural interfaces, particularly in involving the public and those with specialist knowledge in designing guidelines and rules.

Regulation cannot be so onerous, complicated and expensive that it allows ‘Big Tech’ to dominate the emerging field.

The UK should take the lead in creating a new ‘device friendly’ approvals and regulation system. Work should continue to develop and use new means of gathering evidence on the efficacy of devices, such as ‘real-world data’, as alternatives to randomised controlled trials (RCTs).

PRACTICES

- BEIS, the Better Regulation Executive (BRE) and the Department for Health and Social Care (DHSC) are encouraged to adopt neural interfaces as a test case with which to explore new approaches to emerging technology regulation.
- BEIS could consider starting a new round of the Regulators Pioneer Fund, focusing on participatory approaches to constructing regulation of the use of neural interfaces.
- The Medicines and Healthcare products Regulatory Agency (MHRA) could develop a regulatory ‘sandbox’ for neural interfaces with medical applications, focusing on start-ups.
- Development of a new approvals and regulation system for neural interfaces might be coordinated by MHRA, The Health Research Authority (HRA) and NHSX, a new joint organisation for digital, data and technology.

Acknowledgments

NEURAL INTERFACES STEERING GROUP

Chairs

Professor Chris Toumazou FRS FREng, Regius Professor of Engineering and Chair in Biomedical Circuit Design, Imperial College London.

Dr Tim Constandinou, Reader in Neural Microsystems, Department of Electrical and Electronic Engineering, and Deputy Director of the Centre for Bio-inspired Technology, Imperial College London.

Members

Dr Mahnaz Arvaneh, Lecturer, Department of Automatic Control and Systems Engineering, University of Sheffield.

Professor Jane Burridge, Professor of Restorative Neuroscience, University of Southampton.

Dr Sarah Chan, Chancellor's Fellow and Reader, Usher Institute for Population Health Sciences and Informatics, Director, Mason Institute for Medicine, Life Sciences and the Law, University of Edinburgh.

Professor Tim Denison, Professor of Neurotechnology, University of Oxford.

Mr Jinendra Ekanayake, Royal College of Surgeons of England Fellow in Neurovascular Neurosurgery, Leeds General Infirmary, Honorary Senior Clinical Lecturer, Imperial College London.

Professor Sadaf Farooqi, Principal Research Fellow, University of Cambridge.

Dr Caroline Golden, Research Associate, Department of Electrical and Electronic Engineering, Imperial College London.

Dr Rylie Green, Reader, Department of Bioengineering, Imperial College London.

Professor Andrew Jackson, Professor of Neural Interfaces, Newcastle University.

Professor Slawomir J Nasuto, Deputy Research Division Leader, Biomedical Sciences and Biomedical Engineering Division, School of Biomedical Sciences, University of Reading.

Dr Konstantin Nikolic, Associate Professor, Department of Electrical and Electronic Engineering, Imperial College London.

Dr Victor Pikov, Founder and CEO, Medipace Inc.

Professor Rodrigo Quian Quiroga, Director, Centre for Systems Neuroscience, University of Leicester.

Dr Andrew Sims, Head of Department, Northern Medical Physics and Clinical Engineering, Newcastle upon Tyne Hospitals NHS Foundation Trust.

EXTERNAL REVIEWERS

Professor Jon Agar, Professor of Science and Technology Studies, University College London.

Frazer Bennett, Chief Innovation Officer, PA Consulting Group.

Hermann Hauser KBE FRS FREng, Co-Founder, Amadeus Capital Partners.

ROYAL SOCIETY SECRETARIAT

Dr Claire Craig CBE, Chief Science Policy Officer (until July 2019).

Elizabeth Surkovic, Head of Policy, Resilient Futures.

Dr Patrick Noack, Senior Policy Adviser.

Jack Pilkington, Policy Adviser.

James Musisi, Project Co-ordinator.

David Vigar, Consultant Editor.

Lindsay Taylor, Policy Adviser (until September 2018).

Emma Laycock, Policy Intern (until February 2019).

EMERGING TECHNOLOGIES WORKING GROUP

A committee of experts oversees the Royal Society's policy work on emerging technologies and futures. The Royal Society gratefully acknowledges the contribution of this group in the development of the project.

Chair

Professor Andy Hopper CBE FREng FRS, Treasurer, the Royal Society.

Members

Professor Christopher Abell FMedSci FRS, Pro Vice-Chancellor for Research, University of Cambridge.

Dame Helen Ghosh DCB, Master of Balliol College, University of Oxford.

Professor Dame Anne Glover FRS, University of Strathclyde; President, the Royal Society of Edinburgh.

Professor Mark Miodownik MBE FREn, Professor of Materials and Society, University College London.

Dame Angela Strank FREng FRS, Chief Scientist, BP.

The Royal Society would also like to thank those who contributed to the development of this project through taking part in informal interviews, reviewing sections of the report or attending the Neural Interfaces Insights Workshop on 13 November 2018, as well as members of the public who took part in the programme of independent public dialogue commissioned by the Royal Society to complement this perspective.

References

1. Thomson C, Segrave R, Racine E, Carter A. 2018 The impact of deep brain stimulation on personality, identity, and relationships in neurological and psychiatric conditions. Brain Stimul. 12, 500. (https://doi.org/10.1016/j.brs.2018.12.636)

2. Walport, M. 2014 Innovation: Managing risk, not avoiding it. Annual report of the Government Chief Scientific Adviser 2014. See https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/381905/14-1190a-innovation-managing-risk-report.pdf (accessed 11 March 2019).

3. World Health Organisation. 2018 Factsheet on depression. See https://www.who.int/news-room/fact-sheets/detail/depression (accessed 7 February 2019).

4. Huang C et al. 2019 The neuroprotective effect of deep brain stimulation at nucleus basalis of Meynert in transgenic mice with Alzheimer's disease. Brain Stimul. 12, 161–174. See https://www.ncbi.nlm.nih.gov/pubmed/30181106 (accessed 7 February 2019).

5. Urban T. 2017 Neuralink and the brain's magical future. Wait But Why, 20 April 2017. See https://waitbutwhy.com/2017/04/neuralink.html (accessed 7 February 2019).

6. Virilio, P. 1999 Politics of the Very Worst, New York: Semiotext(e), 1999See http://anthropoetics.ucla.edu/ap0602/virilio/ (accessed 7 February 2019).

7. Galič M, Timan T,Koops BJ. 2017 Bentham, Deleuze and beyond: An overview of surveillance theories from the Panopticon to participation. Philos Tech. 30, 9–37. See https://link.springer.com/article/10.1007/s13347-016-0219-1 (accessed 11 February 2019).

8. Dragoni N, Giaretta A,Mazzara M. 2018 The Internet of Hackable Things. (https://doi.org/10.13140/RG.2.2.19643.72482)

9. Pycroft L et al. 2016 Brainjacking: Implant security issues in invasive neuromodulation. World Neurosurg. 92, 454–462 (https://doi.org/10.1016/j.wneu.2016.05.010)

10. Dodge J. 2017 Cyborg self hacking. 30 January 2017. See https://www.youtube.com/watch?v=ihcaNoUJ6BU&feature=youtu.be (accessed 7 February 2017). Also: Kingery K. 2016 Hacking into a bionic ear. See https://pratt.duke.edu/about/news/hacking-bionic-ear (accessed 7 February 2017).

11. Schultz W. 2015. Neuroessentialism: Theoretical and clinical considerations. J. Humanist. Psychol. 58, 607–639. See https://journals.sagepub.com/doi/abs/10.1177/0022167815617296?journalCode=jhpa (accessed 10 February 2019).

12. Corbett-Davies S, Pierson E, Feller A, Goel S and Huq A. 2017. Algorithmic decision making and the cost of fairness. In Proceedings of the 23rd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining (https://doi.org/10.1145/3097983.3098095) Also: Kleinberg J, Mullainathan S, Raghavan M. 2016 Inherent trade-offs in the fair determination of risk scores. Proc. Innov. Theoret. Comp. Sci. See https://arxiv.org/abs/1609.05807 (accessed 11 March 2019). Also: Angwin J, Larson J. 2016 Bias in criminal risk scores is mathematically inevitable, researchers say. ProPublica 30 December 2016. See https://www.propublica.org/article/bias-in-criminal-risk-scores-is-mathematically-inevitable-researchers-say (accessed 7 February 2019).

13. Statistica. 2019 Percentage of households with landline telephones in the United Kingdom (UK) from 1970 to 2017. See https://www.statista.com/statistics/289158/telephone-presence-in-households-in-the-uk/ (accessed 13 February 2019).

14. Wenner Moyer W. 2016 A safe drug to boost brainpower. Sci. Am. 1 March 2016. See https://www.scientificamerican.com/article/a-safe-drug-to-boost-brainpower/ (accessed 7 February 2019).

15. Cury R et al. 2017 Thalamic deep brain stimulation for tremor in Parkinson disease, essential tremor, and dystonia. Neurology 89. (https://doi.org/10.1212/WNL.0000000000004295)

16. Brunoni AR et al. 2016 Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. Br. J. Psychiat. 208, 522–531.

17. Medtronic receives European CE mark approval for deep brain stimulation therapy for refractory epilepsy. 16 September 2010. See http://newsroom.medtronic.com/phoenix.zhtml?c=251324&p=irol-newsArticle&ID=1773303 (accessed 7 February 2019).

18. National Institute for Healthcare and Excellence (NICE). 2017 Mollii suit for spasticity. See https://www.nice.org.uk/advice/mib100 (accessed 7 February 2019).

19. US Food & Drug Administration. 2013 Premarket approval for Neuropace RNS system. See https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100026 (accessed 7 February 2019).

20. NHS England. 2018 Clinical commissioning policy: Deep brain stimulation for refractory epilepsy (all ages). See https://www.england.nhs.uk/wp-content/uploads/2018/03/d04-deep-brain-stimulation-for-refractory-epilepsy.pdf (accessed 7 February 2019).

21. Dalic L, Cook, MJ. 2016 Managing drug-resistant epilepsy: challenges and solutions. Neuropsych. Dis. Treat. 12, 2605–2616. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5068473/ (accessed 7 February 2019).

22. Overstreet E, Hoen M. 2018 Cochlear implants: Considerations regarding the relationship between cognitive load management and outcome. The Hearing Review. See http://www.hearingreview.com/2018/06/cochlear-implants-considerations-regarding-relationship-cognitive-load-management-outcome/ (accessed 7 February 2019).

23. Chuang AT, Margo CE, Greenberg PB. 2014 Retinal implants: A systematic review. Br. J. Ophthalmol. 98, 852–856.

24. Lyons MK. 2011. Deep brain stimulation: Current and future clinical applications. Mayo Clin. Proc. 86, 662–72. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3127561/ (accessed 7 February 2019).

25. Epilepsy Action factsheet. 2017 See https://www.epilepsy.org.uk/info/treatment/deep-brain-stimulation, (accessed 7 February 2019).

26. Professor Sir John Gurdon and 400 others. Letter to The Guardian, 13 September 2016. See https://www.theguardian.com/science/2016/sep/13/primate-research-is-crucial-if-we-are-to-find-cures-for-diseases-like-parkinsons (accessed 7 February 2019).

27. US Food & Drug Administration. 2013 Premarket approval for Neuropace RNS system. See https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100026 (accessed 7 February 2019).

28. NeuroPace press release 2019 NeuroPace Shares Positive Data from Studies of the RNS System at the American Academy of Neurology 2019 Annual Meeting. 9 May 2019 See: https://www.neuropace.com/neuropace-shares-positive-data-from-studies-of-the-rns-system-at-the-american-academy-of-neurology-2019-annual-meeting/ (accessed 1 July 2019)

29. Parc de Salut - Hospital del Mar. 2018 News release: Hospital del Mar successfully uses deep brain stimulation to treat 4 patients with anorexia nervosa, 12 July 2018. See https://www.parcdesalutmar.cat/en/noticies/view.php?ID=3(accessed 7 February 2019). Also: Scientists treat anorexia by hooking brain up to electrodes. Newsweek. 12 July 2018. See https://www.newsweek.com/scientists-treat-anorexia-hooking-brain-electrodes-1020308 (accessed 7 February 2019).

30. de Koning PP, Figee M, van den Munckhof P, Schuurman PR, Denys D. 2011 Current status of deep brain stimulation for obsessive-compulsive disorder: A clinical review of different targets. Curr. Psychiat. Rep. 13, 274–82. (https://doi.org/10.1007/s11920-011-0200-8)

31. Sun FT, Morrell MJ. Wharen RE. 2008 Responsive cortical stimulation for the treatment of epilepsy. Neurotherapeutics 5, 68–74.

32. Wagner FB et al. 2018 Targeted neurotechnology restores walking in humans with spinal cord injury. Nature 563, 65–71. See https://www.nature.com/articles/s41586-018-0649-2 (accessed 7 February 2019).

33. Dones I, Levi V. 2018 Spinal cord stimulation for neuropathic pain: Current trends and future applications. Brain Sciences 8, 138. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6119923/ (accessed 7 February 2019).

34. Bacher D et al. 2015 Neural point-and-click communication by a person with incomplete locked-in syndrome. Neurorehab. Neural Re. 29, 462–471. See https://www.ncbi.nlm.nih.gov/pubmed/25385765 (accessed 7 February 2019).

35. Jarosiewicz B et al. 2015 Virtual typing by people with tetraplegia using a self-calibrating intracortical brain-computer interface. Sci. Transl. Med. 7, 313. See https://www.ncbi.nlm.nih.gov/pubmed/26560357 (accessed 7 February 2019).

36. People with tetraplegia gain rapid use of brain-computer interface. Science Daily. 24 January 2018. See https://www.sciencedaily.com/releases/2018/01/180124123204.htm (accessed 7 February 2019).

37. Wolpaw J et al. 2018 Independent home use of a brain-computer interface by people with amyotrophic lateral sclerosis. Neurology 91. (https://doi.org/10.1212/WNL.0000000000005812)

38. Bournemouth University. The use of Function Electrical Stimulation (FES) in neurological rehabilitation. See https://research.bournemouth.ac.uk/impact/the-use-of-function-electrical-stimulation-fes-in-neurological-rehabilitation/ (accessed 7 February 2019).

39. Sczesny-Kaiser M et al. 2015 HAL® exoskeleton training improves walking parameters and normalizes cortical excitability in primary somatosensory cortex in spinal cord injury patients. J. Neuroeng. Rehabil. 12, 68. (https://doi.org/10.1186/s12984-015-0058-9)

40. McDonald CM. 2012. Clinical approach to the diagnostic evaluation of hereditary and acquired neuromuscular diseases. Phys. Med. Reh. Clin. N. 23, 495–563.

41. Xue G, Chen C, Lu ZL, Dong Q. 2010 Brain imaging techniques and their applications in decision-making research. Acta Psychol. Sin. 42, 120–137.

42. Quian Quiroga R, Reddy L, Kreiman G, Koch C, Fried I. 2005 Invariant visual representation by single neurons in the human brain. Nature 435, 1102–1107. See https://www.nature.com/articles/nature03687(accessed 7 February 2019).

43. Hampson RE et al. 2018 Developing a hippocampal neural prosthetic to facilitate human memory encoding and recall. J. Neural Eng. 15 036014. See https://iopscience.iop.org/article/10.1088/1741-2552/aaaed7/pdf, (accessed 7 February 2019).

44. Human Brain Project. Neuromorphic computing. See https://www.humanbrainproject.eu/en/silicon-brains/ (accessed 7 February 2019).

45. Sabatowski R, Schäfer D, Kasper M, Brunsch H, Radbruch L. 2004 Pain treatment: A historical overview. Curr. Pharm. Design 10, 701–716. (https://doi.org/10.2174/1381612043452974)

46. Sabatowski R, Schäfer D, Kasper M, Brunsch H, Radbruch L. 2004 Pain treatment: A historical overview. Curr. Pharm. Design 10, 701–716. (https://doi.org/10.2174/1381612043452974).

47. The Scientist. 2011 Animal electricity, circa 1781. See https://www.the-scientist.com/foundations/animal-electricity-circa-1781-41872 (accessed 8 February 2019).

48. Lord Cohen of Birkenhead. 1959 Richard Caton (1842-1926) Pioneer electrophysiologist. P. Roy. Soc. Med. 52, 645. See https://journals.sagepub.com/doi/pdf/10.1177/003591575905200816 (accessed 8 February 2019).

49. Pravdich-Neminsky VV. 1913 Experiments on the registration of the electrical phenomena of the mammalian brain. Zbl. Physiol. 27, 951–960.

50. The Burton Report. 2019 The history of neurostimulation: Part I. See https://www.burtonreport.com/infspine/nshistneurostimparti.htm (accessed 8 February 2019).

51. Berger H. 1929 Uber das Elektrenkephalogramm des Menschen. First report. Arch. Psychiat. Nervenkr. 87, 527–570. (https://doi.org/10.1007/BF01797193) Also: Tudor M, Tudor L, Tudor K. 2005 Hans Berger (1873-1941)--the history of electroencephalography. Acta Med. Croatica 59, 307–313. See https://www.ncbi.nlm.nih.gov/pubmed/16334737 (accessed 8 February 2019).

52. Aquilina O. 2006 A brief history of cardiac pacing. Images Paediatr. Cardiol. 8, 17–81. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3232561/ (accessed 8 February 2019).

53. Gibbs FA, Davis H, Lennox WG. 1935 The electro-encephalogram in epilepsy and in conditions of impaired consciousness. Arch. NeurPsych. 34, 1133–1148. (https://doi.org/10.1001/archneurpsyc.1935.02250240002001)

54. Endler NS. 1988 The origins of electroconvulsive therapy. J. ECT 4. See https://journals.lww.com/ectjournal/Abstract/1988/04010/The_Origins_of_Electroconvulsive_Therapy__ECT_.3.aspx (accessed 8 February 2019).

55. Sironi VA. 2011 Origin and evolution of deep brain stimulation. Front. Integr. Neurosci. 5. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157831/ (accessed 8 February 2019).

56. Eshraghi AA, Nazarian R, Telischi FF, Rajguru SM, Truy E, Gupta C. 2012 The cochlear implant: Historical aspects and future prospects. Anat. Rec. (Hoboken) 295, 1967–1980. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4921065/ (accessed 8 February 2019).

57. Sironi VA. 2011 Origin and evolution of deep brain stimulation. Front. Integr. Neurosci. 5. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3157831/ (accessed 8 February 2019).

58. Moore GE, 1965 Cramming more components onto integrated circuits. Electronics 38, See https://newsroom.intel.com/wp-content/uploads/sites/11/2018/05/moores-law-electronics.pdf (accessed 8 February 2019).

59. Lutters B, Koehler PJ. 2016 Brainwaves in concert: The 20th century sonification of the electroencephalogram. Brain 139, 2809–2814 (https://doi.org/10.1093/brain/aww207)

60. Mudry A, Mills M. 2013 The early history of the cochlear implant: A retrospective. JAMA Otolaryngol. 139, 446–453. See https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/1688121 (accessed 8 February 2019).

61. Fetz EE. 1969 Operant conditioning of cortical unit activity. Science 163, 955–958.

62. Vidal JJ. 1973 Toward direct brain computer communication. Annu. Rev. Biophys. Bio. 2, 157–180. See http://web.cs.ucla.edu/~vidal/BCI.pdf (accessed 8 February 2019).).

63. Maura DD. 1974 Transcutaneous stimulator and stimulation method. United States Patent 3,817,254. See https://patentimages.storage.googleapis.com/c7/d9/b1/abc6b8cf8dc553/US3817254.pdf (accessed 8 February 2019).

64. Bozinovski S, Sestakov M, Bozinovska L. 1988 Using EEG alpha rhythm to control a mobile robot. In: Harris G, Walker C (eds) Proc. IEEE Conf.Med. Biol. Soc. 3, 1515–1516.

65. Chen XL, Xiong YY, Xu GL, Liu XF. 2013 Deep brain stimulation. Intervent. Neurol. 1, 200–212.

66. Kennedy PR, Bakay RA. 1998 Restoration of neural output from a paralyzed patient by a direct brain connection. Neuroreport 9, 1707–1711. (https://doi.org/10.1097/00001756-199806010-00007).

67. Hochberg LR et al. 2006 Neuronal ensemble control of prosthetic devices by a human with tetraplegia. Nature 442, 164–171.

68. Collinger JL et al. 2013 7 degree-of-freedom neuroprosthetic control by an individual with tetraplegia. Lancet 381(9866), 557–564.

69. US Food & Drug Administration. 2013 Premarket approval for Neuropace RNS system. See https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P100026 (accessed 7 February 2019).

70. Second Sight. 2013 Second Sight medical products receives FDA approval for Argus II system. See http://investors.secondsight.com/news-releases/news-release-details/second-sight-medical-products-receives-fda-approval-argus-ii (accessed 9 February 2019).

71. Crunchbase. 2019 Neuralink. See https://www.crunchbase.com/organization/neuralink#section-overview (accessed 9 February 2019).

72. Neuralink. 2019. See https://www.neuralink.com/ (accessed 9 February 2019).

73. Johnson B. 2016 Introducing Kernel: An HI company. See https://bryanjohnson.co/kernel-an-hi-company/ (accessed 9 February 2019).

74. Kernel. 2019 See https://kernel.co/ (accessed 9 February 2019).

75. Statt N. 2017 Facebook is working on a way to let you type with your brain. See https://www.theverge.com/2017/4/19/15360798/facebook-brain-computer-interface-ai-ar-f8-2017 (accessed 9 February 2019). Also: Mark Zuckerberg confirms Facebook is working on mind-reading technology. The Telegraph. 19 April 2017. See https://www.telegraph.co.uk/technology/2017/04/19/mark-zuckerberg-confirms-facebook-working-mind-reading-technology/ (accessed 9 February 2019).

76. DARPA. 2017 Towards a high-resolution, implantable neural interface. See https://www.darpa.mil/news-events/2017-07-10 (accessed 9 February 2019).

77. Johnson BC et al. 2018 StimDust: A 6.5mm3, wireless ultrasonic peripheral nerve stimulator with 82% peak chip efficiency. IEEE Cust. Integr. Cir. (http://dx.doi.org/10.1109/CICC.2018.8357047)

78. Maskeliunas R, Damasevicius R, Martisius I,Vasiljevas M. 2016 Consumer-grade EEG devices: Are they usable for control tasks? PeerJ 4, e1746. (https://doi.org/10.7717/peerj.1746)

79. Valve psychologist explores controlling games directly with your brain. Venture Beat. 24 March 2019. See https://venturebeat.com/2019/03/24/valve-psychologist-explores-controlling-games-directly-with-your-brain/ (accessed 3 July 2019).

80. Katona J, Kovari, A. 2015 EEG-based computer control interface for brain-machine interaction. Int. J. Online Biomed. Eng. 11. See https://online-journals.org/index.php/i-joe/article/view/5119 (accessed 7 February 2019).

81. Synesthesia suit. See http://rezinfinite.com/synesthesia-suit/ (accessed 7 February 2019).

82. How to build a brain cap. See https://www.instructables.com/id/How-To-Build-a-Brain-Cap-tDCS/ (accessed 7 February 2019).

83. The Brain Stimulator website. See https://thebrainstimulator.net/ (accessed 7 February 2019).

84. 49 Reinhart, RMG, Nguyen, JA. 2019 Working memory revived in older adults by synchronizing rhythmic brain circuits. Nat. Neurosci. 22(5), 820-827

85. Kim D. 2012 Practical use and risk of Modafinil, a novel waking drug. Environ. Health Toxicol. 27. (https://dx.doi.org/10.5620%2Feht.2012.27.e2012007)

86. Eliyahu U, Berlin S, Hadad E, Heled Y, Moran D. 2007 Psychostimulants and Military Operations. Mil. Med. 172, 383.

87. Vitor-Costa M et al. 2015 Improving cycling performance: Transcranial direct current stimulation increases time to exhaustion in cycling. PLoS ONE 10. See https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0144916 (accessed 7 February 2019).

88. Wurzman R, Hamilton RH, Pascual-Leone A, Fox MD. 2016 An open letter concerning do-it-yourself users of transcranial direct current stimulation. Ann. Neurol. 80, 1–4. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6050584/ (accessed 11 February 2019).

89. Schambra HM, Bikson M, Wager TD, DosSantos MF, DaSilva AF. 2014 It's all in your head: Reinforcing the placebo response with tDCS. Brain Stimul. 7, 623–624. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4108558/ (accessed 11 February 2019).

90. Al Emondi. Next-generation nonsurgical neurotechnology. See https://www.darpa.mil/program/next-generation-nonsurgical-neurotechnology (accessed 7 February 2019).

91. DARPA. 2017 Towards a high-resolution, implantable neural interface. See https://www.darpa.mil/news-events/2017-07-10 (accessed 7 February 2019).

92. United Rentals, Project Uptime. 2018 Wearables that detect fatigue. See https://www.unitedrentals.com/project-uptime/technology/wearables-detect-fatigue#/ (accessed 7 February 2019).

93. Lee BG, Lee BL, Chung WY. 2014 Mobile healthcare for automatic driving sleep-onset detection using wavelet-based EEG and respiration signals. Sensors-Basel 14, 17915–17936. See https://www.ncbi.nlm.nih.gov/pubmed/25264954 (accessed 7 February 2019).

94. Agarwal S, Dutta T. 2015 Neuromarketing and consumer neuroscience: Current understanding and the way forward. Decision. 2015 42, 457–462.

95. Neuromarketing Science & Business Association Code of Ethics. See https://www.nmsba.com/buying-neuromarketing/code-of-ethics (accessed 7 February 2019

96. Wadesona A, Nijholtb A, Nama CS. 2015 Artistic brain-computer interfaces: State-of-the-art control mechanisms. Prog. Brain. Res. 2, 70–75. See https://pdfs.semanticscholar.org/6b9a/5a69dbc2dbf5f338f9b7c5dba9d983f96aa5.pdf (accessed 7 February 2019).

97. For example, DNAFit. See https://www.dnafit.com/ (accessed 7 February 2019).

98. International Data Corporation. Worldwide wearables market ticks up 5.5% due to gains in emerging markets, says IDC. 4 September 2018. See https://www.idc.com/getdoc.jsp?containerId=prUS44247418 (accessed 7 February 2019).

99. Neural Interfaces: A public dialogue to inform future development. Ongoing consultation carried out for the Royal Society

100. Romanelli P et al. 2018 A novel neural prosthesis providing long-term electrocorticography recording and cortical stimulation for epilepsy and brain-computer interface. J. Neurosurg. 1, 1–14. (https://doi.org/10.3171/2017.10. JNS17400)

101. Homer ML, Nurmikko AV, Donoghue JP, Hochberg LR. 2013 Sensors and decoding for intracortical brain computer interfaces. Annu. Rev. Biomed. Eng. 15, 383–405

102. Iota Biosciences. 2019 "Neural dust" biotech startup iota completes $15 million funding, expands leadership team. See https://iota.bio/iota-completes-15million-funding-expands-leadership/ (accessed 9 February 2019).

103. Neely RM, Piech DK, Santacruz, SR, Maharbiz MM, Carmena JM. 2018 Recent advances in neural dust: Towards a neural interface platform. Curr. Opin. Neurobiol. 50, 64–71.

104. Seo D et al. 2016 Wireless recording in the peripheral nervous system with ultrasonic neural dust. Neuron 91, 529–539. (https://doi.org/10.1016/j.neuron.2016.06.034)

105. Elon Musk & Neuralink. 2019 An integrated brain-machine interface platform with thousands of channels. 16 July 2019. See https://assets.documentcloud.org/documents/6204648/Neuralink-White-Paper.pdf (accessed 5 August 2019)

106. Howard Hughes Medical Institute 2017. New Silicon Probes Record Activity of Hundreds of Neurons Simultaneously. See: https://www.hhmi.org/news/new-silicon-probes-record-activity-hundreds-neurons-simultaneously (accessed 6 AUgust 2019).

107. Jun JJ et al. 2017 Fully integrated silicon probes for high-density recording of neural activity. Nature 551, 232–236.

108. Neuropixels. 2019 See: https://www.neuropixels.org/about (accessed 5 August 2019).

109. Rajah G, Saber H, Singh R, Rangel-Castilla L. 2018 Endovascular delivery of leads and stentrodes and their applications to deep brain stimulation and neuromodulation: A review. Neurosurg. Focus 45, E19.

110. Rajah G, Saber H, Singh R, Rangel-Castilla L. 2018 Endovascular delivery of leads and stentrodes and their applications to deep brain stimulation and neuromodulation: A review. Neurosurg. Focus 45, E19.

111. Oxley T et al. 2016 Minimally invasive endovascular stent-electrode array for high-fidelity, chronic recordings of cortical neural activity. Nat. Biotechnol. 34, 320–327. See https://www.nature.com/articles/nbt.3428 (accessed 9 February 2019). Also: Wheelchair application explained in interview with Thomas Oxley in: Medagadget. 2017 Stentrode minimally invasive brain-machine interface. See https://www.medgadget.com/2017/02/stentrode-minimally-invasive-brain-machine-interface-interview-dr-thomas-oxley-neurologist-royal-melbourne-hospital.html (accessed 9 February 2019).

112. DARPA. 2016 Minimally invasive "stentrode" shows potential as neural interface for brain. See https://www.darpa.mil/news-events/2016-02-08 (accessed 9 February 2019).

113. Mahmoudi P, Veladi H, Pakdel FG. 2017 Optogenetics, tools and applications in neurobiology. J.Med. Signals. Sens. 7, 71–79. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5437765/ (accessed 9 February 2019).

114. Gefvert B. 2016 Optogenetics: Ten years after - Optogenetics progresses in clinical trials. See https://www.bioopticsworld.com/articles/print/volume-9/issue-9/optogenetics-ten-years-after-optogenetics-progresses-in-clinical-trials.html (accessed 9 February 2019). Also: ClinicalTrials.gov. 2015 updated 2018 RST-001 Phase I/II Trial for advanced retinitis pigmentosa. See https://clinicaltrials.gov/ct2/show/NCT02556736 (accessed 9 February 2019).

115. Lyons MK. 2011. Deep brain stimulation: Current and future clinical applications. Mayo Clin. Proc. 86, 662–672. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3127561/ (accessed 9 February 2019).

116. Milby AH, Halpern CH, Baltuch GH. 2008 Vagus nerve stimulation for epilepsy and depression. Neurotherapeutics 5, 75–85.

117. Childs J, DeLeon J, Nickel E, Kroener S. 2017 Vagus nerve stimulation reduces cocaine seeking and alters plasticity in the extinction network. Learn. Memory 15, 35–42. (https://doi.org/10.1101/lm.043539.116)

118. Health Quality Ontario. 2017 Retinal prosthesis system for advanced retinitis pigmentosa: A health technology assessment update. Ont. Health Technol. Assess. Ser. 17, 1–62. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5692298/ (accessed 9 February 2019).

119. Orlov IV, Stolbkov YK, Gerasimenko YP. 2018 Vestibular prosthetics: Concepts, approaches, results Neurosci. Behav. Physi. 48, 711–720. See https://doi.org/10.1007/s11055-018-0621-5 (accessed 9 February 2019).

120. Tozer A. 2018 The brain scanning helmet about to revolutionise our understanding of the brain. See https://www.technologynetworks.com/neuroscience/articles/the-wearable-brain-scanner-new-meg-helmet-298853 (accessed 7 February 2019).

121. Narayan A. 2009 The fMRI brain scan: A better lie detector? Time. 20 July 2009. See http://content.time.com/time/health/article/0,8599,1911546-1,00.html (accessed 7 February 2019).

122. Lowenberg K. (2008), Neuro-Cola: Neuroscience's ability to measure consumer preference. Stanford Center for Law & the Biosciences Blog. 7 October 2008. See: https://law.stanford.edu/2008/10/07/neuro-cola-neurosciences-ability-to-measure-consumer-preference-part-1/ (accessed 7 February 2019).

123. Davies D et al. 2016. Comparison of near infrared spectroscopy with functional MRI for detection of physiological changes in the brain independent of superficial tissue. Lancet 387 (Special issue S34).

124. Scarapicchia V, Brown C, Mayo C, Gawryluk JR. 2017 Functional magnetic resonance imaging and functional near-infrared spectroscopy: Insights from combined recording studies. Front. Hum. Neurosci 11. (https://doi.org/10.3389/fnhum.2017.00419).

125. Krueger E, Scheeren EM, Nogueira-Neto GN, Button VLSN, Nohama P. 2014 Advances and perspectives of mechanomyography. Revista Brasileira de Engenharia Biomédica 30, 384–401. (https://dx.doi.org/10.1590/1517-3151.0541) Also: Burridge J. 2018 Medical applications of outside the body neural interface technologies. Royal Society Working Paper.

126. Dubljevi V, Saigle V, Racine E. 2014 The rising tide of tDCS in the media and academic literature. Neuron 82, 731–736.

127. Lefaucheur J-P et al. 2017 Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). Int. J. Clin. Neuropsych. 128, 56–92. Also: Bucur M, Papagno C. 2018 A systematic review of noninvasive brain stimulation for post-stroke depression. J. Affect. Disorders 238. (https://doi.org/10.1016/j.jad.2018.05.026).

128. Janicak PG, Dokucu ME. 2015 Transcranial magnetic stimulation for the treatment of major depression. Neuropsych. Dis. Treat. 11, 1549–1560.

129. National Institute for Health and Care Excellence (NICE). 2015 Repetitive transcranial magnetic stimulation for depression, Interventional procedures guidance. See https://www.nice.org.uk/guidance/ipg542/chapter/1-Recommendations (accessed 8 February 2019).

130. rTMS Centre Sheffield. 2018 TMS on the NHS – NHS availability. See https://www.rtmscentre.co.uk/tms-on-the-nhs/ (accessed 9 February 2019).

131. Magstim. 2018 NHS clinical trial could pave the way for new depression treatment. See https://www.magstim.com/2018/11/tms-nhs-clinical-trial/# (accessed 9 February 2019).

132. Simeral JD, Kim SP, Black MJ, Donoghue JP, Hochberg LR. 2011 Neural control of cursor trajectory and click by a human with tetraplegia 1000 days after implant of an intracortical microelectrode array. J. Neural Eng. 8 025027. See https://www.ncbi.nlm.nih.gov/pubmed/21436513 (accessed 7 February 2019).

133. Bacher D et al. 2015 Neural point-and-click communication by a person with incomplete locked-in syndrome. Neurorehab. Neural Re. 29, 462–471. See https://www.ncbi.nlm.nih.gov/pubmed/25385765, (accessed 7 February 2019). Also: Jarosiewicz B et al. 2015 Virtual typing by people with tetraplegia using a self-calibrating intracortical brain-computer interface. Sci. Transl. Med. 11, 313. See https://www.ncbi.nlm.nih.gov/pubmed/26560357 (accessed 7 February 2019). Also: People with tetraplegia gain rapid use of brain-computer interface. See www.sciencedaily.com/releases/2018/01/180124123204.htm (accessed 7 February 2019).

134. Melcer E, Astolfi M, Remaley M, Berenzweig A, Giurgica-Tiron T. 2018 CTRL-Labs: Hand activity estimation and real-time control from neuromuscular signals. Extended Abstracts of the 2018 CHI Conference on Human Factors in Computing Systems See: https://dl.acm.org/citation.cfm?id=3186520&dl=ACM&coll=DL (accessed 7 February 2019).

135. Mai XQ, Luo Ji, Wu JH, Luo YJ. 2004 "Aha!" Effects in a guessing riddle task: An event-related potential study. Hum. Brain Mapp. 22, 261–270. See http://enginpsych.psych.ac.cn/upload/20130107180338802763706.pdf (accessed 7 February 2019).

136. Pais-Vieira M, Lebedev M, Kunicki C, Wang J,Nicolelis MAL. 2013 A brain-to-brain interface for real-time sharing of sensorimotor information. Sci. Rep-UK 3 1319.

137. Jiang L, Stocco A, Losey DM, Abernethy JA, Prat CS, Rao RPN. 2018 BrainNet: A multi-person brain-to-brain interface for direct collaboration between brains. Preprint. Cornell University. See https://www.biorxiv.org/content/biorxiv/early/2018/09/26/425066.full.pdf(accessed 8 February 2019).

138. NHS Healthy Body website. See https://www.nhs.uk/live-well/healthy-body/top-5-causes-of-premature-death/ (accessed 7 February 2019).

139. University of Southampton. 2016 New wireless sleeve to help people recover arm use after stroke. See https://www.southampton.ac.uk/news/2016/01/m-mark.page (accessed 8 February 2019)

140. Adama S, Bogdan M. 2018 Stroke rehabilitation and Parkinson's disease tremor reduction using BCIs combined with FES. Int. J. Priv. Heal. Info. Manag. 6, 20–36. (https://doi.org/10.4018/IJPHIM.2018010102)

141. University of Southampton. 2016 Enabling stroke rehabilitation. See https://www.southampton.ac.uk/news/2016/04/enabling-stroke-rehabilitation.page (accessed 8 February 2019).

142. Helping Hand. The New Yorker. 23 November 2015. See https://www.newyorker.com/magazine/2015/11/23/helping-hand-annals-of-medicine-karen-russell (accessed 8 February 2019).

143. Overstreet E, Hoen M. 2018 Cochlear implants: Considerations regarding the relationship between cognitive load management and outcome. The Hearing Review. See http://www.hearingreview.com/2018/06/cochlear-implants-considerations-regarding-relationship-cognitive-load-management-outcome/ (accessed 7 February 2019).

144. LeMasurier M, Gillespie PG. 2005 Hair-cell mechanotransduction and cochlear amplification. Neuron 48.

145. Bionic ears – let's hear it for cochlear implants. The Guardian. 16 March 2014. See https://www.theguardian.com/science/2014/mar/16/bionic-ears-cochlear-implants-transformed-lives-children (accessed 8 February 2019). Also: ENT doctor. Cochlear implants. See http://entdoctor.org.uk/html/cochlear_implants.html (accessed 8 February 2019).

146. Poitras Tucker B. 1998 Deaf culture, cochlear implants, and elective disability. The Hastings Center report. 28, 6–14. (https://doi.org/10.2307/3528607). Also: Praderio C. 2017 Why some people turned down a 'medical miracle' and decided to stay deaf. See https://www.thisisinsider.com/why-deaf-people-turn-down-cochlear-implants-2016-12(accessed 8 February 2019).

147. Hearing Link factsheet. See https://www.hearinglink.org/your-hearing/about-hearing/facts-about-deafness-hearing-loss/ (accessed 8 February, 2019).

148. Neurable. 2017 A game you can control with your mind. See http://neurable.com/news/game-you-can-control-your-mind (accessed 19 February 2019).

149. Metz R. 2017 Mind-controlled VR game really works. See https://www.technologyreview.com/s/608574/mind-controlled-vr-game-really-works/ (accessed 19 February 2019).

150. Mishra J, Anguera JA, Gazzaley A. 2016 Video games for neuro-cognitive optimization. Neuron 90, 214–218. See https://www.sciencedirect.com/science/article/pii/S0896627316300691 (accessed 8 February 2019).

151. Trimble. Neurable and Trimble partner to explore the use of brain-computer interfaces for the transportation and AEC industries. 3 January 2019. See http://investor.trimble.com/news-releases/news-release-details/neurable-and-trimble-partner-explore-use-brain-computer (accessed 8 February 2019).

152. Ke Y et al. 2019 The effects of transcranial direct current stimulation (tDCS) on working memory training in healthy young adults. Front. Hum. Neurosci. 13, 19. See https://www.frontiersin.org/articles/10.3389/fnhum.2019.00019/full (accessed 11 February 2019).

153. Miler J, Meron D, Baldwin D, Garner M. 2017 The effect of prefrontal transcranial direct current stimulation on attention network function in healthy volunteers. Neuromodulation 21. (https://doi.org/10.1111/ner.12629)

154. Edwards DJ et al. 2017 Transcranial direct current stimulation and sports performance. Front. Hum. Neurosci.11, 243. (https://doi.org/10.3389/fnhum.2017.00243)

155. Thair H, Holloway AL, Newport R,Smith AD. 2017 Transcranial direct current stimulation (tDCS): A beginner's guide for design and implementation. Front. Neurosci. 11, 641. (https://doi.org/doi:10.3389/fnins.2017.00641)

156. The Brain Stimulator. I've never used tDCS before, what types of feelings/sensations should I expect? See https://thebrainstimulator.net/faq/ive-never-used-tdcs-types-feelingssensations-expect/ (accessed 19 February 2019).

157. Nelson J et al. 2016 The effects of transcranial direct current stimulation (tDCS) on multitasking throughput capacity. Front. Hum. Neurosci. 10, 589. (https://doi.org/doi:10.3389/fnhum.2016.00589)

158. Wurzman R, Hamilton RH, Pascual-Leone A, Fox MD. 2016. An open letter concerning do-it-yourself users of transcranial direct current stimulation. Ann. Neurol. 80, 1–4. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6050584/ (accessed 11 February 2019).

159. BrainyQuote.com. See https://www.brainyquote.com/quotes/mary_lou_jepsen_841487 (accessed 8 February 2019).

160. Recode. Full transcript: Mary Lou Jepsen on Too Embarrassed to Ask, live at SXSW. 30 March 2017. See https://www.recode.net/2017/3/30/15130136/transcript-mary-lou-jepsen-one-laptop-per-child-too-embarrassed-to-ask-live-sxsw (accessed 8 February 2019).

161. Elon Musk & Neuralink. 2019 An integrated brain-machine interface platform with thousands of channels. 16 July 2019. See https://assets.documentcloud.org/documents/6204648/Neuralink-White-Paper.pdf(accessed 5 August 2019)

162. Tozer A. 2018 The brain scanning helmet about to revolutionise our understanding of the brain. See https://www.technologynetworks.com/neuroscience/articles/the-wearable-brain-scanner-new-meg-helmet-298853 (accessed 7 February 2019).

163. Elon Musk & Neuralink. 2019 An integrated brain-machine interface platform with thousands of channels. 16 July 2019. See https://assets.documentcloud.org/documents/6204648/Neuralink-White-Paper.pdf(accessed 5 August 2019)

164. Adi R. 2018 I tried the wristband that lets you control computers with your brain. See https://www.theverge.com/2018/6/6/17433516/ctrl-labs-brain-computer-interface-armband-hands-on-preview (accessed 8 February 2018). Quotes Thomas Reardon, CEO, CTRL-Labs: 'There's nothing you can do with a chip in your brain that we can't do better'.

165. Gilja V et al. 2012 A high-performance neural prosthesis enabled by control algorithm design. Nat. Neurosci. 15, 1752–7.

166. Nanalyze. 2018 CTRL-Labs uses AI for brain-computer interface. See https://www.nanalyze.com/2018/06/ctrl-labs-ai-brain-computer-interface/ (accessed 11 February 2019).

167. Furber S, Temple S. 2007 Neural systems engineering. J. R. Soc. Interface 4, 193-206. (https://doi.org/10.1098/rsif.2006.0177)

168. Anikeeva P, 2018 Why you shouldn't upload your brain to a computer. See https://www.youtube.com/watch?v=MZ3Q638aMIA (accessed 19 February 2019).

169. BrainFacts.org. 2017 Your complex brain. See: https://www.brainfacts.org/core-concepts/your-complex-brain (accessed 7 February 2019).

170. Masetti M. 2015 How many stars are there in the Milky Way? See https://asd.gsfc.nasa.gov/blueshift/index.php/2015/07/22/how-many-stars-in-the-milky-way/(accessed 7 February 2019).

171. Adolphs R. 2015 The unsolved problems of neuroscience. Trends Cogn. Sci. 19, 173–175.

172. National Geographic video. 2014 Beautiful 3-D brain scans show every synapse. See https://caltechletters.org/science/brainception (accessed 7 February 2019).

173. Yuste R, Bargmann C. 2017 Toward a global BRAIN initiative. Cell 168. (http://dx.doi.org/10.1016/j.cell.2017.02.023)

174. Human Brain Project. 2017 Overview. See https://www.humanbrainproject.eu/en/science/overview/ (accessed 8 February 2019).

175. Human Brain Project. 2018 The Human Brain Project has entered its third phase. See https://www.humanbrainproject.eu/en/follow-hbp/news/the-human-brain-project-has-entered-its-third-phase/ (accessed 8 February 2019).

176. Yuste R, Bargmann C. 2017 Toward a global BRAIN initiative. Cell 168. (http://dx.doi.org/10.1016/j.cell.2017.02.023)

177. Neurotech Reports. 2018 The Market for Neurotechnology: 2018–2022. See http://www.neurotechreports.com/pages/execsum.html (accessed 8 February 2019).

178. R&D Magazine. 2018 Global R&D funding forecast. See https://digital.rdmag.com/researchanddevelopment/2018_global_r_d_funding_forecast?pg=4#pg4(accessed 8 February 2019).

179. Department of Defense. 2018 Fiscal Year (FY) 2019 budget estimates page 51. See https://www.darpa.mil/attachments/DARPAFY19PresidentsBudgetRequest.pdf (accessed 8 February 2019).

180. Crunchbase. 2019 Neuroscience companies – Leaderboard. See https://www.crunchbase.com/hub/neuroscience-companies/top/org_top_rank_delta_d30_list#section-leaderboard (accessed 19 February 2019).

181. Angel. 2019 Neuroscience startups. See https://angel.co/neuroscience (accessed 19 February 2019).

182. Johnson B. 2018. See https://medium.com/future-literacy/hi-i-am-bryan-johnson-5d833d49e70e (accessed 8 February 2019).

183. Crunchbase. 2019. Neuralink. See https://www.crunchbase.com/organization/neuralink#section-overview (accessed 1 July 2019).

184. Neuralink. See https://neuralink.com/ (accessed 8 February 2019).

185. GSK. 2016 GSK and Verily to establish Galvani Bioelectronics – a new company dedicated to the development of bioelectronic medicines. 1 August 2016. See https://www.gsk.com/en-gb/media/press-releases/gsk-and-verily-to-establish-galvani-bioelectronics-a-new-company-dedicated-to-the-development-of-bioelectronic-medicines/ (accessed 8 February 2019).

186. Galvani. 2016 About us. See https://www.galvani.bio/ (accessed 8 February 2019).

187. Moses DA,Leonard MK, Makin, JG, Chang, EF. 2019 Real-time decoding of question-and-answer speech dialogue using human cortical activity. Nature Communications 10 Article 3096.

188. Facebook. 2019 Imagining a new interface: Hands-free communication without saying a word. See: https://tech.fb.com/imagining-a-new-interface-hands-free-communication-without-saying-a-word/

189. The Guardian. 2019 Elon Musk unveils plan to build mind-reading implants 17 July 2019. See https://www.theguardian.com/technology/2019/jul/17/elon-musk-neuralink-brain-implants-mind-reading-artificial-intelligence (accessed 5 August 2019).

190. Urban T. 2017 Neuralink and the brain's magical future. Wait But Why. 20 April 2017. See https://waitbutwhy.com/2017/04/neuralink.html (accessed 7 February 2019). 'If you have two brain interfaces, you could actually do an uncompressed direct conceptual communication with another person.'

191. QS Top Universities 2019 The World's Top 100 Universities. See: https://www.topuniversities.com/student-info/choosing-university/worlds-top-100-universities (accessed 1 July 2019)

192. University College London. Brain Sciences. See https://www.ucl.ac.uk/brain-sciences/research (accessed 7 February 2019).

193. QS Top Universities 2019 Subject rankings. See: https://www.topuniversities.com/university-rankings/university-subject-rankings/2018/engineering-electrical-electronic (accessed 1 July 2019)

194. UK Government Office for Life Sciences. 2018. Bioscience and Health Technology Sector Statistics 2018. See https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/798583/Bioscience_and_Health_technology_Sector_2018.pdf (accessed 3 July 2019).

195. Department for Exiting the European Union 2017. Sectoral Analysis – Life Sciences Sector, 21 December 2017 (See: https://www.parliament.uk/documents/commons-committees/Exiting-the-European-Union/17-19/Sectoral%20Analyses/21-Life-Sciences-Report.pdf, accessed 26 June 2019).

196. Creative Industries Federation 2019 Statistics. See: https://www.creativeindustriesfederation.com/statistics (accessed 1 July 2019).

197. UKIE press release 2019 UK consumer spend on games grows 10% to a record £5.7bn in 2018. 2 April 2019 See: https://ukie.org.uk/news/2019/04/uk-consumer-spend-games-grows-10-record-%C2%A357bn-2018 (accessed 1 July 2019).

198. TIGA press release 2019 TIGA calls on Government to introduce further productivity measures. 5 June 2019 See https://tiga.org/news/tiga-calls-on-government-to-introduce-further-productivity-measures (accessed 1 July 2019)

199. UKIE 2019 Games Map. See: https://gamesmap.uk/#/map (accessed 1 July 2019)

200. Health Data Research UK 2019 Health Data Research UK is uniting the UK's health data to enable discoveries that improve people's lives. See https://www.hdruk.ac.uk/about/ (accessed 1 July 2019)

201. OECD 2018 OECD Regulatory Policy Outlook 2018. See https://read.oecd-ilibrary.org/governance/oecd-regulatory-policy-outlook-2018_9789264303072-en#page241 (accessed 1 July 2019)

202. HM Government 2019 Regulation for the Fourth Industrial Revolution. See: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/807792/regulation-fourth-industrial-strategy-white-paper-web.pdf (accessed 1 July 2019)

203. Zhou AJ et al. 2017 WAND: A 128-channel, closed-loop, wireless artifact-free neuromodulation device. Nat. Biomed. Eng. 3, 15–26. See https://www.nature.com/articles/s41551-018-0323-x and https://arxiv.org/ftp/arxiv/papers/1708/1708.00556.pdf (accessed 7 February 2019).

204. Samotus O, Parrent A, Jog, M. 2018 Spinal cord stimulation therapy for gait dysfunction in advanced parkinson's disease patients. Mov. Disord. 33, 783-792. See: https://www.ncbi.nlm.nih.gov/pubmed/29442369 (accessed 4 July 2019).

205. World Health Organisation. 2018 Depression. See https://www.who.int/news-room/fact-sheets/detail/depression (accessed 7 February 2019).

206. Hearables will monitor your brain and body to augment your life. IEEE Spectr.. 1 May 2019. See https://spectrum.ieee.org/consumer-electronics/audiovideo/hearables-will-monitor-your-brain-and-body-to-augment-your-life (accessed 3 July 2019).

207. The Guardian. 2019 Elon Musk unveils plan to build mind-reading implants 17 July 2019. See https://www.theguardian.com/technology/2019/jul/17/elon-musk-neuralink-brain-implants-mind-reading-artificial-intelligence (accessed 5 August 2019).

208. INSIGHTEC. 2018 INSIGHTEC for neurosurgery. See: https://www.insightec.com/clinical/neurosurgery (accessed 1 July 2019).

209. Edelman BJ, Meng J, Suma D, Zurn C, Nagarajan E, Baxter BS, Cline CC, He B. 2019 Noninvasive neuroimaging enhances continuous neural tracking for robotic device control. Sci. Robot. 4, 31. See https://robotics.sciencemag.org/content/4/31/eaaw6844 (accessed 1 July 2019).

210. For example, the 'Beddit' sleep monitor. See https://www.beddit.com/ (accessed 7 February 2019).

211. For example, Ebb. See https://ebbsleep.com/learn-about-ebb/ (accessed 7 February 2019).

212. University of Alabama at Birmingham. 2018 Clinical trial record on effect of deep brain stimulation (DBS) on sleep architecture in patients with movement disorders. See https://clinicaltrials.gov/ct2/show/NCT01169324 (accessed 7 February 2019).

213. MIT News. 2017 Brain controlled robots. See http://news.mit.edu/2017/brain-controlled-robots-0306 (accessed 7 February 2019).

214. Hatsopoulos NG, Donoghue JP. 2009 The science of neural interface systems. Ann. Rev. Neurosci. 32, 249–266. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2921719/ (accessed 7 February 2019).

215. Fast Company. 2018 This neural operating system lets paralyzed, voiceless patients communicate. See https://www.fastcompany.com/40559440/this-neural-operating-system-lets-paralyzed-voiceless-patients-communicate (accessed 19 February 2019). Also: Nuro. 2019. See https://nuro.ca/#products (accessed 19 February 2019).

216. Elon Musk & Neuralink. 2019 An integrated brain-machine interface platform with thousands of channels. 16 July 2019. See https://assets.documentcloud.org/documents/6204648/Neuralink-White-Paper.pdf(accessed 5 August 2019)

217. Jun JJ et al. 2017 Fully integrated silicon probes for high-density recording of neural activity. Nature 551, 232–236. See: https://www.nature.com/articles/nature24636 (accessed 6 August 2019)

218. National Institute of Mental Health (US). 2016 Brain stimulation therapies. See https://www.nimh.nih.gov/health/topics/brain-stimulation-therapies/brain-stimulation-therapies.shtml (accessed 7 February 2019).

219. Alzheimer's Society. 2019 Facts for the media. See https://www.alzheimers.org.uk/about-us/news-and-media/facts-media (accessed 7 February 2019).

220. Aldehri M, Temel Y, Alnaami I, Jahanshahi A, Hescham S. 2018 Deep brain stimulation for Alzheimer's disease: An update. Surg. Neurol. Int. 9, 58. See https://www.ncbi.nlm.nih.gov/pubmed/29576909 (accessed 7 February 2019).

221. Lv Q, Du A, Wei W, Li Y, Liu G, Wang XP. 2018 Deep brain stimulation: A potential treatment for dementia in Alzheimer's disease (AD) and Parkinson's disease dementia (PDD). Front. Neurosci. 12, 360. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5986883/ (accessed 8 February 2019).

222. BIOS press release 2018 BIOS announces ground-breaking AI-led research results. See: https://www.bios.health/groundbreakingresearchresults (accessed 1 July 2019)

223. Parc de Salut - Hospital del Mar. 2018 News release: Hospital del Mar successfully uses deep brain stimulation to treat 4 patients with anorexia nervosa. See https://www.parcdesalutmar.cat/en/noticies/view.php?ID=3(accessed 7 February 2019).

224. Forget the Facebook leak: China is mining data directly from workers' brains on an industrial scale. South China Morning Post. 29 April 2018. See https://www.scmp.com/news/china/society/article/2143899/forget-facebook-leak-china-mining-data-directly-workers-brains (accessed 7 February 2019). Also: 'Mind-reading' tech being used to monitor Chinese workers' emotions. The Telegraph. 30 April 2018. See https://www.telegraph.co.uk/news/2018/04/30/mind-reading-tech-used-monitor-chinese-workers-emotions/ (accessed 19 February 2019).

225. Jiang L, Stocco A, Losey DM, Abernethy JA, Prat CS, Rao RPN. 2018 BrainNet: A multi-person brain-to-brain interface for direct collaboration between brains. Preprint. Cornell University. See https://www.biorxiv.org/content/biorxiv/early/2018/09/26/425066.full.pdf (accessed 8 February 2019).

226. Burke JF, Merkow MB, Jacobs J, Kahana MJ, Zaghloul KA. 2015 Brain computer interface to enhance episodic memory in human participants Front. Hum. Neurosci. 8. See https://www.frontiersin.org/articles/10.3389/fnhum.2014.01055/full (accessed 7 February 2019). Also: Hampson RE et al. 2018 Developing a hippocampal neural prosthetic to facilitate human memory encoding and recall. J. Neural Eng. 15. (https://doi.org/10.1088/1741-2552/aaaed7)

227. Ramirez S et al. 2013 Creating a false memory in the hippocampus. Science 26, 387–391.

228. Yoo S-S, Kim H, Filandrianos E, Taghados SJ, Park S. 2013 Non-invasive brain-to-brain interface (BBI): Establishing functional links between two brains. PLoS ONE 8, e60410. (https://doi.org/10.1371/journal.pone.0060410)

229. DiGiovanna J, Mahmoudi B, Fortes J, Principe JC, Sanchez JC. 2009 Coadaptive brain–machine interface via reinforcement learning. IEEE T. Bio-med. Eng. 56, 54–64.

230. Stealth sharks to patrol the high seas. New Scientist. 1 March 2006. See https://www.newscientist.com/article/mg18925416-300-stealth-sharks-to-patrol-the-high-seas/ (accessed 7 February 2019).Also: Sharks are Pentagon's latest spy recruits. Daily Telegraph. 2 March 2006. See https://www.telegraph.co.uk/news/1511918/Sharks-are-Pentagons-latest-spy-recruits.html (accessed 7 February 2019).

231. Hirotaka S, Maharbiz M. 2010 Recent developments in the remote radio control of insect flight. Front. Neurosci. 4, 1999. See https://www.frontiersin.org/article/10.3389/fnins.2010.00199 (accessed 7 February 2019).

232. Yang J, Huai R, Wang H, Lv C, Su X. 2015 A robo-pigeon based on an innovative multi-mode telestimulation system. Biomed. Mater. Eng. 26, S357–S363. See https://pdfs.semanticscholar.org/1d6d/cbb4e6de21589725ad066e7673b87be97086.pdf (accessed 7 February 2019).

233. DARPA 60 years 1958–2018. See https://www.darpa.mil/attachments/DARAPA60_publication-no-ads.pdf (accessed 11 February 2019).

234. World Health Organisation. 2001 Mental disorders affect one in four people. See https://www.who.int/whr/2001/media_centre/press_release/en/ (accessed 8 February 2019).

235. World Health Organisation. 2018 Depression. See https://www.who.int/news-room/fact-sheets/detail/depression (accessed 8 July 2019).

236. Ionescu DF, Rosenbaum JF, Alpert JE. 2015 Pharmacological approaches to the challenge of treatment-resistant depression. Dialogues. Clin. Neurosci. 17, 111–126. See https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4518696/ (accessed 19 February 2019).

237. Delaloye S, Holtzheimer PE. 2014 Deep brain stimulation in the treatment of depression. Dialogues. Clin. Neurosci. 16, 83-91.

238. Bewernick BH et al. 2010 Nucleus accumbens deep brain stimulation decreases ratings of depression and anxiety in treatment-resistant depression. Biol. Psychiat. 67, 110–116. See https://www.ncbi.nlm.nih.gov/pubmed/19914605 (accessed 8 February 2019).

239. George MS et al. 2000 A controlled trial of daily left prefrontal cortex TMS for treating depression. Biol. Psychiat. 48, 962–970. See https://www.ncbi.nlm.nih.gov/pubmed/11082469 (accessed 8 February 2019).

240. National Institute for Health and Care Excellence (NICE). 2015 Repetitive transcranial magnetic stimulation for depression, Interventional procedures guidance. See https://www.nice.org.uk/guidance/ipg542/chapter/1-Recommendations (accessed 8 February 2019).

241. Depressed man has been 'cured' by revolutionary treatment - and it doesn't involve drugs. Daily Mirror. 7 May 2017. See https://www.mirror.co.uk/news/real-life-stories/depressed-man-been-cured-revolutionary-10363105 (accessed 8 February 2019).

242. Cristancho P, Akkineni K, Constantino JN, Carter AR, O'Reardon JP. 2014. Transcranial magnetic stimulation in a 15-year-old patient with autism and comorbid depression. J. ECT 30, e46–47. (https://doi.org/10.1097/YCT.0000000000000156) Also: A brain therapy changed my life. It raises profound questions for the future. The Spectator. 6 July 2017. See https://health.spectator.co.uk/a-brain-therapy-changed-my-life-it-raises-profound-questions-for-the-future/ (accessed 8 February 2019).

243. Welsh firm Magstim in £2m trial to tackle depression. BBC. 23 November 2019. See https://www.bbc.co.uk/news/uk-wales-46309114 (accessed 19 February 2019). Also: Smart TMS website RTMS: Repetitive transcranial magnetic stimulation treatment. See https://www.smarttms.co.uk/tms-treatment/nhs-availability/ (accessed 8 February 2019).

244. National Institute for Health Research (NIHR). 2018 BRIGhTMIND: Brain imaging guided transcranial magnetic stimulation in depression. See https://ukctg.nihr.ac.uk/trials/trial-details/trial-details?trialId=14281, accessed 8 April 2019).

245. National Institute for Health and Care Excellence (NICE). 2009 Vagus nerve stimulation for treatment-resistant depression Interventional procedures guidance. See https://www.nice.org.uk/guidance/ipg330/chapter/1-Guidance (accessed 8 February 2019).

246. Medical News Today. 2018 Severe depression: Vagus nerve stimulator improves lives. See https://www.medicalnewstoday.com/articles/322854.php (accessed 8 February 2019).

247. Singh A, Kar SK. 2017 How electroconvulsive therapy works: Understanding the neurobiological mechanisms. Clin. Psychopharm. Neu. 15, 210–221. Also: MIND. 2016 Electroconvulsive therapy. See https://www.mind.org.uk/information-support/drugs-and-treatments/electroconvulsive-therapy-ect/#.XEBiWVz7Q2w (accessed 8 February 2019).

248. National Human Genome Research Institute. 2018 The Ethical, Legal and Social Implications (ELSI) research program. See https://www.genome.gov/10001618/the-elsi-research-program/ (accessed 8 February 2019).

249. Human Fertilisation and Embryology Authority (HFEA). 2018 IVF regulation: Ensuring safe and ethical treatment. See https://www.hfea.gov.uk/about-us/news-and-press-releases/2018-news-and-press-releases/ivf-regulation-ensuring-safe-and-ethical-treatment/ (accessed 8 February 2019).

250. Engineering and Physical Sciences Research Council (EPSRC). 2019 Framework for responsible innovation. See https://epsrc.ukri.org/index.cfm/research/framework/ (accessed 8 February 2019).

251. Yuste R et al. 2017 Four ethical priorities for neurotechnologies and AI. Nature 551, 159–163. See https://www.nature.com/news/four-ethical-priorities-for-neurotechnologies-and-ai-1.22960 (accessed 8 February 2019).

252. Poitras Tucker B. 1998 Deaf culture, cochlear implants, and elective disability. The Hastings Center report. 28, 6-14. (https://doi.org/10.2307/3528607) Also: Insider. 2017 See https://www.thisisinsider.com/why-deaf-people-turn-down-cochlear-implants-2016-12 (accessed 8 February 2019).

253. Yuste R et al. 2017 Four ethical priorities for neurotechnologies and AI. Nature 551, 159–163. See https://www.nature.com/news/four-ethical-priorities-for-neurotechnologies-and-ai-1.22960 (accessed 8 February 2019).

254. Pitchbook. 2019 CTRL-Labs. See https://pitchbook.com/profiles/company/164078-83 (accessed 8 February 2019). Also: CNBC. 2018 Top VC deals: Google and Amazon both backed CTRL Labs, and Chinese AI firm SenseTime raised $620 million. See https://www.cnbc.com/2018/06/01/google-and-amazon-back-ctrl-labs-sensetime-raises-620-million.html (accessed 8 February 2019).

255. Business Insider. 2019 A group of Mark Zuckerberg-funded researchers is testing implantable brain devices as part of a $5 billion quest to end disease. See https://www.businessinsider.com/chan-zuckerberg-research-implantable-brain-device-primates-2018-12?r=US&IR=T (accessed 8 February

256. Bushey R. 2017 Chan Zuckerberg Biohub reveal recipients of $50m grant for ambitious disease research efforts. R&D Magazine. 15 February 2017. See https://www.rdmag.com/article/2017/02/chan-zuckerberg-biohub-reveal-recipients-50m-grant-ambitious-disease-research-efforts (accessed 8 February 2019).

257. Chan P. 2019 "Luck is not a national strategy. We need to build strategies that take luck out of the equation for every person." See https://chanzuckerberg.com/about/our-approach/ (accessed 8 February 2019).

258. Quartz. 2017 Survey: Facebook is the big tech company that people trust least. See https://qz.com/1085588/survey-facebook-is-the-big-tech-company-that-people-trust-least/ (accessed 8 February 2019).

259. Science Daily. 2010 Psychological research conducted in 'WEIRD' nations may not apply to global populations. See https://www.sciencedaily.com/releases/2010/06/100630132850.htm (accessed 8 February 2019).

260. Krauss A. 2018 Why all randomised controlled trials produce biased results. Ann. Med. 50, 312–322. See https://www.tandfonline.com/doi/full/10.1080/07853890.2018.1453233 (accessed 8 February 2019).

261. Pollitzer E. 2012 From ideas to markets: The gender factor. Prepared for the November 2012 Gender Summit, Brussels. See https://www.express.co.uk/news/uk/978731/women-car-crash-dummies-gender-health-research (accessed 8 February 2019).

262. Buolamwini J, Gebru T. 2018 Gender Shades: Intersectional accuracy disparities in commercial gender classification. Proceedings of the 1st Conference on Fairness, Accountability and Transparency, in Proceedings of Machine Learning Research 81, 77–91. See http://proceedings.mlr.press/v81/buolamwini18a/buolamwini18a.pdf (accessed 8 February 2019). Also: Discriminating algorithms: 5 times AI showed prejudice. New Scientist. 12 April 2018 updated 27 April 2018. See https://www.newscientist.com/article/2166207-discriminating-algorithms-5-times-ai-showed-prejudice (accessed 8 February 2019).

263. Wareable. 2017 Wearables still haven't solved the problems of skin science, but new ideas are coming. See https://www.wareable.com/health-and-wellbeing/skin-science-complex-wearables-4441 (accessed 8 February 2019).

264. MarketWatch. 2015 Skin tone not a new issue for heart monitors. See https://www.marketwatch.com/story/skin-tone-not-a-new-issue-for-heart-monitors-2015-04-30 (accessed 14 February 2019).

265. Carstensen J. 2018. Brain-computer interfaces raise fresh AI privacy and bias concerns. See https://www.all-turtles.com/2018/09/10/brain-computer-interfaces-raise-fresh-ai-privacy-and-bias-concerns/ (accessed 8 February 2019).

266. Akbari H, Khalighinejad B, Herrero JL, Mehta AD, Mesgarani N. 2019 Towards reconstructing intelligible speech from the human auditory cortex Sci. Rep. 9, 874. (https://doi.org/10.1038/s41598-018-37359-z)

267. Anumanchipalli G, Chartier, J, Chang, E F 2019 Speech synthesis from neural decoding of spoken sentences. Nature. 568, 493-498. (See: https://www.nature.com/articles/s41586-019-1119-1, accessed 1 July 2019)

268. Shen G, Horikawa T, Majima K, Kamitani Y. 2019 Deep image reconstruction from human brain activity. PLoS Comput. Biol. 15, e1006633. (https://doi.org/10.1371/journal.pcbi.1006633)

269. Huth AG, Lee T, Nishimoto S, Bilenko NY, Vu AT, Gallant JL. 2016 Decoding the semantic content of natural movies from human brain activity. Front. Syst. Neurosci. 10. (https://doi.org/10.3389/fnsys.2016.00081)

270. Jiang L, Stocco A, Losey DM, Abernethy JA, Prat CS, Rao RPN. 2018 BrainNet: A multi-person brain-to-brain interface for direct collaboration between brains. Preprint. Cornell University. See https://www.biorxiv.org/content/biorxiv/early/2018/09/26/425066.full.pdf (accessed 8 February 2019).

271. Pais-Vieira M, Lebedev M, Kunicki C, Wang J, Nicolelis MAL. 2013 A brain-to-brain interface for real-time sharing of sensorimotor information. Sci. Rep-UK 3 1319.

272. Li M, Xu H, Liu X, Lu S. 2018. Emotion recognition from multichannel EEG signals using K-nearest neighbor classification. Technol. Health Care 26, 509–519.

273. Dutta T. 2015 Neuromarketing and consumer neuroscience: Current understanding and the way forward. Decision 42, 457–462.

274. The Royal Society. 2019 Protecting privacy in practice: The current use, development and limits of Privacy Enhancing Technologies in data analysis. See https://royalsociety.org/topics-policy/projects/privacy-enhancing-technologies/ (accessed 3 March 2019).

275. Annual Report of the Government Chief Scientific Adviser. 2014. Innovation: Managing risk, not avoiding it. See https://www.gov.uk/government/publications/innovation-managing-risk-not-avoiding-it (accessed 8 February 2019).

276. National Human Genome Research Institute. 2018 The Ethical, Legal and Social Implications (ELSI) research program. See https://www.genome.gov/10001618/the-elsi-research-program/ (accessed 8 February 2019).

277. National Institute for Health and Care Excellence (NICE). 2017 Mollii suit for spasticity - Medtech innovation briefing, 28 March 2017. See https://www.nice.org.uk/advice/mib100/resources/mollii-suit-for-spasticity-pdf-2285963207581381 (accessed 8 February 2019).

278. National Institute for Health and Care Excellence (NICE) 2017 Mollii suit for spasticity - Medtech innovation briefing, 28 March 2017. (See: https://www.nice.org.uk/advice/mib100/resources/mollii-suit-for-spasticity-pdf-2285963207581381, accessed 8 February 2019).

279. Remotion. 2018 Video. See http://www.remotion.co.uk/videos (accessed 8 February 2019).

280. Burridge J. 2018 Medical applications of outside the body neural interface technologies. Royal Society Working Paper.

281. National Institute for Health and Care Excellence (NICE). 2017 Mollii suit for spasticity - Medtech innovation briefing, 28 March 2017. See https://www.nice.org.uk/advice/mib100/resources/mollii-suit-for-spasticity-pdf-2285963207581381 (accessed 8 February 2019).

282. UK Government. 2018. Business Secretary hosts first cross-government working group on future regulation, See https://www.gov.uk/government/news/business-secretary-hosts-first-cross-government-working-group-on-future-regulation (accessed 8 February 2019).

283. NESTA. 2019 Anticipatory regulation. See https://www.nesta.org.uk/feature/innovation-methods/anticipatory-regulation/ (accessed 8 February 2019).

284. Wellcome. 2019 A blueprint for the oversight of emerging science and technologies. (See: https://wellcome.ac.uk/reports/blueprint-oversight-emerging-science-and-technologies, accessed 29 March 2019).

285. Department for Business, Energy and Industrial Strategy (BEIS). 2019 Regulation for the Fourth Industrial Revolution. (See: https://www.gov.uk/government/publications/regulation-for-the-fourth-industrial-revolution, accessed 1 July 2019).

286. Department for Business, Energy and Industrial Strategy (BEIS). 2019 UK and World Economic Forum to lead regulation revolution to foster industries of the future. (See: https://www.gov.uk/government/news/uk-and-world-economic-forum-to-lead-regulation-revolution-to-foster-industries-of-the-future, accessed 8 July 2019).

287. US Food & Drug Administration (FDA). 2019 Implanted brain-computer interface (BCI) devices for patients with paralysis or amputation - Non-clinical testing and clinical considerations - Draft guidance for industry and food and drug administration staff, 25 February 2019. (See: https://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM631786.pdf, accessed 8 February 2019).

288. National Institute for Health and Care Excellence (NICE). 2019 Evidence Standards Framework for Digital Health Technologies. See: https://www.nice.org.uk/Media/Default/About/what-we-do/our-programmes/evidence-standards-framework/digital-evidence-standards-framework.pdf (accessed 29 March 2019).

289. Department for Health and Social Care (DHSC). 2018 Code of conduct for data-driven health and care technology. See: https://www.gov.uk/government/publications/code-of-conduct-for-data-driven-health-and-care-technology (accessed 29 March 2019).

290. Yuste R et al. 2017 Four ethical priorities for neurotechnologies and AI. Nature 551, 159–163. See https://www.nature.com/news/four-ethical-priorities-for-neurotechnologies-and-ai-1.22960(accessed 8 February 2019).

The Royal Society is a self-governing Fellowship of many of the world's most distinguished scientists drawn from all areas of science, engineering, and medicine. The Society's fundamental purpose, as it has been since its foundation in 1660, is to recognise, promote, and support excellence in science and to encourage the development and use of science for the benefit of humanity.

The Society's strategic priorities emphasise its commitment to the highest quality science, to curiosity-driven research, and to the development and use of science for the benefit of society. These priorities are:

• Promoting excellence in science

• Supporting international scientific collaboration

• Demonstrating the importance of science to everyone

For further information
The Royal Society
6 – 9 Carlton House Terrace
London SW1Y 5AG

T +44 20 7451 2500
E science.policy@royalsociety.org
W royalsociety.org

Registered Charity No 207043

9 781782 524205

ISBN: 978-1-78252-420-5
Issued: September 2019 DES6094