Technology Touching Life

Strategic Framework

1. Five Year Vision_________________________________________________________ 1
2. Background_____________________________________________________________ 2
3. What is Technology Touching Life________________________________________ 2
4. Technology Touching Life Scope__________________________________________ 5
   4.1 Transformative Capabilities_____________________________________________ 6
   4.2 Research outside the scope of Technology Touching Life___________________ 9
5. Delivering TTL as a cross-Council programme_________________________________ 10
Annex 1: Examples of areas of biological challenge within TTL____________________ 13

1. Five Year Vision
Technology Touching Life (TTL) is a BBSRC, EPSRC and MRC joint initiative to foster interdisciplinary research into innovative, and potentially disruptive, technological capabilities that will drive world-leading basic discovery research in the health and life sciences. To achieve this, we aim to stimulate and support pioneering interdisciplinary leaders and collaborations across the interface of engineering, physical, and life sciences (both biomedical and biological), with developments driven by both technological innovation and scientific question.

Activities within TTL will build on the strengths of the UK research base by enabling effective collaboration, community building and peer review across disciplinary interfaces. TTL will help position the UK as one of the best places in the world for researchers at these disciplinary interfaces to co-conceive, co-develop and co-deliver game-changing technologies. In doing so we will ensure the UK leads future waves of life sciences discovery and capitalise on our vibrant research base to maximise the benefit of research 'at the interface' for our economy and society.
2. Background

New technologies often have their origins in innovative research and development in the engineering and physical sciences and play a crucial role in advancing life sciences research. Particularly revolutionary past examples include Magnetic Resonance Imaging, DNA sequencing and super-resolution microscopy, each of which involved fundamental innovation in engineering and physical sciences (EPS) methods being integrated within a technological platform that opened up new opportunities for basic, discovery research.

Through Technology Touching Life the BBSRC, EPSRC and MRC are highlighting interdisciplinary technology research as a topic of mutual strategic importance. The strategy for TTL has been developed with input from members of the academic community through our collective advisory structures, engagement with the community via an e-consultation and an Expert Group. The TTL strategy builds on the recommendations from the Maxwell report\(^1\), the Government's Science and Innovation strategy\(^2\), as well as studies focused on the opportunities and challenges at this disciplinary interface (\(e.g.\)\(^3\), \(^4\)). This is a long term commitment, aiming to nurture the adventurous research that leads to the discovery of ground-breaking technologies and technology-enabled research in the life sciences.

3. What is Technology Touching Life?

The Research Councils are uniquely positioned to stimulate this collaboration and develop strong working models across the disciplines. A strategic focus on TTL is needed now to deliver the next generation of technological advances and capabilities that keep UK research at the forefront. The TTL programme aims to build substantially upon our existing individual activities and enable interdisciplinary technology research to support basic 'discovery' science.

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\(^2\) Our plan for growth:science and innovation


\(^3\) Research at the intersection of the Physical and Life Sciences. The National Academies Press.

https://www.nap.edu/read/12809/chapter/1 (accessed October 14 2016)

\(^4\) Evaluating Interdisciplinary Research: a practical guide (Professor Veronica Strang and Professor Tom McLeish) https://www.dur.ac.uk/ias/news/?itemno=25309 (accessed October 14 2016)
"Novel tools, techniques and instruments that enable advanced capabilities and innovative approaches with wide-ranging potential for generating new fundamental understanding in the health and life sciences"
understanding to feasibility and proof of concept in experimental models ranging from molecule to human. We expect that the new tools and capabilities generated are likely to feed into more translational research and development programs, including existing Research Council mechanisms (e.g. EPSRC Impact Acceleration Accounts, BBSRC Follow on Fund, MRC Confidence in Concept) and Innovate UK Emerging Technologies.

Figure 1. Word Cloud generated from the Technology Touching Life e-consultation responses.
4. Technology Touching Life Scope

The linkage of excellent fundamental EPS science to tractable life science challenges was identified as important by the Maxwell Report and the TTL consultation. The aim of TTL is to foster interdisciplinary research into innovative and potentially disruptive technological capabilities that will drive world-leading basic discovery research in the health and life sciences. The main areas of relevant research are articulated here to illustrate the scope of TTL, including emerging areas of EPS innovation and key research questions in the health and life sciences, which together can stimulate research generating transformative technological capabilities for discovery research. This is not an exhaustive or exclusive set of topics, but is presented as a guide to the scope of TTL and to enable the development of future areas for investment. The partner councils anticipate supporting research into a diverse range of technologies and scientific challenges through Technology Touching Life and will assess the range and balance of research as the program progresses.

The TTL theme seeks to develop approaches that expand the current scientific paradigm. The next breakthrough technology could address a range of current technical challenges with respect to sensitivity, resolution, reliability, integration, speed, selectivity, conditions, or context.

The complexity of biological systems means that life scientists need to look beyond the genome to determine how organisms function. To do so, they must perturb, measure, and increasingly integrate the analysis of many different
parameters, at the molecule/cell/tissue/organism level, to derive overall understanding of the processes they are interested in. Furthermore, technologies that operate accurately, safely and effectively within or close to the living system will allow life science researchers to understand how biological processes operate 'as they are' in the organism i.e. under physiological conditions. Current techniques can be limited with respect to speed, resolution, invasiveness or integration, or be strong in one parameter but not all, thus limiting their impact in real life situations. The co-development of new techniques and technologies based on novel engineering and physical sciences will enable step changes in life sciences.

There is substantial scope for novel Engineering and Physical Sciences (EPS) research to be brought together with life sciences questions in order to create field-changing approaches and develop new hypotheses. Fundamental EPS research in fields including physics, chemistry, engineering and ICT should be developed in TTL in partnership with life sciences researchers, driven by and also driving key life sciences questions. The combination of basic research in both fields is crucial to transforming capabilities and enabling insight and understanding beyond current levels.

Illustrative examples of impacts in the health and life sciences are given in Annex 1.

4.1 Transformative Capabilities

Perturb

Altering the structure or function of a biological system and observing its response can generate a range of outputs informative to the understanding of normal physiology and pathophysiology. Perturbation can be internal or external in mechanism, applied in vitro or in vivo, and take place across a range of relevant scales (molecule, cell, and organism). Perturbation is a common strategy that allows biologists to understand more about the system they are studying and a variety of tools, techniques and methodologies have been developed to enable this e.g. optogenetics uses light to control modified cells within a tissue, externally applied mechanical stress influences cell morphology in vitro, and implantable electrodes can selectively modulate nerve stimulation in humans and animals.

Advances in technology will allow interrogation of systems with greater precision, control, ease of use, reduced off-target effects and cost, and under
more physiologically relevant conditions. New technologies may require novel miniaturisation and nanofabrication methods, use of advanced materials, sensors with enhanced specificity and sensitivity, or novel signal detection mechanisms. Instruments may also require re-engineering to lessen the effects of damaging energy, mechanical and chemical inputs used during experimentation.

Research areas may include, but are not limited to:

- Inhibition and control of biological behaviour using chemical, biochemical, or physical tools in order to understand biological characteristics and responses

- Physical and mechanical control of biomolecules, cells, and cellular systems, and use of this control to understand the relationship between physical forces and biological function

- Micro and nanotechnology for precision manipulation either in-vivo using implantable systems, or in vitro using approaches including microfluidics, electronics, or photonics

Measure

Biological systems and processes occur at a range of length scales (from atoms to molecules to cells to whole organisms) and time frames, (from very fast events such as neuron firing to much slower processes like developmental transitions as organisms grow or age). New approaches to the measurement and characterisation of biological systems are required in order to surpass current limits of resolution, speed and sensitivity could enable data acquisition that reveals novel insights into a range of biological mechanisms and disease processes. Transformative technological innovations for the life sciences will not only be based on measuring beyond what is currently possible but also detecting and accurately quantifying novel targets and by increasingly non-invasive approaches.

Solutions are likely to require innovation in areas such as photonics, imaging, sensor design, label development, detector sensitivity, and data processing.

Research areas may include, but are not limited to:

- Improving and developing imaging and microscopy techniques with respect to both length scale and time scale resolution, non-invasive and
deep-tissue imaging, imaging under physiological conditions (including in-humans)

- Technologies or combinations of technologies for the measurement of multiple biological parameters on demand, across scales, continuously, and/or over long time periods, with in-build integration and interpretation of data to reduce subjectivity

- New sensing and measurement techniques to enable the identification, characterisation and quantification of biological behaviours and processes with increased sensitivity, at smaller scales, continuously, and under biologically relevant conditions

**Analyse**

Developing approaches to the sensing and analysis of biological systems, including the synthesis and integration of output data from multiple techniques, will facilitate and enhance understanding of biological phenomena and systems. Technological outputs from research in this area may enable phenotyping from the cellular to whole organism level and generate better functional understanding of key processes such as drug resistance, cell signalling and physiological adaptation to the environment.

Integrated characterisation of biological phenomena and systems will require innovation in a broad range of areas such as analytical science, chemical biology, sensor technology, device design, microsystems and electronics, robotics and automation, and data processing and integration. This includes image processing, tools for signal detection, and advances in machine learning and artificial intelligence to enable intelligent system design.

Alongside physical tools and technologies, new computational tools and analysis methods will be required to support the extraction, processing and analysis of data. Challenges will be framed by the data outputs from the technology but may include areas such as improving detection of signals from noise, integrating sensor data, signal processing and automated approaches to recognise patterns and features within data (e.g. using machine learning). It is expected that these new computational tools will provide a key link for users between technology-enabled experimentation and the derivation of new knowledge.

Examples of relevant challenges:
• Integrating measurements across hierarchical scales of biological organisation in order to understand how (for example) the structure and interactions of biomolecules influences the behaviours of cells, tissues, and organisms

• Real-time analysis of the structure and function of cells and sub-cellular structures, and consequent understanding of their influence on behaviour

• Multiscale imaging correlating gross morphology with molecular details

• Ultra-small scale sampling and detection of biomolecules using highly sensitive techniques to understand how composition, turnover or localisation changes in response to developmental, physiological or environmental changes

4.2 Research outside of the Scope of Technology Touching Life

In defining the scope of TTL, we recognise that not all research to develop technologies for biological or biomedical applications falls within this space; much already has a clear home at one Research Council or with Innovate UK.

Examples of research that is embedded within other areas of the Research Councils' strategy include:

- Medical/Clinical devices (in development for end-point clinical utility rather than basic research purposes)
- **Healthcare Technologies** & Biomedical engineering
- Research solely focusing on data analysis or mathematical/statistical approaches that are not integrated into a broader technology led project e.g. data mining/re-use, development of databases for sharing research data.
- Large scale infrastructure, or direct application of off-the-shelf technology to research
- Incremental technology development that does not incorporate developments based on EPS approaches.

There are other avenues that support excellent science in these areas and the ambition of TTL is distinct, highly focused towards next generation technologies to transform research approaches in the health and life sciences.
5. Delivering TTL as a Cross-Council program
Implementation and delivery of the Technology Touching Life initiative will occur via a range of approaches and mechanisms. Interventions will need to include fostering “first-contact” between disciplines, establishing national networks, accelerating development of areas which already have some momentum, enhancing interdisciplinary peer review, and supporting research programmes of different scales. Successful delivery of the TTL strategy will also entail broad consideration of the contributory factors, including support for the people leading and carrying out the research and the availability of necessary equipment and infrastructure.

Community Building Activities
In order to enable the community to respond to the challenges set by Technology Touching Life and to develop new collaborative relationships across the physical and life sciences, a key intervention will be supporting national networks in this area, enabling the community to build capacity primed to respond to funding opportunities.

Pump Priming & Proof-of-Principle
In order to test and develop innovative and sometimes risky research at the interface between disciplines, pump prime or proof-of-principle funding will be a crucial intervention. We will explore the benefits of aligning this with national networks where appropriate. It is important to recognise that even when pump-
priming funding does not lead to a promising lead, such projects provide significant added value from the perspective of skills and expertise development that the project helps to build.

**Larger-scale Investment**

The partner Councils will publicise our cohesive approach to decision making to specifically encourage investigator-led applications within the remit of Technology Touching Life by the research community. The [Cross-Council Funding Agreement](#) allows us to act with agility to support such applications at any time through our responsive funding mechanisms.

The partner councils will seek to build on the ideas and collaborations that emerge through the Networks, maintaining momentum and community engagement in this area. The councils will work with the community and expert advisors to identify and prioritise potential future interventions which would contribute to the long term goal of supporting truly interdisciplinary research and training in this area.

We will work closely with existing investments (including the Francis Crick Institute, BBSRC and MRC Institutes and the proposed Rosalind Franklin Institute) and UK HEIs to ensure TTL complements and builds on the current UK research landscape. Furthermore, we will seek to identify and maximise opportunities relevant to TTL arising from new activities and investments, as and when they arise.

**Cross-Council Peer Review**

A key objective within TTL is to further facilitate and build confidence in peer review of proposals which lie at this interface between the physical and life sciences. The proposed approach will focus on setting and communicating clear expectations to applicants and reviewers, enhancing support for the TTL interdisciplinary interface across all BBSRC, EPSRC and MRC activities rather than instigating bespoke processes.

Aspects of the proposed approach include;

- Ensuring an appropriate mix of interdisciplinary researchers from across the remit of TTL are involved in assessment and decision making;

- Providing more direct instructions, and clarify our expectations, to reviewers and Board/Panel members regarding assessment of interdisciplinary proposals;

- Identifying a collective pool of reviewers available to all the Councils that are experienced in research spanning disciplinary boundaries, or who can recognise the added value of combining expertise, tools or techniques from multiple disciplines;
- Regularly evaluating the outcomes of activities aligning with the TTL theme and continuous improvement and strengthening of our approach.
Annex 1: Examples of Areas of Biological Challenge within TTL

The following are intended to be illustrative examples of the potential transformations which could be realised in health and life sciences research by the development and implementation of new technological approaches developed through TTL. They are not intended to be a prescriptive set of challenges or topics. The Research Councils intend to work with the community to further develop the challenges within TTL.

**Bridging length scales**

Tackling the capability boundaries of existing technologies, developing creative ways to circumvent physical limitations and integrating complementary methods will transform our understanding of the functional connectivity of processes that operate at different organisational hierarchies.

Examples:

- Addressing the gaps between the capabilities of light microscopy and structural biology imaging technologies
- Deep tissue imaging and multiscale approaches to correlate gross morphology with molecular details

**Localising and quantifying targets**

The complexity of living systems necessitates building complex models to derive an overall understanding of the processes operating in health and disease. Development of systems approaches to life science questions requires accurate localisation and quantitation of systems components to enable the development of models with realistic predictive capabilities.

Examples:

- Ultra-small scale sampling and detection of biomolecules using highly sensitive techniques to understand how composition, turnover or localisation changes in response to developmental, physiological or environmental changes.
- Novel analytical and '-omics' approaches to characterise the complete chemical composition of sub-cellular compartments, e.g. to understand and model changes in response to drug therapies.
**Insights from perturbing systems**

Altering the structure or function of a biological system and observing its response can generate a range of outputs that are informative to the understanding of normal physiology and pathophysiology. Perturbation can be internal or external in mechanism, applied in vitro or in vivo, and can reveal properties of the system that may not be apparent by observation alone.

Examples:

- Externally applied physical/mechanical stress to influence cell morphology in vitro could reveal the relationship between physical forces and biological function, informing areas such as tissue engineering and developmental biology.
- Exploiting advances in optics to harness optogenetic techniques for control of cells using light within a tissue.

**Populations to individuals**

Organisms consist of multiple components; for example, multiple cell types that make up a tissue or molecules that make up a cell membrane. While the behaviours of populations or groups of these molecules has progressed our understanding of how they function together, significant further insight is expected from understanding the impact of variation of individuals within these similar populations on biological processes.

Examples

- Implantable electrodes that can selectively modulate nerve stimulation in humans and animals
- Microfluidic approaches to separate, quantify and measure individual cells and cell types from populations

**Real-time observation and monitoring in vivo**

Instruments may require re-engineering to lessen the effects of damaging energy, mechanical and chemical inputs used during experimentation. New technologies may require novel miniaturisation and nanofabrication methods, use of advanced materials, sensors with enhanced specificity and sensitivity, or novel signal detection mechanisms
Examples:

- Real-time analysis of the movement and dynamics of sub-cellular structures to generate understanding of their responses to drug treatment or environmental stress.
- *In vivo* sensors that can detect changes in metabolite concentrations and the physio-chemical environment continuously and/or over long time periods, with in-built analytical and signal processing capabilities to reduce subjectivity and produce useful outputs for researchers.

**New modes of labelling and detection**

Detection remains a key challenge within the life sciences, owing to the complex organisation of biological structures, the diversity of biochemical targets, and problems of toxicity, selectivity and specificity. Combining these new capabilities in chemical and analytical tools to identify specific and/or complex biomolecules with innovation in sensor design and imaging platform technologies could lead to a step change in our ability to investigate key questions relevant to health and disease in a range of systems.

Examples:

- Developing novel contrast reagents and chemical probes, improving delivery technologies and reducing off-target effects, to enhance imaging capabilities.
- Development of novel sensing modalities that employ advances in materials science and nanotechnology to achieve high sensitivity and selectivity towards key metabolites.
- Novel imaging, sensor and analytical capabilities for rare molecules and molecular signatures which could enable early detection and predictive diagnosis of disease.