DID WE REALISE OUR POTENTIAL?

Celebrating 20 years of the mission led Research Councils

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Have the mission led Research Councils realised their potential? Before I try and answer this, I'd like to invite you to reflect a little about purpose, not only for the Research Councils but also for yourselves as individuals, and on the nature of leadership that brings about change.

Why is it that you do what you do – as researchers, as leaders, as administrators, and why is it the Research Councils do what they do? To quote the Pythons, why is it that you get up half an hour before you went to bed, to finish that proposal, catch that early flight or prepare that lecture? It's not getting the money – that's just a result, available from pretty much any job. And I don't mean WHAT is it that you do – the day to day tasks that take up your time – filling in forms, sitting in meetings, or HOW is it that you do it – reading papers, synthesizing ideas, designing experiments. I mean WHY do you do it? And beyond that, WHY do you choose to follow the leaders that inspire you and guide you?

Some of you may recall that August last year saw the 50th anniversary of Martin Luther King's Washington DC speech where he proclaimed 'I have a dream'. Notice he said 'I have a dream' and not 'I have a plan'! The Dream is the thing that inspires us and unites us, and that effective leaders like Dr King capture, so that we all think, act and communicate in the same way. To quote Simon Sinek's 2009 TED Talk, "People don't buy WHAT you do, they buy WHY you do it". People are inspired by what great leaders believe, even though ultimately they do it for themselves.

... riding this wave of disruption ...

We live in an era of unprecedented disruption. The current churn rate of companies entering and leaving the S&P500 means that by 2027, 75% will have changed. In 2011 Kodak was replaced by a cloud computing firm and the New York Times was replaced by Netflix. On average, glaciers have thinned by over 10 metres since 1980, and the concentration of CO_2 has increased from 280 to 380 parts per million since the pre-industrial era. Wealth and population are concentrating in cities, with middle classes booming in the BRIC countries and squeezed in the West. Here in the UK, we are privileged to live in one of the wealthiest, most cultured and most organised countries in the world, with great institutions to guide us, and great people to inspire us. So my 'Why', my 'Dream' is clear – I want to keep it that way – I want disruption to work in our favour so that we capture the value from change to the benefit of Us. I want to be part of the Next Wave, not the Last Wave, so that Britain is not only Great, (to quote the strapline on the Government's Industrial Strategy) but will continue to be Great. I believe this so much, that I wrote it into the headline on my Linked In page. I went with my 'Why' and not my 'What', because it's who I am.

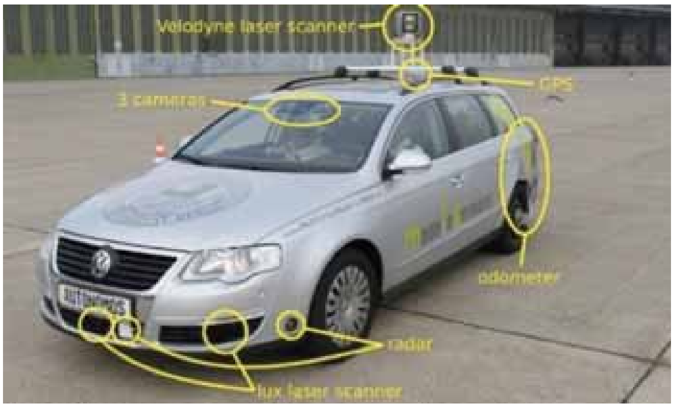
... inspired by what great leaders believe ...

Innovation is at the heart of riding this wave of disruption. It will create the new generations of products, services, and businesses that will make Britain productive and competitive internationally, help us monitor and intervene for our environment, make our cities function effectively. It's important to distinguish this Innovation from the Invention that precedes it. *Invention* for me is largely what we do here through the Research Councils, and is the process of turning money into ideas. Innovation, on the other hand, is largely what happens afterwards, and is the process of turning these ideas back into money again, but with a significantly larger transfer function! I like the strapline over the entrance to iRobot's headquarters in Boston – 'Make Money, Have Fun'. They know their Why! And the EPSRC too – 'Pioneering Research and Skills'. 'The Heart of Discovery and Innovation'. But what I'd really like is this innovation money to be sticky money – I'd like it to stick in the UK, I'd like it to stick to companies, universities and the Research Councils, and I think it's OK if some of it actually sticks to all of us as individuals too!

So how do we make Innovation happen from Invention? Well, there's no formula, and certainly no gantt chart, but there are lessons learned from exemplars that are working. For example, the autonomous car is coming, development programs are up and running in BMW, Audi and Google, and soon there will be demonstration vehicles driving around Milton Keynes as part of the LUTZ project, derived from EPSRC funded R&D at Oxford. However, this innovation really started at the break of dawn on March 13, 2004, when 15 vehicles left a starting gate in the desert outside of Barstow, California as part of a DARPA grand challenge. The goal was to autonomously navigate 142 miles across the desert to Primm, Nevada. None finished the course, and the top scoring vehicle travelled a nerve racking 7.5 miles! Not deterred, the teams came back in subsequent years, using competition to continually improve, and even raise the bar into urban environments. Similarly, autonomous underwater vehicles are now searching for the MH370 wreckage at 5000m depth in the Pacific, and Subsea7 in Aberdeen are now operating commercially the world's first Autonomous Inspection Vehicle in deep-water oilfields, based on EPSRC funded research spun out from Heriot-Watt. These also started life as freely-flooding prototypes in various AUVFests of the 1990s and 2000s. What both of these disruptive innovations have in common is the dream – I Have a Dream, not I Have A Plan. The key to reaching a tipping point where corporate interest takes over from public investment is the compelling demonstration, supported by the community, covered by media, embraced by the public, that captures the imaginations of business and market leaders, and from which a compelling disruption can flow. And one thing is sure – if we in the UK don't do it, somebody else will. So we have to compete to survive.

... The key to reaching a tipping point ...

Last year the Government launched its Industrial Strategy, and the Minister for Universities and Science launched the 8 (now 9) Great Technologies to spearhead the technology push from invention to innovation. In parallel, BIS, EPSRC and TSB have set up an unprecedented set of organisations and instruments to stimulate the innovation ecosystem, following reports from Hauser, Dyson, Witty and others. Leadership councils, special interest groups, catapults, catalysts, innovation and knowledge centres, knowledge transfer networks and more are the result. Inside the EPSRC alone, change has been everywhere. 113 CDT's have achieved impressive financial leverage and focus training around cohorts, creativity and innovation. We have impact acceleration accounts, public engagement, we write about pathways to impact and national importance in our proposals, and of course we have the REF. For the grey hairs amongst us, it's worth thinking back to how things were in 1994 – the uproar and controversy that surrounded the idea that research should have relevance to beneficiaries, and the new tick box on the reviewers' form. So as a nation we are taking the translation of invention into innovation seriously, but have we realised our potential?



Certainly there are stellar examples of success – LEDs from research into gallium nitride research, telecommunications from fibre optic research, and of course ARM. In the media, Marcus du Sautoy, Jim Al-Khallili and even Brian Cox. And the headline coverage of the Astra Zeneca takeover by Pfizer demonstrates the extent to which science and innovation are seen to be important in national life. Many more academics and their PhD students are having a go, offering themselves into CTO and engineering roles in spin outs, recognising that effective technology transfer is about the movement of people, not just licences.

So we have made great strides, and the juggernaut of culture change is rolling. No longer is it the case that our Researchers are from Venus and Industrialists are from Mars. The UK continues to punch above its weight in scientific output, citations and international collaboration, second only to the US, partly thanks to ring fenced Government funding and FEC on grants. But set against my 'Why', we haven't yet realised our potential. Where are our Googles, Facebooks, Apples and Amazons? Even Estonia managed to produce Skype! And why are there so few with a research and innovation background in this weekend's Sunday Times Rich List – including me? It only takes a mere £85M to make it into one of the top 1,000!

... juggernaut of culture change is rolling ...

Government and its agencies have created a stimulating and richly supported environment to promote UK invention and innovation. Ultimately, whether or not the Research Councils and the TSB realise their potential, is actually up to Us – the recipients of their support. Do we treat it as a form of public subsidy for our lifestyles and our businesses, or do we think of it as an investment to be nurtured, from which great things might flourish, that will keep Britain ahead in a disruptive and globalised world?

So I leave you with one challenge, to help us realise our potential. Can you write down your 'Why'? Not your 'What' or your 'How', but your 'Why'. And can you write it in one sentence that you can say in the lift or to your teams. Effective leaders start with 'Why'.

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We live in an age of rapid change. This is particularly so in science and technology where the rates of change in many areas are exponential. Over the past 50 years the computing power on a specific area of material has doubled roughly every two years – following what has come to be known as Moore's Law. When Moore wrote his 1965 paper he only had four data points – the earliest in 1962 – but the line he drew through them leads to the present we are now in. In 1972 the Intel 8008 microprocessor had 3500 transistors forty years later the Intel Ivy Bridge processor contains 1.4 billion.

These rates of change apply at every level in computing – not just to how many components we can fit on a chip or the minimum feature sizes used to build the chips in our computers and electronic devices, they apply to the speed of a microprocessor, they apply to the amount of information we can store in our memory technology.

... Computational tools and methods have refashioned science ...

This computational power has underpinned much other progress in STEM – whether it is proteomics or synthetic chemistry, astronomy or cryptography.

Computational tools and methods have refashioned science and technology. The digital ecosystem that has emerged has shaped the way research is conducted. The collection, analysis, interpretation and publication of scientific results is mediated by the Internet and World Wide Web, a social network of scientists collaborate and compete through their agency.

It is increasingly apparent that the problems we face nationally and internationally, locally and globally demand innovation, co-ordination and collaboration. This will be a defining characteristic of STEM research as we move further into the 21st Century. The Research Councils have been important in supporting and promoting this transformation in the nature of STEM – as the world has become a mixed reality of the digital and the physical.

Twenty years on from the ROPA report we can say that UK Research is World Class. Evidence can be provided from numerous sources but one recent BIS 2013 report[1] shows that the UK with just 0.9% global population and 3.2% of research expenditure is responsible for 4.1% of the world's researchers, 9.5% of downloads and 15.9% of the world's most highly-cited articles.

The ubiquity of data about STEM on the Web enables us to be much more precise about the impact of the investments the Research Councils make. Whether it is value for money, citation rates or international benchmarks.

... much more precise about the impact of the investments ...

The mission driven characterisation of our Research Councils has enabled a rational structure for funding research to emerge. This has helped promote collaboration and coordination. The challenge is around the right balance of investments. Are we able to be as agile as we need when the pace of innovation is accelerating?

Notwithstanding this challenge of balance and agility the Research Councils must take a significant part of the credit for our international performance.

But there are other reasons why our STEM landscape is in reasonable shape. Learned Societies and Professional Bodies have also become more mission driven. They have become more collaborative as they recognise the interdisciplinary challenge of many of the problems confronting us. For example, the Royal Society and the Royal Academy of Engineering do significant work together.

Another reason that the Research Councils have been successful is that STEM is seen to be indispensable to the security and the economic and social well-being of the country.

One of the notable features of the past two decades has been the continuity of the Ministerial appointments that oversee STEM and Research Council supported R&D. Two incumbents between them held the office for 12 years (David Sainsbury 1998-2006, David Willets 2010-14). The commitment of these Ministers from across the political divide did much to secure the funding of STEM as well as associated R&D within Government.

We now have a network of Chief Scientific Advisers, across Departments of Government and across the devolved Administrations; there are Horizon Scanning and Foresight activities within a Government office of Science and a Chief Scientific Adviser, providing advice at the highest level. A number of Select and other Committees focus on S&T within Parliament. This has both raised the profile of STEM but also helped furnish policies with real evidence bases.

... interdisciplinary challenge of many of the problems ...

The health of STEM in the UK might be regarded as surprising given our relative under-investment in it. The facts are bald and striking. The most recent global comparative data from UNESCO 2008-10[2] indicates that the UK invests 1.7% of GDP in S&T research. This is against a G20 average of 2.04%; it certainly contrasts with the aspiring knowledge economy that is South Korea which invests 3.7% of GDP.

If we take public funding of R&D the position is even starker. The G8 average is .79% of GDP – in the UK it is .57% – hardly an inspiring level of investment given the inspirational work that gets done.

Whilst we certainly punch above our weight in terms of the impact of the work funded by the Research Councils the UK as a whole still fails to exploit the fruits of its S&T at scale. The recent REF (Research Excellence Framework) exercise supervised by HEFCE is furnishing ample numbers of impact case studies that represent diverse forms of exploitation from the research done in UK Universities[3]. But the overall problem remains one of scaling. We are very successful at generating innovative start-ups that invariably are acquired by foreign companies. We produce too few global brands from our world-class research. The reasons for this are well rehearsed and being currently reviewed again by the Information Economy Council[4]. But we do not appear to have the investment infrastructure, incentivisation, inclination or culture to successfully scale our innovation.

... citizen level engagement with sciences ...

A noteworthy development over the last twenty years has been the extent of citizen level engagement with science and technology. There has always been an aspiration that STEM subjects should better engage with the general public. The development of the Internet and World Wide Web over the past two decades has provided a dramatic new means by which individuals can participate directly, as never before, in the process of discovery, analysis and innovation.

... much wider participation in the knowledge economy ...

As of July 2014 members of the public had contributed hundreds of millions of classifications to the citizen science astronomy site Galaxy Zoo. Beginning in 2007 astronomers at the University of Oxford had built a site that enabled people to quickly learn the task of classifying images of galaxies. The first project comprised a data set made up of a million galaxies imaged by the Sloan Digital Sky Survey – far more images than the handful of professional astronomers could deal with. Within 24 hours of launch the site was achieving 70,000 classifications an hour. More than 50 million classifications were received by the project during its first year, contributed by more than 150,000 people and resulting in many scientific insights.

From 2009 as the UK Government began to make more of its non-personal public data openly available a broad range of community based groups have taken the data and built innovative applications using it. Individuals, groups, public bodies, private corporations large and small have benefited from the availability of data at scale on the Web. News businesses, new applications and new services have been built using this new data resource. Moreover, the skills needed to exploit this new abundant resource are being fostered, in part, by the development of computing learning platforms such as the UK's Raspberry Pi.

... punch above our weight ...

When Tim Berners-Lee famously tweeted at the opening of the London Olympics that "this is for everyone" – it spoke to new possibilities and new realities – realising our potential through much wider participation in the knowledge economy.

Whilst these are positive developments there are very real challenges confronting research and development in our Institutions of Higher Education. As a consequence there are real challenges facing our Research Councils if they are to continue to be successful.

The funding of UK HE is being radically rebalanced. Universities are increasingly dependent on the money received from teaching. In general research loses money. Even on the full economic cost model that Research Councils use to fund Universities only 75% of costs are recovered. Increasing numbers of Research Council initiatives require Universities to match fund or else make substantial contributions towards the cost of doing research. Universities must often find 50% of major equipment costs. These are real and material concerns – the system is under stress. For all our success in realising our potential we need a secure and well-funded R&D capability if it is to continue into the future.

References

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SYNTHETIC BIOLOGY: writing the future with biomolecules

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Summary: Synthetic biology is an emerging field that aims to make the engineering of biology easier, more reliable and more predictable. It combines understanding and methods from the biological and physical sciences with engineering principles and approaches. It is a truly multidisciplinary endeavour that requires input from experimental scientists, theoreticians, engineers and social scientists to succeed. If it takes root, the promises are considerable, and synthetic biology will have an impact on how we think about basic research in the biological sciences through to how we exploit it in the biotech, pharma and agrichem sectors. Through coordinated efforts from government, the Research Councils, industry and the academic research community over the past 7 years, the UK has built an extremely strong base for synthetic-biology research. This is largely founded in the universities and basic-research facilities, but there are strong links with industry. The challenges ahead are to grow this base to deliver high-quality basic science, which, in turn, will lead to applications underpinning UK SMEs and industry.

Synthetic biology is beginning to mean a lot of different things to many different people. Therefore, for clarity: in my view, synthetic biology simply aims to make the engineering of biologically inspired systems more predictable and more useful. Ideally, it involves the development and combination of experimental components and methods (some people call these biobricks) with mathematical and computational modelling to deliver solutions to biological problems. These could include different approaches in fundamental science, such as exploring simplified chemical systems that mimic biological molecules, cells and functions; or improvements on how we produce drugs, biofuels and foodstuffs in bacteria, yeasts and plants more efficiently.

... The UK has an extremely strong base for synthetic-biology research ...

I say "ideally" because the current vision for synthetic biology involves applying concepts such as *abstraction, modularisation,* and *standardisation* to biology. However, synthetic biology is still in its infancy and biologists do not fully agree on what the *standards* should be; or understand what can be *abstracted* from biology; or even know with certainty whether or not biological systems really are *modular* allowing them to be chopped and changed at will. As a result, it is not possible to say where this new field is heading, or what approaches will succeed ultimately. One thing is clear, however: the synthetic-biology wagon is rolling, it is picking up steam, and it will change the way that we think about biology and how we exploit it. The UK must be part of these developments; indeed, we must help lead and shape them both nationally and internationally.

Broadly speaking, there are four approaches to synthetic biology: first, one might consider a top-down approach that I refer to as Genome Engineering, and others call Synthetic Genomics. It is now possible to synthesise chemically and stitch together large pieces of DNA of the size of whole chromosomes, or even small genomes from natural organisms. The advantage of doing this rather than using traditional DNA manipulations is that in this process unwanted DNA can be excised, and new genes with specific uses can be incorporated. The resulting synthetic DNA can be 'booted up' inside living cells, and selected genes used. This approach is championed by George Church, J Craig Venter and others in the USA. Notable UK activity is from Imperial College who contribute to the Yeast 2.0 project.

In a second approach, which I call Biomolecular Engineering and is also known as Metabolic Engineering, useful genes, or even whole pathways of genes, are cloned from one organism into more tractable hosts, usually bacteria or yeasts. Here the aim is to get the best of both worlds and produce functional molecules, such as biofuels, fine chemicals or pharmaceuticals, cheaply in bulk and in organisms that are easy to grow. One of the world leaders here is Jay Keasling at Berkeley. The UK has considerable strength in this area both in academe and industry, and particularly in enzyme engineering.

The third approach is Biomolecular Design. It is distinct from those described above in that the molecular targets are created *de novo*. As such, this approach is more basic, higher risk and further from applications than the first two approaches. That said, if we do manage to make stable and functional proteins or other biomolecules to order, it would place us in a strong position to engineer known or novel proteins for useful purposes, a principle at the very heart of synthetic biology. The UK is strong in this area with a good base of young and established academic research groups, including experts at the University of Bristol.

The final approach, Protocell Construction, is very much at the basic-science end of synthetic biology. Little research in this area can currently claim to be geared to foreseeable applications. Its aim is to produce entities that mimic the properties and behaviours of biological cells, but without using any of the natural building blocks, eg DNA, lipids, proteins.

... One ambition is to build synthetic cells ...

The ambition is to build synthetic cells in order to understand the rudiments and origins of natural cellular systems. The UK has growing activity in this area.

I will now describe what my group at Bristol does. Although DNA is the ultimate programming language of biology, we do not work at that level yet. We design and engineer protein molecules. This is because proteins are the workhorses of biology: they provide much of the structural scaffolding found within and outside cells; they help store, transfer and translate the genetic information in biology by interacting with, manipulating and controlling DNA and RNA molecules; and they provide biology's catalysts, making sure that reactions that convert one type of energy or molecule into another happen at the right time, in the correct place, and at a useful speed. In short, proteins do pretty much everything in biology apart from storing and passing on the genetic information.

... New genes with specific uses can be incorporated into biological systems ...

In these respects, engineering protein molecules would seem an eminently sensible place to begin in synthetic biology. However, this turns out to be difficult: unlike the relatively straightforward codes that link the linear chemistry of DNA and RNA molecules to their structures and functions, we do not have similar instructions for how to write functional pieces of proteins. This is because protein functions are much more varied and complicated than those for DNA and RNA. It gets worse: in many cases, and unlike mutations in DNA and RNA, we cannot easily predict how changes in protein chemistry might affect the protein's shape, stability and function. This is precisely why the more-traditional synthetic biologists (sensibly) choose to engineer DNA and the genes that encode natural proteins, rather than starting from scratch and inventing new genes and new proteins; it is these natural genes and gene products that synthetic biologists often refer to as biobricks.

By analysing natural proteins, my group is learning some of the "rules" by which they are put together and function. We then apply these rules to engineer existing natural proteins to alter their functions, and also to create completely new proteins *de novo*. Protein structures and functions that we are targeting include: channel-forming structures that can span membranes to communicate between cells and sense the environment; fibrous proteins that can be induced to form gels to support the growth of human cells and tissue for use in regenerative medicine; and large cage-like assemblies of small protein modules, which might be used to deliver drugs to specific cells in the body.

... Synthetic biologists will be creating new biomolecules, which may create public unease ...

I close with two further topics with national and global impacts: the first is about funding; and the other relates to topics such as public perception, regulation and responsible innovation around synthetic biology.

Regarding funding, the UK leads the way. This began with the RCUK's establishment of 7 Synthetic Biology Networks in 2007, which started to mobilise the research community. In 2012 a small group, established by David Willetts MP, published the Synthetic Biology Roadmap for the UK. Key recommendations of this were the creation of an Innovation Knowledge Centre, Centres for Doctoral Training, Research Centres, and Centres for DNA Synthesis. Over the past two years, and with Research Council, Government and industrial funding all of these have been achieved. These foundations still need to be supported with responsive-mode funds, seedcorn investment for spinning out applications and so on. However, the key message is that this is an extremely strong and healthy start for UK synthetic biology, which is unparalleled anywhere in the world.

My final thought might be seen as a word of warning. We have to tread carefully, and to be seen to be doing so, as we step into this new territory. Synthetic biologists will be creating new biomolecules; they will be questioning what life is; and they will develop capabilities to engineer living cells and organisms beyond those currently possible, or even currently imaginable. All of this makes lay people, pressure groups, regulators and even some scientists feel uneasy. We must tackle this head-on, through informed and open discussions with all parties. Above all, we must illustrate the benefits of synthetic biology while being cognisant of the concerns of others. My own views on this align with many more-eminent synthetic biologists: that is, we are likely to pass more opportunities over by not venturing into synthetic biology, than we are to risk harm to our planet and the future of the human race by embracing it. We must do synthetic biology, we must do it well and responsibly, and we in the UK must take the lead on this.