A transformative roadmap for neurotechnology in the UK

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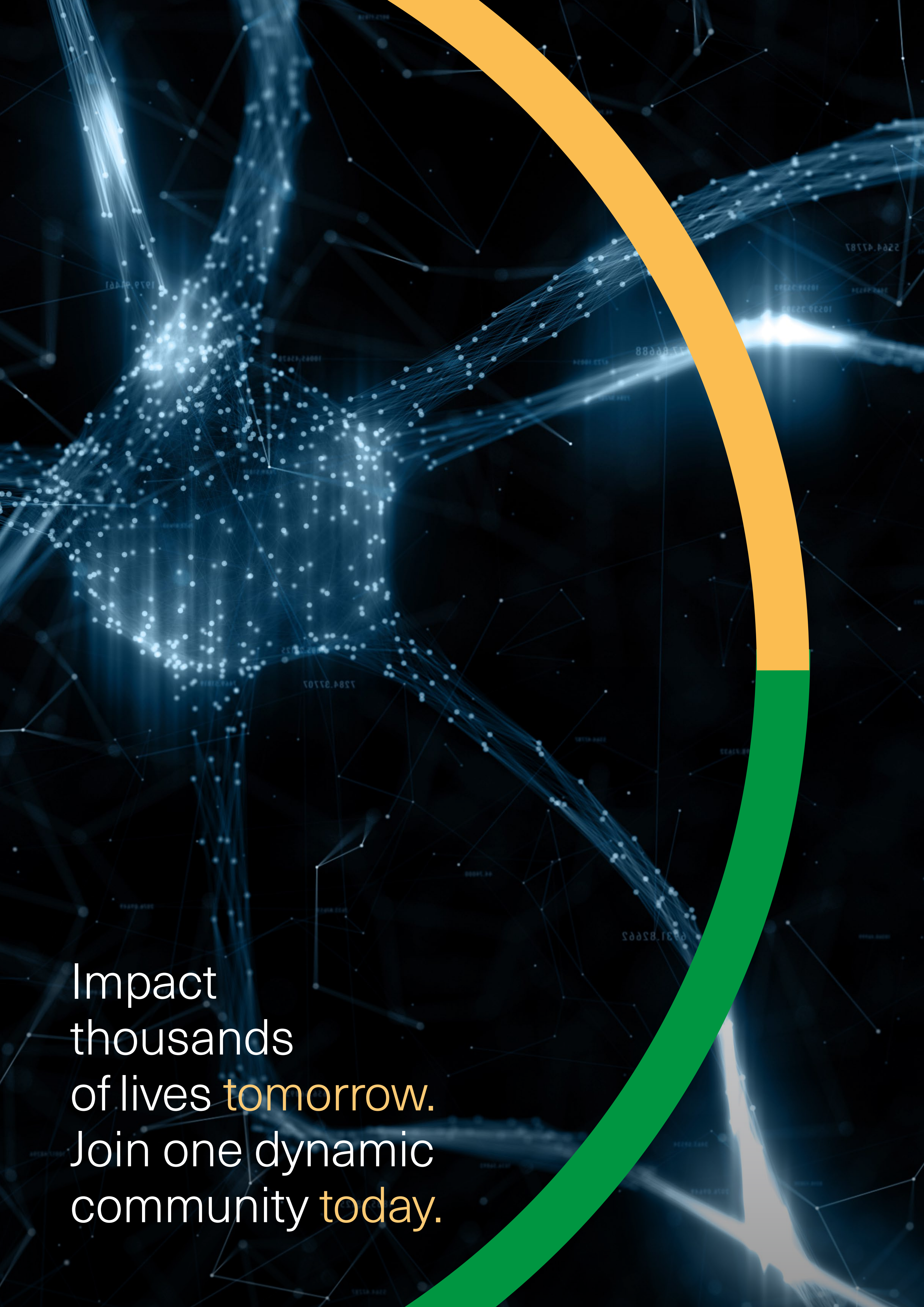
ktn Innovation Networks

Neurotechnology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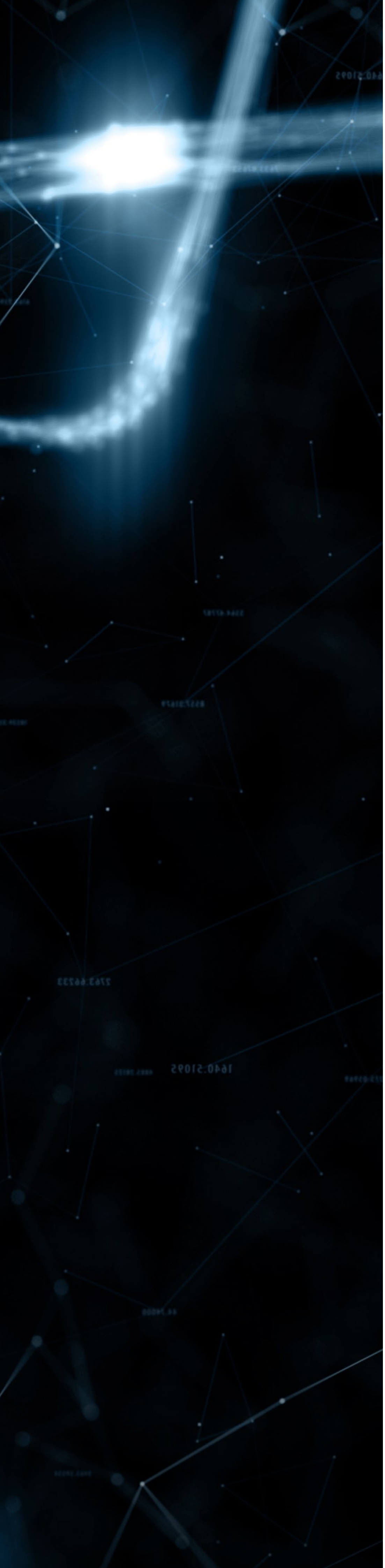

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Foreword

Dr Lothar Krinke, CEO, Magstim Group

The development of cost-effective treatments for disorders of the brain and nervous system is one of the most important challenges of the first half of this century. The societal cost of neurodegenerative and psychiatric disease is already hugely significant and is increasing rapidly as our population ages. At the same time, advances in technology from diverse fields such as imaging, microelectronics, AI and neuroscience, make it feasible to better understand the fundamentals of brain physiology and etiology at an unprecedented scale and precision. This is the gateway to next-generation device-based neurotechnology therapies.

The rapid deployment of government-industry partnerships to authorize, develop and distribute COVID-19 vaccines has proven the value of a focused collaboration on a massive scale.

This transformative roadmap for neurotechnology in the UK is a unique proposal that will ensure that the UK accelerates its leadership position in this field. It is a call to action directed at government, universities, and industry to establish collaborative, yet pre-competitive, mechanisms that will accelerate development of a meaningful and highly effective neurotechnology.

The roadmap provides a focus for funding research and its translation and proposes actions to lower real and perceived barriers to progress in neurotechnology. The proposals in it call for the development of specialised researchers and the education of a skilled workforce and the formation of an accelerator that will ensure that new concepts can be rapidly tested and developed.

A particularly valuable and unique concept is the proposal to shape UK regulatory processes for rapid and safe testing of human neurotechnology devices. This will make the UK particularly attractive for new and established companies.

The document proposes the development of a framework to ensure ethics is at the forefront of developments in the field of brain device interfaces - promoting achievable goals for this emerging technology. Yet, readers will be inspired by the opportunity to transform the neurotechnology landscape and will be convinced that the roadmap is ambitious, but realistic and practical.

As the CEO of a UK based global neurotechnology company, I urge all parties to endorse and support the implementation of the roadmap.

Executive Summary

Neurotechnology, defined in this document as “the application of engineering principles to the understanding, engagement, and repair of the human nervous system,” is undergoing rapid advancements. A number of key research areas show progress; from neuroscience, through computing power to AI, imaging, materials technology, sensors and manufacturing. It is already used in a variety of clinical settings, for example, to restore hearing to profoundly deaf patients (cochlear implants), treat movement disorders such as Parkinson’s (deep brain stimulation), alleviate depression (transcranial magnetic stimulation), and is at the cusp of restoring vision to sufferers of degenerative retinal conditions (retinal prostheses). More broadly, techniques such as virtual reality are being employed to treat social anxiety.

Recent developments are increasing the sophistication and capability of neurotechnology devices, opening up the opportunity to address many more neurological conditions that have proven resistant to pharmaceutical or therapeutic interventions. In order to improve the quality of life for this patient cohort, which is only increasing due to the UK’s aging population, we propose a strategic investment to enhance our synthesis of engineering science and the nervous system through the creation of centres of research and translation excellence. To ensure these novel treatments successfully translate and become available to clinicians and patients, this initiative needs to occur in parallel with a co-ordinated investment in, and coordination with, the business community.

This clinical and commercial opportunity has been recognised internationally, with significant public and private investment being made. The US government alone has invested $1.8bn since 2013 and other nations have since joined this global effort.

Our understanding of how the brain functions, and how technology can interface with it, has progressed dramatically, with significant clinical impact and commercial opportunity rapidly emerging.

The UK has already established the beginnings of an exciting neurotechnology community, comprising high-tech SMEs, University spin-outs and leading academic groupings. A major investment in this area will allow the UK to build upon its existing strengths and take an international lead in neurotechnology; growing a major medical technology, championing its ethical adoption and becoming home to the next generation of technology giants.

Key recommendations

Over the last 2 years, KTN has conducted a broad consultation with key stakeholders associated with neurotechnology research and innovation through in-depth workshops, an online survey and many 1-1 meetings. In this paper we set out a roadmap for a UK Neurotechnology Programme with three underpinning recommendations, which we believe will transform UK neurotechnology research, establish a strong national ecosystem and industrial sector, improve the quality of life for patients, reduce pressure on the NHS and better prepare the UK for the challenges of an ageing population. These are:

Acceleration of the UK neurotechnology sector

We recommend a dual approach, with the aim of taking first-in-human research through to business adoption. Firstly, investment in research and translation capability and coordination is required to bring together the broad scientific community needed to take on this challenge and help drive the discovery science through to commercialisation. Secondly, the formation of a Neurotechnology Accelerator, which will harness and grow existing infrastructure to transform the UK's cutting edge, but nascent, neurotechnology manufacturing capabilities. It will provide vital commercialisation support and act as the voice of the community and a conduit to the regulator.

Ethics, regulations, data, privacy and security

A new approach to regulations creating greater flexibility in the testing and adoption of emerging neurotechnologies, while ensuring their ethical implementation and exploitation. This will help set standards and regulations enabling UK businesses to operate at the highest ethical levels and lead in the commercial development. We recommend that a set of international protocols and standards for the use of neurotechnology devices, and especially brain machine interfaces, be developed and adopted, utilising a "systems thinking" approach. These must be secure by default (cyber and neural), rather than just by design, to prevent the issues currently seen with Internet of Things devices.

People/talent

Preparing the next generation of graduates, technical staff and apprentices is a vital component of this emerging field. We recommend a series of investments to support the multi-disciplinary training requirements needed across the sector. This includes fellowships for clinicians to work on device development, enhanced support for entrepreneurs to spin-out companies and schemes to support early-career researchers so that they can develop into future leaders. This would be supplemented by a Doctoral Training Centre in neurotechnology, which builds upon the success of the Imperial College centre.

Why focus on neurotechnology?

Neurotechnology plays a central role in unlocking the secrets of how the human brain works – a scientific endeavour that is as important as the development of the internet or decoding the human genome. This enhanced understanding is critical, not only to the continued development of the next generation of neural interface technologies, but also to the development of more targeted pharmacological approaches and clinical interventions for neurological conditions.

There is currently a global effort to accelerate this development, spurred on by tremendous advances in diverse fields such as neuroscience, electronics, computing and system integration. Without a similar focussed UK effort, the potential benefits arising from our long-term research investments and excellence and the rapidly developing but currently small, high-tech industrial base, are at risk of being lost to other countries.

Below, we outline some of the principal societal benefits that will result from a determined push in neurotechnology.

Improving healthcare and quality of life
Millions of people around the world suffer from often debilitating and otherwise intractable neurological conditions, including neurodegenerative diseases, brain injuries/damage and mental health disorders. For example, psychosis, severe depression and bipolar disorder cause an enormous burden of illness, on average reducing healthy life by 12 years, working life by 14 years, and life expectancy by 9 years[1].

The combined cost of care globally, especially for dementia, mood disorders, and anxiety disorders, amounts to hundreds of billions of pounds annually. In Europe, mental illnesses (e.g., depression, anxiety disorders, and alcohol and other drug use disorders) alone affect more than one in six people, with an estimated total cost of over €600 billion in 2015 (OECD/EU, 2018). In the UK, mental illness is the leading cause of illness, with costs estimated at 4.5% of UK GDP (£70 billion in 2014)[2,3]. In 2012-13, the NHS spent £3.3 billion on neurological services, amounting to 3.5% of NHS expenditure[4].

These costs are set to soar. For example, a report by the World Economic Forum and the Harvard School of Public Health predicted that mental health disorders could cost the global economy up to $16 trillion between 2010-2030[5].

Neurotechnology has an important part to play in addressing some of these conditions; both in enhancing the evidenced-based, clinically-informed assessment of conditions and crucially, in their treatment. For example, depth electrodes can be used to identify epileptic brain tissue, vagus nerve stimulators are used to treat severe forms of schizophrenia and obsessive-compulsive disorders and deep brain stimulators are finding application in areas outside of Parkinson's, such as depression and dementia.

The UK is already making a significant contribution to this field, both academically and through innovative companies, some of which are listed on the following page.

122,000
people suffer from Parkinson's disease in the UK[6]

Bristol based **Bioinduction** have developed a new deep brain stimulator, Picostim, that is one third of the size of current devices. Picostim can be implanted in a single surgical step allowing twice the number of surgeries to be scheduled than is currently the case. An initial health economic study indicates this could save the NHS up to £14 million a year for the treatment of Parkinson's disease alone.

850,000
people suffer from dementia (including Alzheimer's) in the UK[7]

Based in Belfast, Northern Ireland, **BrainWaveBank** have developed a suite of tools that can be used at home or in the clinic and tracks brain activity and cognitive performance. A wearable device sends brain activity readings to their AI-powered cloud platform. This allows doctors and scientists to remotely track how a patient's brain health develops over time, to power the next generation of therapies for Alzheimer's disease, depression and other conditions.

4.4%
of the world's populations suffer from depression[8]

Transcranial magnetic stimulation (TMS), an effective, non-invasive outpatient treatment option for people with depression was pioneered in the UK and is now being driven forward by Wales-based Magstim. In the UK, the National Institute for Health and Care Excellence, (NICE) has approved TMS as a safe treatment[10] and it is now subject to a large study to assess its potential and value[11]. Clear clinical evidence shows that TMS can have successful impact on treating severe depression.

7.4m
people living with heart and circulatory disease in the UK[9]

BIOS Health, based in Cambridge, are developing a full-stack neural interface platform that uses artificial intelligence to decode and encode the signals from the brain to the body to treat chronic health conditions, replacing drugs with computer generated neural signals. By understanding and correcting signals in real time, they are aiming to treat chronic cardiac illnesses in an effective, automated and personalized way.

400,000
people in the UK suffer from rheumatoid arthritis

A third of people suffering from rheumatoid arthritis are forced to stop working within 2 years of onset, rising to half within 10 years[13]. The National Audit Office estimates that rheumatoid arthritis costs the NHS £560 million annually , with wider costs to the UK economy of £ 3.8-4.8 bn per year[14]. **Galvani Bioelectronics**, a partnership between GSK and Verily Life Sciences (part of Google's parent company Alphabet), is planning to invest £540m over seven years to develop tiny implantable devices to treat a range of debilitating chronic diseases caused by inflammation, such as rheumatoid arthritis.

1.2m
stroke survivors in the UK[12]

NeuroCONCISE, based in Londonderry, Northern Ireland, develop AI-enabled, wearable neurotechnology that translates brainwaves into control signals allowing wearers to communicate or interact with technology without movement. This brain-computer interface technology can drive novel assistive devices for the physically impaired, new assessment protocols for disorders of consciousness and rehabilitative devices to support stroke rehabilitation. Stroke rehab trials with neurotechnology have demonstrated clinically important functional recovery, providing more than twice the functional recovery as other therapies and state-of-the-art rehab technologies.

Non-medical applications of neurotechnology

Neurotechnology products targeting non-medical applications are becoming increasingly popular and available on the market. In particular, wearable neurotechnology that measure electroencephalography (non-invasively), enables users to interact with devices and their environment through a brain-computer interface (BCI). These interfaces, where the user actively modulates their brain activity to relay intent or commands to the computer or device, have traditionally been the target for alternative and augmentative communication (AAC) devices and assistive technologies. However, they are now seeing increased interest in areas such as, computer gaming (neurogaming), recreation and educational products to encourage and support learning through neuroscience.

Wearable neurotechnologies, which passively monitor brain activity, are targeting human enhancement and augmentation applications. Examples include cognitive load monitoring, operator drowsiness/vigilance detection, early reaction systems (detecting neural response before physical response), video game-player monitoring/enhancement and e-sport performance. In general, these passive brain-computer interfaces target better human-machine and human-computer interactions and have seen interest in military applications.

Transcranial electrical stimulation (TES) and transcranial magnetic stimulation (TMS) devices, which modulate brain circuitry using electrical or magnetic stimulation, have mainly been evaluated in research programmes. However, they are now commercially available in products reporting a range of human enhancements including, in visual perception, memory, reading, decision-making and physical performance aspects – these are now being evaluated in military funded programmes.

In general, non-medical applications are attracting early adopters of neurotechnology. The funding and investment are originating from outside the medical sector and are helping to drive the demand for neurotechnology products. The gaming sector, an area where the UK has a strong international reputation, is a good example of this. Revenue from such demand is supporting innovation within early stage neurotechnology start-ups that are targeting medical applications, which typically present more development, efficacy and regulatory related challenges.

UK neurotechnology

The UK has a world leading research base in fundamental neuroscience, medical imaging, bioelectronic medicines, brain-computer interfaces and neural prosthetics. We aim to bring to bear these combined forces to ensure that the UK establishes a leading role in neurotechnology. Moreover, there is relevant regional excellence across the country, for example, non-invasive neurotechnology in Northern Ireland, photonics in Scotland, dementia research in Wales, optogenetics in the north east of England, mental health in the Midlands and clinical, experimental and computational neuroscience in the South[16]. The real potential will be realised if this fragmented excellence can be brought together with common aims and a shared strategy, to establish the critical mass needed to compete internationally.

An innovation infrastructure is also emerging that can support the pre-competitive landscape and accelerate the commercialisation of new neurotechnologies:

- The new £5.2 million Wellcome Trust funded Manufacture of Active Implant and Surgical Instruments (MAISI) facility prototyping for first-in-patient medical devices;
- The UK Dementia Research Institute is the single biggest investment the UK has ever made in dementia thanks to a £290 million investment;
- NIHR MindTech is a national centre focusing on the development, adoption and evaluation of new technologies for mental healthcare and dementia.
- The Henry Royce Institute is the UK's national institute for advanced materials research, which is investigating material biocompatibility and lifespan - crucial for the encapsulation of next-generation active implantable devices. Harnessing the UK's internationally leading materials research base will give a competitive advantage to UK R&D in this area;
- The Centre for Process Innovation helps companies commercialise new medical devices.

This is supplemented by commercial capabilities, such as that found at Bioinduction Ltd., which has a class-3 AIMD (Active Implantable Medical Device) manufacturing clean room through its subsidiary FineTech Medical and is pursuing clinical trials for Parkinson's Disease, and the development of new bioelectronic research tools in collaboration with Oxford University.

Importantly, the UK's centralised national healthcare system – the National Health Service (NHS) – is a fully-integrated system offering neurotechnology scientists, researchers and innovators access to large, diverse, longitudinal datasets to help their R&D efforts. For companies targeting medical applications, it offers a national-scale market into which safe new devices and processes can be trialled and launched. The UK has an exemplary reputation for good ethical standards and open collaboration between industry and academia, with an internationally renowned regulatory landscape that is taking a new approach to accelerate responsible innovation in emerging technologies.

Neurotechnology funding

In today's global market, expertise, reputation and competitiveness are important factors in a nation's welfare. With investment in this area there is the opportunity for the UK to build upon existing activity to establish an internationally leading position in neurotechnology.

The importance of this field is being widely recognised internationally as demonstrated by the recent major investments by the USA, Canada, the EU, China, South Korea, and Japan (see Table 1), which also underlines the immediacy of the opportunity. A comparison with UK spending is shown in Figure 1.

A paper published by the OECD in 2019 found that, worldwide, over 16,000 patents in health-related neurotechnology had been filed between 2008 and 2016, with a significant upward trend[17]. The USA (9,518), China (3,436), Korea (823), and Japan (603) led the charge.

Table 1. International investments in brain research

US BRAIN Initiative US$1.8 billion since 2013 plus $500 million a year until 2023[18]	**EU Human Brain Project** €1 billion over 10 years (launched in 2013)[19]	**China Brain Project** A 15-year project established in 2016
Korea Brain Initiative 51.3 billion KRW committed to brain research in 2021 alone[20]	**Australian Brain Initiative** AU$500 million over 5 years, launched in 2016[21]	**Japan Brain/MINDS** 40 billion Yen from 2014-2024[22]
Canadian Brain Research Strategy Can$230 million invested in brain research from 2011-2019[23]		

The US is the largest investor in absolute terms, investing $500m a year in its BRAIN Initiative (although it should be noted that there are no public figures for China's investment in this area which is likely to be substantial).

When comparing brain related investments (of which an increasing proportion is based around neurotechnology) to a country's GDP (Figure 1), it is apparent that Australia and Korea are heavily investing in brain related research. Australia has a strong background in neuroprosthetics, notably the cochlear implant[24], while Korea has identified neurotechnology as an important response to the country's rapidly ageing population[25].

Over the last 10 years, on average, UKRI has invested around £9 million per year in neurotechnology related research. The majority of this investment has been through EPSRC and MRC (Figure 2). Though this investment in discovery research has helped establish the underpinning expertise, it is clear that further investment is needed to accelerate the pace of research and ensure a steady pipeline of new technologies to drive the UK sector forward. Alongside this it is also essential that there is a translational pathway in place so that the UK can benefit from breakthrough research rather than it being commercialised overseas.

Industry around the world is also investing in neurotechnology. Notable examples include:

- $100 million investment into Kernel, 'a neuroscience company focused on developing technologies to understand and treat neurological diseases and radically improving our cognition'
- $158 million invested in Neuralink, to develop 'ultra-high bandwidth brain-machine interfaces to connect humans and computers'
- Galvani Bioelectronics, formed by GSK and Verily Life Sciences – part of Google's parent company, Alphabet – is planning to invest £540 million over seven years to develop 'tiny implantable devices to change precise electrical signals in nerves to treat a range of debilitating chronic diseases'

KTN has conducted a survey of the UK neurotechnology community, where 39% of our respondents expect that it will take 1-3 years to bring their neurotechnology device to market. A further 24% expect it will take 4-7 years (Figure 3). There are notable exceptions such as Magstim which already have products on the market, but with many companies nearing the stage of commercialisation, this suggests there is a greater role for Innovate UK, for example, through focussed neurotechnology Biomedical Catalyst competitions. We expect the first wave of neurotechnologies that will reach the market to be predominantly non-invasive, such as wearable neurotechnology for brain-computer interfaces. In order to support the emergence of invasive and non-invasive devices, we propose a £10m Innovate UK call, allowing up to 20 neurotechnology companies to partner with researchers over the course of a 5-year period.

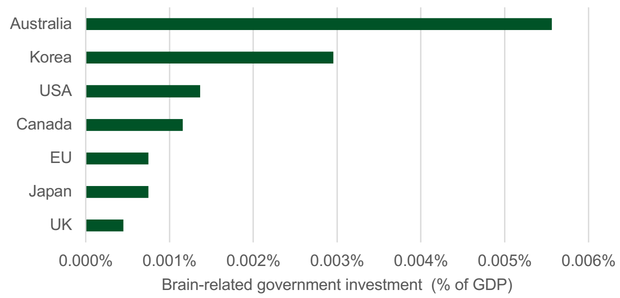


Figure 1. Large scale strategic government investments in brain-related R&D (see Table 1) as a percentage of a country's GDP (2019 World Bank data).

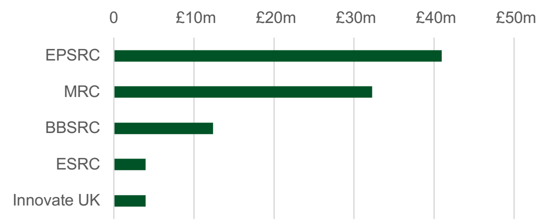
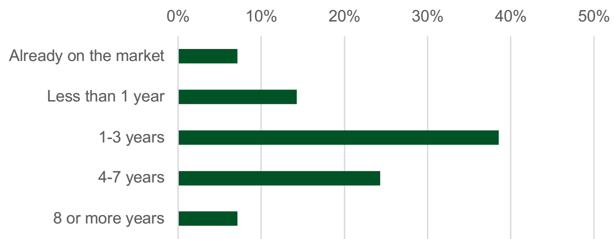


Figure 2. UKRI funding in neurotechnology between 2011-2020. Data from Gateway to Research, see link for list of keywords[26].

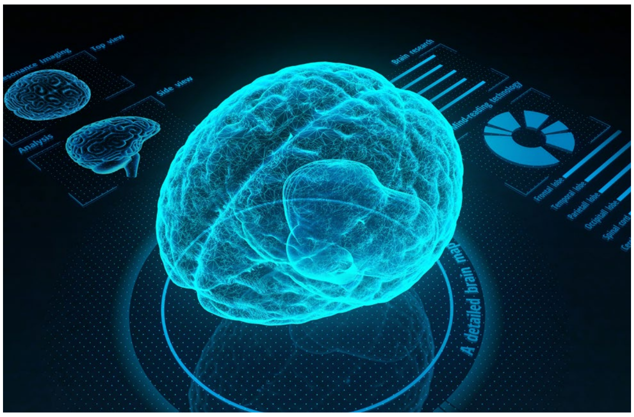


Estimated time for neurotechnology device to reach market ("How long do you expect it will take to bring your neurotechnology device to market (Technology Readiness Level 9)?"). Data from KTN Neurotechnology Survey, January 2021.

Barriers to commercialisation and key recommendations

The UK has established the beginnings of an exciting neurotechnology community, comprising high-tech SMEs, University spin-outs and leading academic groupings. However, as an emerging technology, it is fragmented and lacks the supporting infrastructure and organisational capability of more mature sectors, as found in the pharmaceutical industry. As a consequence, in the UK, pathways to successful commercialisation have yet to be fully established at scale. Equally, the relatively small size and the focussed nature of much of the UK activity restricts the diversity of in-house skills and general level of resource. Our recent survey and deep-dive workshops have highlighted the barriers to commercialisation (Figure 4) and are summarised as follows:

- The difficulty of securing funding and navigating the regulatory landscape adds time and cost to innovators' development journeys, which stretches resources. Importantly, it also inhibits venture capital investors whose return horizons tend to be relatively short;
- Neurotechnology innovators – especially those working on medical applications – often do not have the time, expertise, or resource to navigate the complex regulatory landscape, placing an onerous burden on them that distracts from their mission-critical R&D work;
- Many innovators lack the time and resources to seek out appropriate clinical collaborators.
- In line with many emerging high-tech companies, neurotechnology innovators struggle to compete with larger sectors to attract people with the right blend of skills;
- Through a lack of resource, innovators neglect the potential to develop complementary non-medical applications of their technology that could underwrite the development of medical applications. There is no integrated national strategy where different sectors (e.g. gaming and health) can support each other and create complementary innovations;
- Neurotechnology innovators operate in silos either by accident, tradition, bureaucracy, clinical specialisms, or to protect intellectual property, which stands in the way of the open information sharing and efficient communication needed for transdisciplinary innovation.



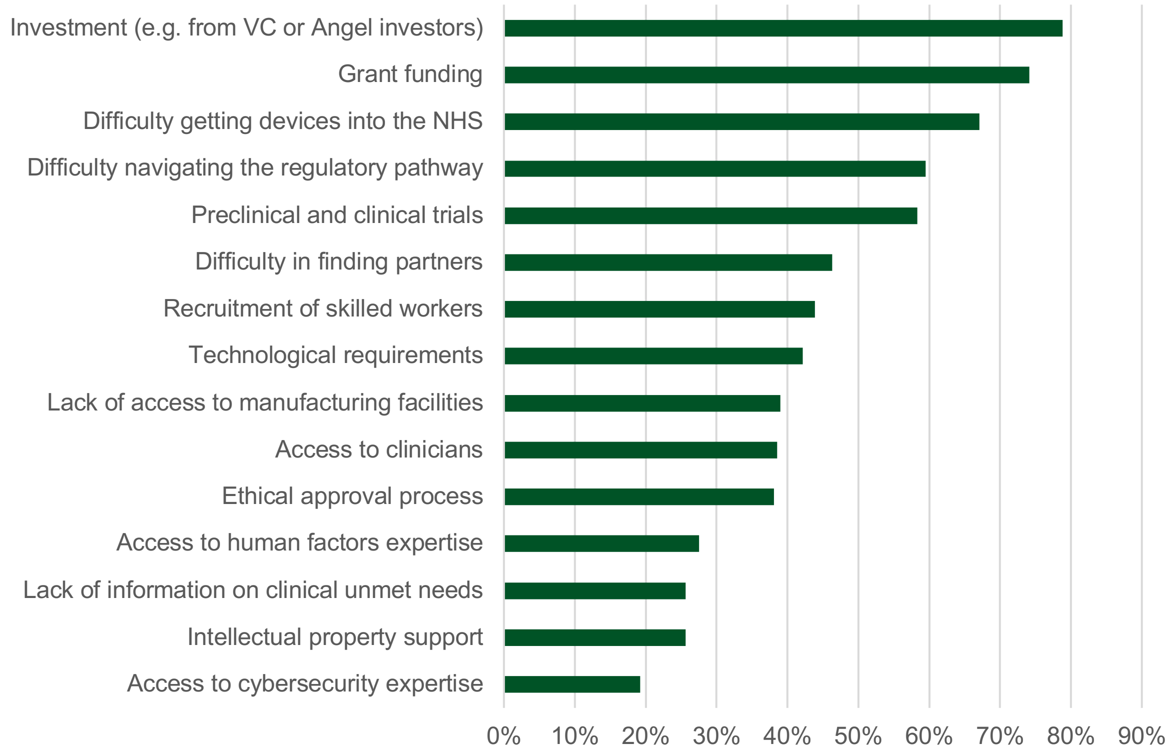


Figure 4. Percentage of respondents who rated barriers to commercialisation as moderate or major. Data from KTN Neurotechnology Survey, January 2021.

We have identified three key areas that could help to overcome these barriers and catalyse the translation of cutting edge neurotechnology research, growing this as a major high-tech industrial sector.

1. Accelerating UK Neurotechnology Research and Innovation

This is a core part of this neurotechnology strategy, where we aim to ensure that there is excellence right across the sector – from applied research through to clinical/commercial translation. It requires:

- Support for the research community to ensure that the pipeline for discovery science is reinforced. This should be done through UKRI and other funders through a coordinated and targeted neurotechnology funding initiative.
- The creation of a Neurotechnology Accelerator, which will establish a world-first national neurotechnology infrastructure and manufacturing ecosystem, drawing together key academic, government, and industry partners and building a translational, commercial pipeline from the laboratory to the NHS. The Accelerator will establish critical mass and help coordinate the community around a national strategy.

Research

We propose a focussed investment in neurotechnology research over an initial 5-year period. The aim will be to draw the neurotechnology research sector together and capitalise on the outstanding engineering, neuroscience and clinical expertise across the UK. This initiative will boost the UK research community through the following funding mechanisms:

- Multi-institutional Programme grant style awards in invasive and non-invasive neurotechnology. These programmes will unify academic, industrial and clinical teams from across the UK through a central transformative research vision, which will fit with a broad national strategy for neurotechnology. Six of these large grants (totalling £30M) will allow the existing UK neurotechnology research and innovation community to self-organise, so that major centres of excellence emerge that reflect the UK's strengths in this area. Furthermore, they will provide infrastructure support for first-in-human testing and translation that will complement the Neurotechnology Accelerator.
- A funding call for responsive mode grants to support investigator-led research programmes in new areas of neurotechnology, ensuring a healthy pipeline of research. An investment of £4.5M will allow up to 9 awards over the first 3 years of this initiative.
- A cross-council Fellowship call, that will allow the most promising early-career researchers to develop independent research profiles, along the lines of what the Turing Fellowships are doing for the Artificial Intelligence community. A £5M fund, would allow 5 prestigious fellowships in neurotechnology and ensure support for the future leaders of this field.

The Neurotechnology Accelerator

We propose the formation of a Neurotechnology Accelerator that will become an essential test bed for device developers and provide key infrastructure to industry - a crucial steppingstone in making the UK internationally competitive in this area. This facility will support industry in the translation of cutting-edge research and will engage with colleges and universities in developing training courses for the required skilled workforce. This step-change in the UK neurotechnology sector will necessitate the creation of larger manufacturing facilities, so as to fulfil the UK's growing device pipeline. We anticipate that the cost for this accelerator will be approximately £10m per year over the first 5 years of the programme.

Manufacturing

In order to make the UK a world leader in neurotechnology, it must have the manufacturing capability to realise this ambition. There are already some specialised facilities capable of manufacturing non-invasive neurotechnology in the UK, while the Centre for Process Innovation has significant expertise in prototyping and assisting companies to commercialise wearable devices. However, there is a need to enhance the capability to manufacture implantable devices at sufficient scale to undertake pivotal clinical trials so that the UK can capitalise on its outstanding academic and research capacity and capture some of the >£5B/annum revenue (10% CAGR)[27] of the neurotechnology sector.

The crucial next step in infrastructure development is a facility that can manufacture devices for clinical trials that will get them to the point of approval (15-500 devices). There are already many devices in development and with strong support there is the prospect of the UK becoming a leading neurotechnology manufacturing hub. To fully exploit this opportunity, the UK will need to grow a world-class manufacturing capability that will require custom built facilities for this new type of technology.

The £5.2 million Wellcome Trust funded Manufacture of Active Implant and Surgical Instruments (MAISI) Facility will open in 2021 and equip the UK with new capability to manufacture prototypes for specialist Class II and III medical devices for first-in-patient studies. This collaboration, between King's College London, UCL, and Newcastle University, is an important first step in creating a manufacturing ecosystem for implantable devices and is an exemplar of what can be achieved through strategic investment and critical mass.

The UK already has some expertise in implantable device manufacturing. For example, Finetech Medical is a manufacturer of neuro-stimulator implants. Finetech has one of the very few facilities in Europe capable of manufacturing Class III active implantable medical devices. Through Bioinduction, Finetech is also supporting academic research at Oxford

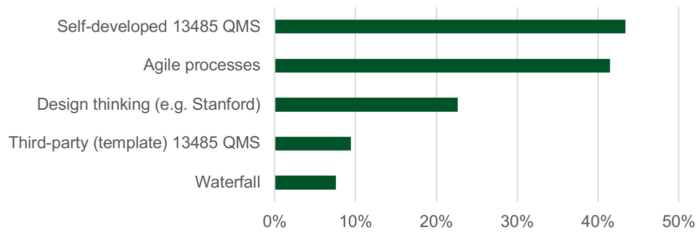


Figure 5. Project management tools used by neurotechnology developers. Data from KTN Neurotechnology Survey, January 2021

(MRC Brain Network Dynamics Unit) to develop bioelectronic research tools which could deploy across the UK for first-in-human research. While they have secured MHRA approval for a first-in-human trial, the proposed initiative will enable a scale-up that benefits the broader UK research ecosystem. We propose building on these and other existing capabilities (such as the National Manufacturing Institute Scotland) to grow the UK's cutting edge neurotechnology manufacturing capabilities.

Providing the capability to scale up neurotechnology manufacturing in the UK will not only create a vibrant eco-system of neurotechnology companies and suppliers, it will also provide the UK with sovereign capability in this vital sector of the future. The alternative is to lose ground and market opportunities to other countries, notably the USA and China, where high levels of investment are leading to significant market growth. With the correct investment the UK will be well-placed to capitalise on this emerging international market.

Commercialisation support

The Accelerator will become the "go-to" contact point for neurotechnology innovators, providing advice at an early stage to save costly and time-consuming corrections and ensuring they are developing the right devices, in the right way for the right market. The main areas of support would include:

- A consultation at the outset of device development to identify a commercialisation pathway
- Direct support on regulations, clinical trials, ethical approvals and health economics
- Access to quality management systems.
  - 43% of people developing neurotechnology devices use self-developed 13485 quality management systems (Figure 5). There is an opportunity to streamline this through third party templates.

One of the aims of the Neurotechnology Accelerator will be to get companies "NHS ready". This will allow them to engage with the Academic Health Science Networks or secure support from funders, such as SBRI Healthcare, in order to translate their innovations into the NHS. The Accelerator will work closely with the Department of International Trade who can assist companies in identifying and exporting their innovations to other markets.

It will act as a conduit to the regulator, well connected to the international scene and able to advise on the fast-changing technology ecosystem. Indeed, we will strongly advocate for a joint role with MHRA's Innovation Office.

The Neurotechnology Accelerator will also be a focal point for the ecosystem, a meeting place to bring together people with different expertise and ideas. It will champion and coordinate the sector, creating a stronger, united voice for the UK community.

National Institute for Health and Care Excellence (NICE)
In 2019, the NHS Long Term Plan committed to accelerate the uptake of selected innovative medical devices, diagnostics and digital products to patients faster, by developing the MedTech Funding Mandate policy, which will launch on 1st April 2021.

In order for neurotechnology to be given positive medical technology guidance, NICE requires that the technology provides an increase in clinical benefits while costing no more to the NHS than current care. For diagnostics guidance and technology appraisal guidance, the technology must be cost effective at a cost per quality adjusted life year threshold set by an independent committee during the appraisal.

A key opportunity is for NICE to engage the accelerator on best-practices and standard models to help innovators and entrepreneurs define a viable healthcare economic strategy amenable to NHS listing.

2. Ethics, regulations and data security

Advances in neurotechnology promise better health, better memory, better concentration, healthier ageing and an enhanced understanding of how the brain functions. However, no technological development is risk-free, and neurotechnology presents some important challenges with respect to technical readiness, investment risks, public acceptance, governance, privacy, security, data ownership and social equity. There are fundamental ethical issues that an ambitious R&D initiative must identify and acknowledge. A system of checks and balances needs to be established in order to ensure responsible research is maintained as neurotechnology R&D accelerates. An important part of this is to engage openly with the public, especially patients and the other stakeholder groups most affected, to ensure their trust and confidence. As well as proven efficacy and safety, this means clear and authoritative communication to avoid misinformation, dispel unwarranted stigma, and denounce unsubstantiated hype.

Ethical framework

Given the far-reaching implications inherent in developing sophisticated interfaces to the human brain, it is vital that an ethical framework is in place from the outset.

The UK is considered a leader in exploring and driving the ethical use of AI and emerging technologies as a result of being home to organisations such as the Centre for Data Ethics and Innovation, the Ada Lovelace Institute and the Alan Turing Institute. It can draw on its considerable experience of the way that comparable technological developments were successfully managed, not least in the Human Genome Project and the way the Human Fertilisation and Embryology Authority oversees technological development. Indeed, the Nuffield Council on Bioethics[28] has already laid the groundwork for an ethical framework for neurotechnology and Australia has implemented a neuroethical framework[29] as part of its brain initiative.

We echo the Royal Society's recommendation for UKRI to develop a funding call to explore the ethics of neurotechnology. We also recommend the formation of a Neuroethics Working Group, led by the Royal Society, to develop a comprehensive ethical framework by which neurotechnology is developed, safeguarding all stakeholders fairly at every step of the R&D life cycle. The Neuroethics Working Group should consult with a broad range of stakeholders including the public, patient groups, charities, government, academia and industry.

Regulatory opportunities

We support the Royal Society's recommendation that the UK should seek to encourage multidisciplinary collaboration across industries to develop neural interfaces at the same time as developing an anticipatory approach to how they are regulated.[30]
To aid this, the neurotechnology sector should develop close ties with the UK Government's recently established Regulatory Horizons Council (RHC). This

is "an independent expert committee that identifies the implications of technological innovation, and provides government with impartial, expert advice on the regulatory reform required to support its rapid and safe introduction"[31]. Insights from this report and the KTN's recent Neurotechnology Survey on the challenges of navigating the regulatory pathway, have fed into the RHC's ongoing study on regulatory reform around medical devices and the RHC have selected neurotechnology as one of only three new priority areas – highlighting the importance of this area.

In light of Brexit, the UK has a unique opportunity for a new regulatory regime which has greater flexibility in the testing and adoption of emerging neurotechnologies. There are some specific areas which are particularly ripe for innovation:

- Setting up an "investigational device" pathway to facilitate first-in-human studies, similar to the investigational device exemption (IDE) process used by the FDA. Such a process can help innovators ethically test new concepts with right-sized design controls for early feasibility work.
- Working to establish an "open-source quality management system" with toolkits, training and templates to help educate researchers and SMEs on the process, reinforce best practices, and lower barriers to adoption.
- Supporting tools to simplify the pathway (e.g., an Australian-style regulatory flow chart to demystify the pathway).
- Develop an international regulatory framework which will allow the adoption of standards and protocols that ensure the technology is secure by default.

Data, privacy and security

Since neurotechnology detects, digitizes, interprets, and acts on personal information contained in neural activity, and this information is personal, it gives rise to concerns about breaches of privacy. Questions that must be considered include:

- How can we effectively guard against this data being abused or hacked?
- If this data is to be stored, how long for, where, and who should be in charge of it?
- If data can be recorded from the brain and neural activity modulated, how can we ensure that this data is secure?

MHRA and vaccine approvals and the ventilator challenge

Covid-19 demonstrated the capability of the UK regulatory environment to adjust quickly to a rapidly evolving situation. For example, the MHRA was the first to approve vaccinations for distribution. The approval was based on a rigorous assessment of clinical evidence, yet the processes applied facilitated continuous reviews with experts and a collaborative engagement with industry.

Likewise, the UK Ventilator Challenge helped rally academic and industry efforts to address a material shortfall based on model estimates. A specification was circulated focusing on the core requirements required for the emergency system, and a clinical testing site was created to facilitate rapid – days, not weeks – validation of designs that provided real-time feedback to teams and the MHRA. On-site regulatory support, supply chain management, and team formation was also facilitated by government. Understanding it is still an evolving situation, the response of UK regulators to Covid-19 demonstrates the capability to respond to a dynamic environment, while still maintaining rigor in the scientific process and maintenance of patient safety.

For neurotechnology to gain wide public acceptance, there must be a framework in place to protect user's neural data. We urge policy makers to develop robust data protection guidance.

While access to cybersecurity expertise is not considered to be a moderate or major barrier to commercialisation by much of the community (Figure 4), this might in part be due to unfamiliarity with the requirements, regulations and best practices - it is essential that neurotechnology innovators embed cybersecurity and data privacy at the outset of device development and not retrospectively. The Neurotechnology Accelerator will provide guidance to innovators and help raise awareness of the importance of cybersecurity.

Privacy

Privacy should be a core part of any neurotechnology and we endorse the recommendation of the Royal Society's iHuman report, (see excerpt below).

Excerpt from the Ethics section of The Royal Society's iHuman Report

Royal Society. iHuman: blurring lines between mind and machine. Royal Society, 2019

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 into 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.

Data

Numerous pieces of legislation, such as the Data Protection Acts 1998 and 2018, as well as the General Data Protection Regulations (GDPR), provide rules on how data should be handled and stored. As the information will be more personal and much of it may be considered medical, additional legislation, as well as industry regulations, standards and protocols may need to be developed to provide a higher level of protection.

Security

The security of the devices falls within two categories, cyber security of the devices and "neural security." The UK should develop industry standards and regulations to ensure that these provide security by default and not just by design.[32]

The current issues with -ware (e.g., Ransom-ware), data breaches and other risks have led to significant security issues for individuals, organisations and states alike and is an increasing risk with pervasive, unsecure IoT (Internet of Things) devices flooding the market. The current internet infrastructure was built to share information and for redundancy, but leaves gaps for security, especially with users unfamiliar with the consequences of the technology. Whilst the devices will have to connect to the internet, developing the framework so that the devices are secure by default rather than just by design would prevent many of the security incidents currently seen in the online world.

FDA's view on Cybersecurity

Taken from https://www.fda.gov/medical-devices/digital-health-center-excellence/cybersecurity

"All legally-marketed medical devices have benefits and risks. The FDA allows devices to be marketed when there is a reasonable assurance that the benefits to patients outweigh the risks.

Medical devices are increasingly connected to the Internet, hospital networks, and other medical devices to provide features that improve health care and increase the ability of health care providers to treat patients. These same features also increase the risk of potential cybersecurity threats. Medical devices, like other computer systems, can be vulnerable to security breaches, potentially impacting the safety and effectiveness of the device.

Threats and vulnerabilities cannot be eliminated; therefore, reducing cybersecurity risks is especially challenging. The heath care environment is complex, and manufacturers, hospitals, and facilities must work together to manage cybersecurity risks."

3. People/talent

Neurotechnology training

As the neurotechnology sector grows, there is an increasing demand for highly skilled graduates and postgraduates, as well as technical staff and apprenticeships. The training requirements are in part met by Imperial College's Centre for Doctoral Training (CDT) in Neurotechnology. This is a good example of multidisciplinary training, coupled with high levels of interaction with industry. The Imperial CDT began the training of a new breed of engineers conversant in engineering, neuroscience and medicine, who understand the multidisciplinary remit of neurotechnology research to ensure that innovative technologies can be evolved for the benefit of the society, in a patient-centric way. However, the CDT will end in 2022, leaving a gap in the training landscape. Recruitment of skilled workers is already an important barrier for the UK neurotechnology sector (see Figure 4), so we recommend further investment in the CDT landscape (at the level of £5M over 5 years) and iCASE studentship programmes, so that UK companies can fill the new jobs that they are creating. The university and college sectors, working together with industry, will have an important role in addressing the broader skills shortage, which includes technical staff and apprenticeships. We need to ensure neurotechnology companies have the support and incentives needed to engage in apprenticeship programmes.

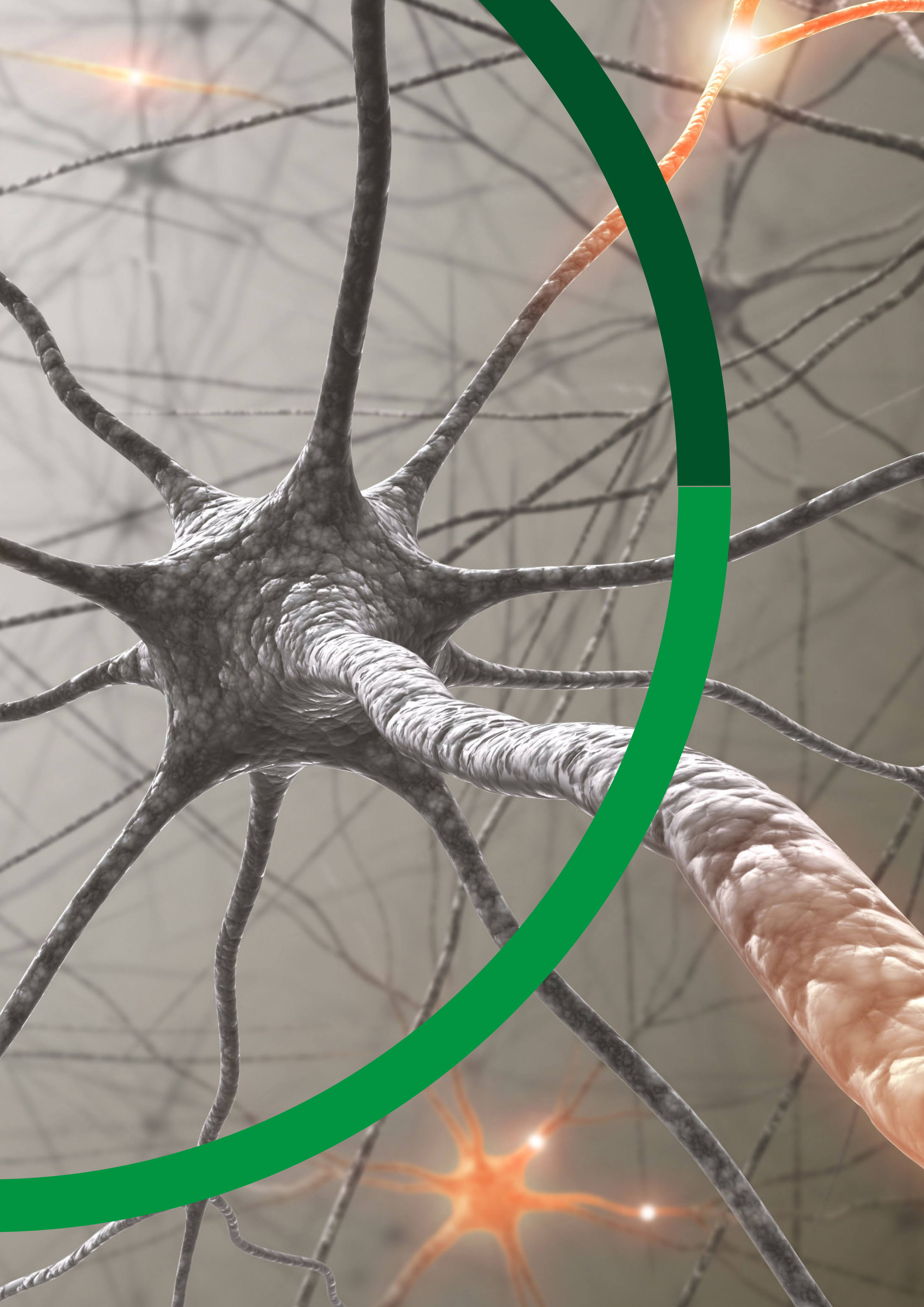
Clinical research fellowships

It is critical to the field that clinicians are given the time and encouragement to conduct research in device development. However, they are under immense time pressure, with little to no time in their job plans for research. We recommend a Fellowship call funding 10 new Clinical Research Fellows, over 5 years and buying out a clinician's time at the level of 2 days per week for research. In order to cement collaborative working, they will be assigned an industry mentor. The Wellcome Trust have also identified this issue and have recently announced PhD Programmes for Health Professionals. This will supplement that programme and give it the neurotechnology focus vital for this sector.

These clinicians will also act as ambassadors, building links between the NHS and the neurotechnology community and act as key contact points for industry. The fellowships will cost approximately £5 million over 5 years, but will result in the emergence of UK clinical leaders in the translation of novel neurotechnology through to the NHS. They will have strong relationships with University researchers and knowledge and relationships with the commercial sector, making them a pivotal part of this multi-disciplinary endeavour.

Enterprise fellowships

Training for the next generation of entrepreneurs is a crucial part of an integrated approach to supporting this sector. More Enterprise Fellowships, for example, those run by the Royal Academy of Engineering, would upskill academics and accelerate the commercialisation of new neurotechnologies emerging from the research base. A small investment of approximately £1M would train up to 20 neurotechnology entrepreneurs and help ensure a healthy commercialisation sector.



How KTN can help

Grow the connections within the community
KTN exists to connect innovators with new partners and opportunities. KTN's Neurotechnology Innovation Network will continue to grow the connections within the community, helping academics, clinicians and companies find new partners and signposting to other organisations that can help commercialise their devices. KTN will also highlight some of the most exciting technology innovations through a series of webinars and workshops.

Create a network of clinical co-developers
It is vital that medical neurotechnology is co-designed with clinicians. Many small companies lack the time and resources to seek out appropriate clinical collaborators. Clinicians, on the other hand, are often eager to be involved at an early stage but can be unaware of the many novel devices that are under development. Over the next two years, KTN will develop a network of clinicians that want to be involved in device development to facilitate collaborations with technologists.

Identify investment opportunities
The UK has a lively start-up scene in neurotechnology. 70% of companies surveyed are looking to secure investment from venture capital or angel investors in the next year. Interestingly, 38% of academics are also looking to raise investment for spin out companies. KTN will run a series of roundtables and showcases to demonstrate to the investor community the enormous opportunities for UK investors in a nascent sector with huge growth potential.

Cross sector collaboration
There are significant opportunities in cross-pollinating technologies across different sectors. Within healthcare, there is much to be learned from the thriving personalised monitoring and self-management initiatives. The gaming industry has also led on areas such as commercialising advanced EEG hardware for e-sports applications, which could be directly applied to stroke rehabilitation. 81% of survey respondents would like to collaborate with other sectors. Neurotechnology innovators are keen to collaborate across a number of different sectors (Figure 6). KTN will run a series of events to facilitate the flow of information and ideas across sectors.

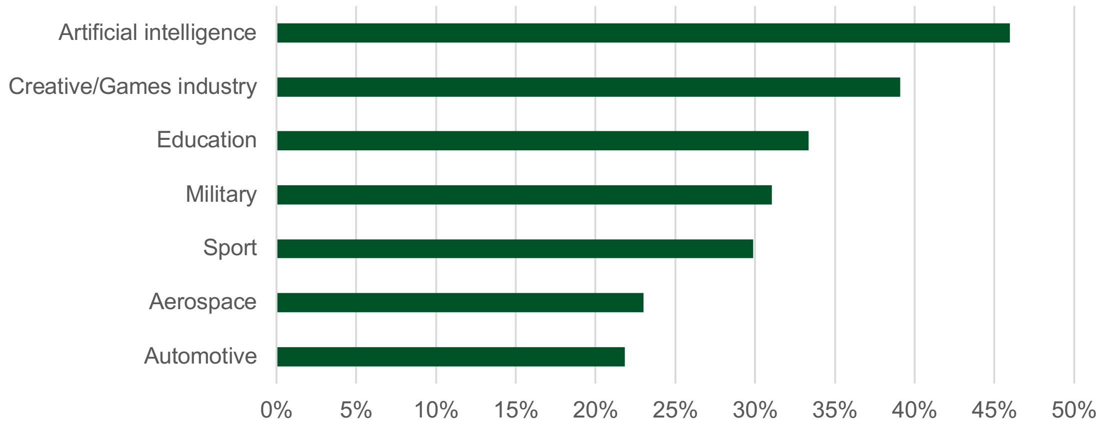


Figure 6. Which sectors the neurotechnology community would most like to collaborate with. Data from KTN Neurotechnology Survey, January 2021

Acknowledgements

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Resources and Further Reading

1 KTN Neurotechnology Special Interest Group: Biodesign Workshop Series 2: Mood and Psychotic Disorders

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29 Carter, Adrian, et al. "A neuroethics framework for the Australian Brain Initiative." Neuron 101.3 (2019): 365-369.

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32 Security by default means that the underlying protocols and principles result in the fundamental infrastructure, principles and ecosystem being secure. Secure by design means that a device which runs on an unsecure infrastructure can be 'hardened' to run securely on that system.

Innovation Networks: Communities that help shape our shared future

KTN exists to connect innovators with new partners and new opportunities beyond their existing thinking – accelerating ambitious ideas into real-world solutions. Our diverse connections span business, government, funders, research and the third sector.

KTN's Innovation Network programme unites some of the best minds and greatest thinkers from across the UK in areas of innovation, development and new technologies. Together, they're charged with finding answers to some of the world's most significant challenges, to help introduce positive change and shape our collective future.

Find out how KTN can be a part of your innovation journey here
https://ktn-uk.org/programme/innovation-networks/

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