New Statesman

# Biotechnology: a greener future

## How tech is helping to build sustainability

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# The road to a better normal

## **Professor Rob Field**, director of the Manchester Institute of Biotechnology (MIB) at The University of Manchester, discusses the potential of biotechnology

When I was appointed Director of the MIB in January, the temporary closure of the institute three months later wasn't something I envisaged. However, as the Sars-CoV-2 coronavirus swept the globe, our students and staff embraced a life of home working. As we adapt to a "new normal", many are asking if Covid-19 could be the catalyst for a better normal.

The pandemic has thrust science and scientists into the spotlight in a manner not seen before. Chief scientists and medics have stood next to politicians to answer questions from members of the public desperate for science to solve the crisis. And the scientific response has been unprecedented. Within a fortnight of the World Health Organisation being informed of a new disease, the virus's genetic sequence was analysed and shared, and now the expectation is that records will be broken in the race for effective vaccines. In the UK we can be proud that our universities, industry and NHS have been at the forefront of research. Scientists have refocussed their energies to tackle the disease. I speak from personal experience; the firm I co-founded, Iceni Diagnostics, adapted our influenza detection technology to produce triage testing kits for coronavirus, supported by Innovate UK funding.

But we need to remember that other global challenges remain. Antimicrobial resistance has not gone away while we focus on Covid-19, and although carbon emissions have dropped during the pandemic, climate change is still very real, and the post-Covid recovery cannot be fuelled by unsustainable consumption. We need a better way of bouncing back.

This supplement will give a glimpse of how biotechnology could help support a sustainable economic reboot. There is a clamour for such a response: in June, a letter to Boris Johnson signed by 213 businesses and business networks pledged support to rebuild the UK economy while accelerating decarbonisation.

Aligned to this goal, the efforts of The University of Manchester in developing biotechnology were recognised in 2019 by the award of the Queen's Anniversary Prize for Higher and Further Education, the sector's most prestigious accolade. The prize recognised the MIB as "a leader in the UK's strategic development of biotechnology and biomanufacturing, through innovative technologies in partnerships with industry".

Note that the partnership aspect is key: innovation with impact cannot occur in an academic silo, but requires close collaboration with industry to enable the translation of science into society.

Covid-19 has shown science at its best: agile yet focused, collaborative while competitive. We can learn from the experience to develop a more resilient and sustainable world. Biotechnology has a large part to play in supporting such a "Clean Growth" recovery.

*Contributions from Dr Kirk J Malone*

**For more information please visit: www.mib.ac.uk**

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# Biomanufacturing: a path to sustainable economic recovery

By **Professor Nigel Scrutton** and **Dr Kirk J Malone**, the director and director of commercialisation at the UK Future Biomanufacturing Research Hub

Industrial biotechnology (IB) is the term for the application of nature's catalysts – enzymes – and biological systems to produce chemicals, materials and energy. The concept is not new: traditional food like bread, cheese and yoghurt are all made using microorganisms. Using the latest developments in biotechnology we are now able to take this approach a step further and engineer nature to produce the medicines, plastics and fuels that underpin society. Through successive investments in the UK's research base we have world-class academic capabilities, creating new approaches that promise to transform bio-production. However, these developments are yet to transition through to large-scale mainstream use.

Let us consider the production of chemicals. The chemical industry is vitally important to the UK economy, with 3,608 businesses employing 153,000 people, giving £19.2bn gross value added on a turnover of £55.5bn. However, the vast majority of this production is from non-renewable petrochemicals. This is at odds with the UK's Paris Agreement obligations to reduce greenhouse gas emissions by 80 per cent by 2050. We need to change.

The OECD has previously highlighted IB as a key enabler to save energy and reduce $CO_2$ emissions. Successive UK governments have also understood the importance of IB; the vision outlined in the 2016 paper *Building a High Value Bioeconomy* outlined the UK's potential to become the "location of choice for global investment in the bioeconomy", to become a "major exporter of process technologies and business models".

Global society needs new technologies to manufacture chemicals essential to modern life in ways that are decoupled from fossil fuels. New alternative biomanufacturing routes promise the opportunity to convert sustainable carbon containing feedstocks, such as food waste and even $CO_2$, into everyday essentials. The UK has the potential to be at the vanguard here: it is recognised as a globally leading nation in a number of important areas of innovation that underpin the bioeconomy, with an excellent policy environment and a high calibre of scientists and intellectual property protection, but often falls down on the required R&D spending.

## The UK could be in the vanguard

As a measure to partly address this capability gap, the UK Research and Innovation-funded Future Biomanufacturing Research Hub (FutureBRH.com) was established in 2019. Based at the Manchester Institute of Biotechnology (The University of Manchester) with spokes at Imperial College London, UCL, Nottingham, the UK Catalysis Hub, IBioIC (Industrial Biotechnology Innovation Centre) and CPI (Centre for Process Innovation), the Future BRH is pioneering new bioproduction technologies. The purpose is to research sustainable biomanufacturing in four key sectors: pharmaceuticals, chemicals, fuels and materials. Positioned at low technology research levels (TRLs 1-3), the aim is to support novel biomanufacturing processes via industrial and academic collaboration. To this end, the Future BRH has established partnerships with major UK and international companies in the petrochemical, personal care and pharmaceutical sectors, along with a number of SMEs with innovative

The Manchester Institute of Biotechnology

technologies. Together, FutureBRH and its partners are researching new biosynthetic routes to medicines, polymers and transport fuels based on sustainable, low-carbon materials.

This focus on biomanufacturing research follows previous strategic investments made by the UK Government in discovery bioscience, in the form of synthetic biology research centres (SBRCs) that have provided new capabilities for the engineering of biology. These centres, at the universities of Bristol, Edinburgh, Imperial College and Manchester, have been at the forefront of creating "biofoundries" equipped with state-of-the-art robotics and analytical equipment to allow the rapid engineering of benign yeast and bacteria. These centres are connected to the Global Biofoundries Alliance to ensure best scientific and ethical practises are shared internationally.

The UK has a firm research base from which to grow a vibrant biomanufacturing economy. The opportunity now facing the government and the manufacturing sector is to implement these frontier technologies at scale for next-generation chemicals biomanufacturing.

The Covid-19 pandemic has put a renewed focus on the UK's supply chains and manufacturing resilience. A shift to bio-based production would reduce our dependence on fossil resources and could transform incumbent processes based upon petrochemicals. Currently, the UK's chemical production is in four main clusters: Hull, Teeside, Runcorn and Grangemouth. Efforts to stimulate biomanufacturing in these areas would be aligned with the "levelling up" strategy, creating high-growth markets. For instance, the market for bio-surfactants is growing at 5.1 per cent compound annual growth rate (CAGR), with demand for bio-plastics pushing growth by 28 per cent CAGR. By 2025, the global IB market has been estimated to be worth up to £360bn.

There is a risk to the UK economy of not supporting biomanufacturing. The pharmaceutical, chemicals and materials manufacturing sectors are highly competitive and global in scale. Failure to support the move towards sustainable biomanufacturing may have a detrimental effect on the existing chemical sector as other countries leapfrog the UK. There is increasing competition from emerging markets, and other developed nations are investing heavily. In Denmark, the Novo Nordisk Foundation has just awarded a grant of £100m to the DTU Biosustain research centre for the sustainable production of biochemicals and green consumer products.

## We must be strategic to build a future

However, the UK cannot do everything and we should be strategic. We do not have the sustainable feedstock capacity to be a significant manufacturer of bulk, low-value bio-based chemicals. Instead, the UK could develop the innovation expertise to export processes and technologies to manufacturing organisations overseas. The UK could focus on manufacturing value-added products, and pursue other opportunities though international partnerships. Further investment to pull through emerging capabilities in chemicals production from novel engineering biology platforms into mainstream manufacturing will push the UK to the front of global markets.

Biomanufacturing requires cross-disciplinary skills, bringing together chemistry, computation, process engineering, microbiology and synthetic biology, in conjunction with research and innovation. But the transition to a sustainable bio-based future cannot occur in isolation in universities, it requires true collaboration with industries across multiple sectors. The step-out nature of this research and development will require co-investment from governments and international bodies to de-risk the science for companies, especially for SMEs. We understand the challenges here: our own spin-out company, C3 BIOTECH, is developing "fuel from waste" technologies that will benefit from economies of scale. With the right investment, biomanufacturing could support the UK's clean growth agenda to decouple pollution from economic development, and allow us to transition to a sustainable manufacturing era post-Covid. ●

**For more information, please visit: www.mib.ac.uk**

**Dr Yvonne Armitage, director of Bio-Key Ltd, on getting the biotechnology message across to government and the wider public**

# How to communicate industrial biotechnology and the bioeconomy

"What's in a name? That which we call a rose/By any other name would smell as sweet." What does Juliet mean exactly when she says this often misquoted soliloquy in Shakespeare's *Romeo and Juliet*? Evidently, she is complaining that a name is meaningless and acts only as a label to distinguish one thing from another. Thus, even if the rose was called something else it would still be as sweet. This applies in many ways to industrial biotechnology (IB) and more broadly the bioeconomy.

Biotechnology is defined simply as a technology that uses living organisms or systems derived from living organisms to make things. But put the word industrial in front to describe the exact use and it somehow makes it less attractive, conjuring images of dirty factories and waste rather than simply pertaining to aspects of industry.

So why are IB and the bioeconomy not commonplace nomenclature in our everyday lives, and why is it important that they should be? To most people the "names" industrial biotechnology and bioeconomy are meaningless, but IB has the potential to help solve some of our current and future societal challenges and is central to the success of the bioeconomy, which simply put is any economic value derived from bio-based products and processes. IB has the capability and the power to enable us to create new medicines and healthcare products, increase the efficiency of food and feed production, help mitigate climate change through the development of cleaner, greener manufacturing processes, to use waste as a feedstock, as well as to create new products that cannot be made any other way. This is undoubtedly the message that we need to get across to both policymakers and the beneficiaries of IB. Every citizen of the UK should understand that a thriving bioeconomy could result in more sustainable living.

Before the publication of the *National Bioeconomy Strategy* in 2018, a survey that asked 1,000 UK citizens if they had heard of the bioeconomy was carried out. Seven out of eight respondents said no; of

## How can we make biotechnology commonplace?

Prince Charles visits a biotech research centre in Havana

those that had heard of the bioeconomy, 94 per cent said it was important. When given more information on the bioeconomy, most participants (87 per cent) thought it was fairly important or very important, indicating that having the right approach and using the right words and information to ensure engagement in a positive way is essential.

The bioeconomy is complex and has an impact across a range of sectors from agrifood to health and from chemicals to transport and energy; so clearly a single explanation will not work and a range of clear, concise and compelling messages needs to be created. Words like biodegradable and biocompostable are used interchangeably and are not properly understood. Bio-based, bio-derived, natural, sustainable are all used and again the terms can be confusing. So how can we ensure that IB and bioeconomy become as commonplace, understood and accepted as digital technology?

The UK IB community knows that there is a need for consistent messages to be developed that clearly articulate the benefits of the technology. This will vary depending on the audience. For policy and decision makers an identified catalogue of successful IB products and processes, together with the need for investment and regulatory framework support, would help. In order to engage a wide range of stakeholders, information that extends beyond the current IB community is needed. And, importantly, inspiring the next generation of school-age students to become scientists and entrepreneurs in this exciting area of technology development is essential.

In recent years there have been a number of resources in the form of videos, booklets and courses that have been generated to educate and inform, that could be more widely promoted.

How to communicate the bioeconomy has been covered in a number of projects funded by the EU. "The RoadToBio" developed a roadmap for the chemical industry to help them understand how to support the aspiration of achieving a 25 per cent share of bio-based products in the organic chemical industry by 2030, compared with 10 per cent in 2016. The main project output was a strategy with accompanying action plan. Importantly, however, an engagement document was delivered that focused on key messages for communication about bio-based products. It provided communication tools to promote bio-based chemicals and easy-to-read information on the roadmap and how to customise the key messages for different target audiences and sectors. Another project, BLOOM, focused entirely on "Boosting European Citizens' Knowledge and Awareness of Bioeconomy Research and Innovation". Again, a range of tools including videos, podcasts and webinars aimed at schools and general public awareness was promoted online and via hubs.

"Very clear, non-ambiguous messaging is needed, but it's in short supply," said Anton Holland, a science communication expert, at the 13th International Congress on Biofuels & Bioenergy and Biofuels & Bioeconomy. "Understanding these varied audiences, knowing how to craft clear messages, and understanding effective approaches like plain language communication and data visualisation are essential tools for all scientific and business professionals whose aim is to advance any aspect of the bioeconomy."

There is no doubt that effective and articulate communication of the opportunities and benefits of IB and the bioeconomy is essential to expedite its widespread use across multiple sectors and to help drive consumer uptake and demand for cleaner, greener products. As an enabling technology IB is simply a member of the toolbox available to researchers developing new products and processes and the bioeconomy. It is absolutely clear that in order for IB to become "business as usual" in multiple industries there needs to be consumer pull, matched with development of world-class technology and conversion to economic value. Ensuring everyone is clear about the technological and socioeconomic benefits should be an overarching aspiration for those delivering these messages to our decision makers and future generations.

IMAGE: RAMON ESPINOSA/AFP VIA GETTY IMAGES

# The race for vaccines

The biopharmaceutical industry is working to bring therapies and vaccines to patients worldwide, says FUJIFILM Diosynth Biotechnologies chief executive officer **Martin Meeson**

FUJIFILM Diosynth Biotechnologies (FDB) is a contract development and manufacturing organisation (CDMO). It offers complete solutions to the biopharmaceutical industry – from preclinical investigations and process development to commercial current good manufacturing practice (GMP) production, fill-finish and final product packaging. It brings its expertise to support companies that are developing therapies and vaccines all the way through the drug development journey.

**Can you walk us through the basics of biotechnology?**

**MM:** Biopharmaceutical manufacturing uses living cells to produce molecules that are too large and too complex to synthesize chemically. This manufacturing is enabled by recombinant DNA technology. This means that genes are engineered into different systems for expression in host cells. There is a wide range of modalities, which include cell culture, microbial fermentation and viral vectors, to mention the most commonly seen in our industry.

**How do you work with other organisations?**

**MM**: As a CDMO, we collaborate with our customers to support them as they advance their medicines through the drug-development process. It is very important to note that our customer owns the process and the product. We can support from the very early stages all the way to providing commercial supply once the products have been approved by the regulatory agencies. As a CDMO we work with a variety of customers, some developing vaccines, some gene therapies, others therapeutics, to name a few. Because of this diversity, drug developers have a variety of requirements. This creates an ever-changing development and manufacturing portfolio that we manage as an organisation.

## The drug development process can be 10-15 years

## How do companies select a CDMO?

**MM**: Customers demand quality, speed and flexibility. Their selection criteria usually involves reviewing a CDMO's technical expertise to develop processes that can be scaled up as demand increases. Customers also consider manufacturing capabilities and available capacity. This is important as customers are driven by timelines. Having a strong compliance track record is an essential part of the selection process. Our quality systems are constantly evaluated through due diligence, customer and regulatory agency audits.

## What does it take to make a biologic therapeutic or a vaccine available to patients?

**MM**: The drug development process can range from ten to 15 years, not including the discovery and very early development stages. This is driven by the need to have stages during human clinical trials, which are typically phase one to phase three. As the product meets clinical trial endpoints, it moves to the next phase. As it moves the number of patients dosed usually increases, all depending on the indication, patient population, frequency of dosing, among many other factors.

As a CDMO, having the ability to scale up processes consistently while meeting the critical quality attributes of the product is essential. One point to make about this process is the current race to deliver a Covid-19 vaccine and other therapeutics to treat Covid-19-related ailments. The challenge that we now face as an industry is that we need to do what takes years at an expedited rate. We have a desperate need to deliver vaccines that will stop the spread of the Covid-19 virus and therapies to halt the mechanism of action inside the body once a person is infected.

## What is the role of a CDMO such as FUJIFILM Diosynth Biotechnology during this crisis?

**MM**: The current pandemic is a complex and challenging situation that has brought together a wide array of parties from private industry, governments, regulatory agencies, academic institutions, suppliers and transportation, to name but a few. There is, of course, the identification of potential vaccines and therapeutic agents and moving them quickly from a research setting into human trials. As this is happening, there is the question of the supply chain to support the efforts of all these groups.

How are they going to deliver the needed doses, whether it is a vaccine or a treatment, globally? Having the ability to move things swiftly into GMP production is extremely important. As a CDMO we are playing a role in this space as we have operational capabilities that can (and are) being quickly ramped up. We have a global footprint with facilities in the United States and Europe that can accommodate the different modalities explored today for Covid-19.

## What are other challenges that you see in your industry at this time of Covid-19?

**MM**: The challenge we have today is to prepare for the future. In order to do this we all need to think of the questions that we need answered in order to provide a solution. We need to strive for balance.

There is a need for lean capacity all over the world, there is a need for a supply chain that will allow for these products to be stored (think future stockpiles) and delivered all over the world. The pandemic has created a global level conversation that we must continue.

# Biotechnology: the sector in numbers*

## The data behind the burgeoning technology, one of the keys to the UK's sustainable future

**80%**

Reduction in greenhouse gas emissions necessary to meet Paris Agreement targets. The OECD says industrial biotechnology (IB) will play a key part in this, saving energy and reducing demand.

**10%**

Employment in industrial biotechnology increased **10%** per annum between 2014 and 2016.

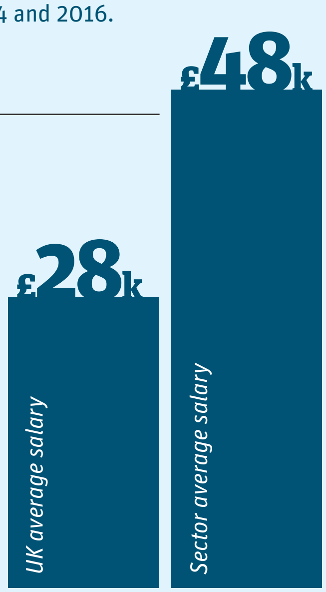
### Employment, growth and Gross Value Added (GVA)

Biotechnology is a fast-growing industry, generating **£3.7bn** in revenue and employing **14,000** staff.

**£19bn**
The GVA of the UK chemical industry

**3,608**
businesses

**153k**
employees




The average salary in the sector is **£48k**. That's **£20k** above the UK average.

## Industrial biotechnology can sustainably produce:

- Personal care products
- Transport fuel
- Biodegradable plastics
- Detergent enzymes
- Pharmaceuticals
- Perfumes

## The benefits of industrial biotechnology

IB products could achieve the equivalent $CO_2$ reductions of taking **490 million** cars off the road.

**£4.5bn** gross value added and **63,000** jobs from "downstream" effects of industrial biotechnology and the sectors using it.

**2.5bn** tonnes of $CO_2$ could be saved every year with the development of IB products.

The development of IB products could save the equivalent of a **68%** reduction in EU total emissions.

**$36bn** worth of markets that IB has the potential to disrupt.

* FIGURES PROVIDED BY THE UNIVERSITY OF MANCHESTER AND THE INDUSTRIAL BIOTECHNOLOGY LEADERSHIP FORUM

# Industrial biotech is taking the UK towards net-zero carbon


**Stephen Webb**, senior portfolio manager at the Biotechnology and Biological Sciences Research Council, on how academia and industry are collaborating to support the UK's green growth future



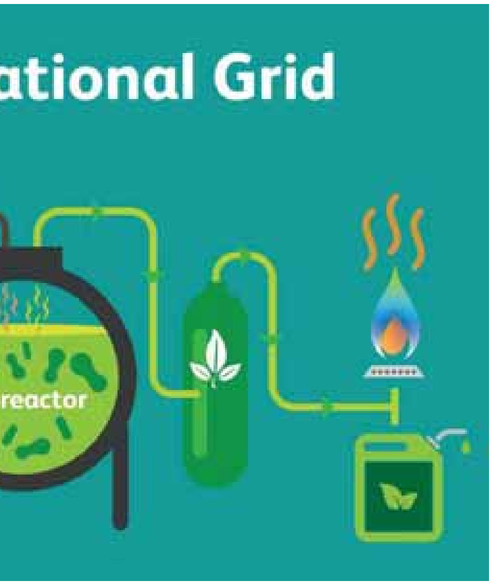
UK industry is directly responsible for a quarter of the UK's greenhouse gas emissions. Industry uses fossil resources such as oil, coal and gas as the raw material to create a range of products, including plastics, bulk chemicals and fertilisers, as well as to provide heat and power for industrial processes such as steelmaking. A by-product of both production and combustion is carbon dioxide ($CO_2$). This gas is almost entirely released to the atmosphere and is thereby a major UK contributor to climate change.

The challenge is to provide alternative sources of raw material and fuel that release no more $CO_2$ into the atmosphere than they take in or, better still, that reduce $CO_2$ levels. When biomass, such as trees from managed forests, is used as the raw material, it can be $CO_2$ neutral, also known as carbon neutral, because no more $CO_2$ is released than was taken in by the tree during its growth. If that released $CO_2$ is itself used as the raw material for further manufacturing processes, and transformed into products such as textiles, paint or insulation, then the $CO_2$ is locked away and the overall process is carbon negative.

Industrial biotechnology is the use of biological resources, including trees, other plants, algae and bacteria, to produce and process materials and chemicals of industrial and societal value. The ability to precisely manipulate the genetic make-up of living organisms has given fresh impetus to industrial biotechnology and is enabling a transformation of $CO_2$-intensive industries.

There are many examples of industrial biotechnology in action. Bacteria can transform industrial waste gases into methane, replacing fossil natural gas as a fuel source and saving thousands of

## Turning CO2 into new products locks it away




**The University of South Wales has been working with NiTech Solutions Ltd to develop a new bioreactor that could use bacteria to convert thousands of tonnes of industrial waste gases each year into a green energy source**

tonnes in $CO_2$ emissions if implemented at full scale, as shown by the University of South Wales and NiTech (see figure). Perennial *Miscanthus* (elephant grass) is being grown by British farmers as a power station fuel in a carbon-negative process – some of the $CO_2$ absorbed by *Miscanthus* as it grows is transferred into the soil and remains there after harvest – and Aberystwyth University and Terravesta are leading efforts to identify optimum *Miscanthus* varieties and growing protocols. Biodegradable plastics are being made from biomass by companies like Biome Bioplastics, in collaboration with several UK universities, without the need for fossil resources. Engineers from the University of Nottingham have demonstrated that genetically-engineered bacteria can transform $CO_2$ from steel plants into industrial chemicals including acetone and isopropanol, displacing petrochemical sources. Enzymes from bacteria have been engineered at the University of Portsmouth to rapidly decompose PET plastic – used for most drinks bottles – enabling new PET plastic products to be manufactured without further raw material input (currently from fossil resources) and, as a bonus, simultaneously avoiding plastic pollution.

The Biotechnology and Biological Sciences Research Council (BBSRC) – part of UK Research and Innovation – plays a vital role in developing the collaborative research ecosystem that is driving industrial biotechnology forwards. It is the principal public funder of UK research and innovation activities for future bio-based manufacturing. It collaborates with academia, industry and government to establish basic scientific knowledge, develop biotechnologies and advance their translation for the benefit of society and UK plc.

Ten years ago, the UK was not in a position to profit from advances in industrial biotechnology. To address this, BBSRC built and nurtured a series of UK-based networks that link academics, businesses and policymakers. This key initiative has resulted in exponential growth of the industrial biotechnology community and brought in many players that had not previously thought that industrial biotechnology had something to offer them. This community is now producing valuable outputs that contribute to reducing the carbon usage of UK industry.

BBSRC's investments were critical to the progress of all the examples described above, but there is still a way to go. These novel processes have demonstrated what is possible, and in some cases they are already in limited commercial use. However, it is still necessary to conduct further research that will optimise and scale these processes to the level of industrial production, increasing their efficiency, reducing their economic costs and ensuring the decarbonisation of British industry.

## A focus on scaling up bio-technologies is needed

Of course, decarbonisation is a global challenge and BBSRC's networks involve members throughout the world. Brazil, for example, has long been a leader in the production of bioethanol (from sugar cane) for motor fuel, but in collaboration with the University of Warwick, they are looking at producing chemicals from the residual sugar cane waste. Argentina and India are collaborating with the UK industrial biotechnology community to explore uses for their waste biomass. UK researchers are members of transnational consortia that have successfully obtained major EU research grants. These international links are testament to the regard in which UK industrial biotech expertise is now held by key players around the world.

Maintaining and expanding the current collaboration between universities, business and policymakers should enable progress in both identifying ways of decarbonising industry in the UK and being a global leader in using bioscience to reduce emissions across the world. Focusing on the translation of these new industrial biotechnologies to large-scale rollout will enable them to play a major part in cutting greenhouse gas emissions. ●

*This report includes contributions from Colin Miles, Alex Amey, Jennifer Swarbrick, Chloe Heywood, Rod Westrop, Joanna Sparks and Elizabeth Saunders*

**For more information on the BBSRC's research and activities see: https://bbsrc.ukri.org/news/topic/biotechnology-impacting-everyday-lives/**

**Lionel Clarke, co-chair of the Engineering Biology Leadership Council, says the UK is at the forefront in the field**

# Growing strong

Synthetic biology is helping accelerate the development of effective solutions to many health, environmental and sustainable manufacturing challenges being faced around the world today. The UK can justifiably claim to be a global leader in aligning and coordinating a government-endorsed approach to the development of synthetic biology and its commercial application. It has produced more research publications on the topic than every other country except the US. Within the past decade, around 150 synthetic biology-related start-ups and small and medium-sized enterprises – the main commercial development channels of this novel technology – have been formed in the UK, attracting over £1.5bn private investment.

Such progress is testament to a massive collective effort, sustained over many decades. The UK's legacy of cutting-edge genomics research derives from Crick and Watson's 1953 discovery that the double-helix encodes information and its subsequent interpretation in the Human Genome Project (HGP) half a century later. Significantly decreasing costs of DNA sequencing made possible in the wake of the HGP, and the consequent capacity to generate masses of information-rich data facilitated the subsequent rapid growth in research. By harnessing rapid developments in data handling and automation while applying clear engineering principles and standards to assist predictability, the concept of synthetic biology – as a technological platform to transform the development of novel biological systems from an empirical process into a digital biodesign and automated construction process – could be realised.

The need to develop effective solutions extremely rapidly in response to the Covid-19 global pandemic has posed the most challenging test – but also the greatest opportunity – for synthetic biology to date. Previously, developing and manufacturing vaccines would typically have necessitated years of empirical effort. Facilitated by the latest synthetic biology techniques, candidate vaccines have been designed in silico, constructed, screened and optimised in just weeks, using the genetic code of the virus as the starting point, bypassing the need to receive physical samples or to cultivate the virus. Techniques using plants as vaccine factories had already been developed, providing a timely option for rapid vaccine production. Other therapies and diagnostic approaches are being developed at an unprecedented rate. Robotic platforms have been reconfigured, permitting thousands of diagnostic tests to be carried out daily.

The availability of such cutting-edge resources today stems largely from the vision of academics more than fifteen years ago followed by a succession of national and international meetings, including workshops co-sponsored by the Royal Society, Royal Academy of Engineering and their counterpart learned societies in the US and China in 2010-11. A public dialogue helped determine UK public interests, concerns and expectations. Following

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**Our approach to vaccines has transformed**

the publication of the UK Synthetic Biology Roadmap in 2012, dedicated financial support from the government and research councils helped establish six synthetic biology research centres to complement the original research centre at Imperial College, together with a centre for doctoral training, a set of biofoundries for genome synthesis and a national centre ("SynbiCITE") to assist the translation and commercialisation of synthetic biology. Informed by the public dialogue and recommended in the roadmap, plans to assist the development and application of responsible research and innovation practices from the earliest stages of investigation were embedded in every research programme.

The UK Synthetic Biology Leadership Council (SBLC) was established to oversee the effective delivery of the key Roadmap recommendations, with a mandate to update plans as needed in the light of ongoing developments and learnings. It was constituted to be co-chaired by an industrialist and senior government minister, initially the Rt Hon David Willetts, author of the prescient 2013 “Eight great technologies” policy.

An online synthetic biology special interest group, open to all, was established to facilitate connectivity with the wider community. This group expanded rapidly to more than 1,000 members – academics, industrialists and other interested individuals. In 2016, the Leadership Council, co-chaired at the time by George Freeman MP, minister for the life sciences, issued a synthetic biology UK strategy document, “Biodesign for the Bioeconomy”. This provided a basis for further engagement with government, supporting its Industrial Strategy and contributing to the development of the UK bioeconomy strategy, launched in December 2018 with the specific goal of doubling the economic contribution of the bioeconomy to the UK by 2030.

In 2019 the SBLC published “Synthetic Biology in the UK 2009-2019 – A Decade of Rapid Progress” summarising the many achievements and commercial applications generated to date. It became apparent that not only had all the main developments envisaged in the roadmap exercise been addressed at least in part within the timeframes set out, but scientific progress had been far greater than anticipated at the outset. For example, rapid, precise, gene editing via CRISPR-Cas9 had not yet been published when the roadmap was written, and the potential for artificial intelligence to aid the processes of machine learning, core to the operation of the automated design-build-test-learn cycle, had not been factored in.

Applications being developed in response to the Covid-19 crisis may be capturing the headlines at present, but this intense focus on rapid technology development and delivery of effective solutions within the health sector is simultaneously honing new skills and techniques that may be applied to the many other challenges also now being faced in developing a more sustainable future as outlined within the UK bioeconomy strategy. To address this new phase of development, the Leadership Council, with its current co-chairman, Nadhim Zahawi MP, has been renamed and reconstituted as the UK Engineering Biology Leadership Council.

Engineering biology is an overarching term that incorporates ongoing basic research and development – synthetic biology – and industrial deployment. It embraces the full range of technologies that must be harnessed to translate biodesign into commercially viable operations, scaling up and out via innovative and distributable operations and generating new jobs and skills capable of delivering widespread economic prosperity. The Bioeconomy Strategy 2030 represents an important stage-gate upon the journey towards establishing manufacturing capabilities no longer dependent upon fossil energy and petrochemical components but instead based upon sustainable biofeedstocks, key to delivering the 2050 national goal of net-zero greenhouse gas emissions. ●

# Bioinnovation: from research to commercialisation

Searching for long-term, sustainable success? Then look beyond the science.
By **Richard Hammond**

**Great ideas to solve big problems**
The idea of manipulating biology to solve problems and make profit is not new. Plants and animals have been selectively bred for thousands of years, and medicines developed from the natural world.

The discovery of DNA accelerated this process, because if you understand the code, you understand how to reprogramme and how to control rather than the messier trial and error that characterised the previous millennia.

In the last ten years, however, two things have changed: much improved tools, techniques and methods to manipulate biology, and wider recognition of the externalities in developing and commercialising new technologies – particularly the environmental costs.

These improvements in technology are exemplified in the appearance of "synthetic biology". This takes biological research and brings it together using engineering principles to solve problems across many sectors, including human health, agriculture, the environment and industrial chemicals.

The UK is at the forefront of this new discipline and there has been significant governmental support through the synthetic biology roadmap and *Biodesign for the Bioeconomy* UK synthetic biology strategic plan.

Synthetic biology takes the ideas of abstraction and rational design-build-test to develop new solutions. This "biodesign" opens up the possibility of developing entirely new bio-based products and therapies.

CRISPR-Cas is a powerful method for precise editing of genes from bacteria to human cells, providing a fundamental biodesign tool. CELLO, a design and simulation software tool, assists people to design genetic logic circuits and simulates the expected performance of the circuit. It builds on the core ideas of abstraction and prediction used to design electronic circuits in silicon, ideas that drove the computer revolution as it separated the design and execution tasks allowing specialisation.

Antha was developed here in the UK as a software tool to define workflows and manage data in the lab. It allows the complex automation and execution of experimental programmes beyond what a human can. Combining tools such as CRISPR-Cas, CELLO and Antha is driving new biotechnology.

Climate change and a focus on the environment has also led to increasing regulation of activities. Consumers are now more aware of the environmental impact of delivering everyday products and services and are looking for alternatives. The popularity of "Green New Deal" policies in the last two years further illustrates the appetite for new thinking. Even the current Covid-19 pandemic is being viewed as the precursor to a bigger global struggle against climate change.

However, commercial success in

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biotechnology remains difficult. There are plenty of problems and lots of new technologies. The challenge is finding a route from idea to market through a complex landscape of needs and concerns. The Cambridge Consultants' Bioinnovation Team collaborates with companies worldwide to identify these routes and navigate them effectively.

**Bioinnovation and sustainability**

Bioinnovation looks beyond the technology to the intersection of tools (biotechnology), rules (governance models) and interests (economic models). It recognises the complexity of delivery and focuses on how to create sustainable value and embraces the reality that there will always be a risk versus reward debate around technological advances – particularly where biotechnology in concerned – and this debate must be had.

Earlier this year an editorial in *Nature* brought economists and scientists together in an effort to align scientific and economic research and unite them into a broader framework. Similarly, in September 2018 the World Economic Forum published an interesting dialogue focused on food systems where they define this model of tools, rules and governance for bioinnovation.

Innovation is required in biotech, governance, and economic models to enable commercial success. Biotechnology gives techniques and methods to develop and supply products and services in a long-term sustainable way, but this alone is not enough. The challenges are very different across sectors from therapeutics to agri-tech to industrial biotech.

Cell therapies are now available where genetically modified cells are infused into patients to treat cancer. This can be highly effective, giving relapsed or refractory patients a cure, and this potential sucess outweighs concerns about using genetically modified materials – but the cost and access to treatments are an increasing issue as benefits are demonstrated.

Conversely, in agriculture genetic modification gives new ways to increase food production and manage the effects of climate change, yet there is strong debate about the willingness to grow and eat modified crops and animals.

Industrial biotech is all about scale and cost. The debate here is typically between interests and technology: is there a green premium society that is prepared to pay for biotech approaches to manufacturing that reduce the environmental impact?

# The UK is at the forefront of synthetic biology

**Routes forward**

There are three tangible actions we can take to drive towards more rapid commercialisation.

We need to break the vertical integration model: today delivery of biotech is highly vertically integrated – one company takes on everything from research to volume manufacture. This forces organisations to be generalists. Other industries commercialise and thrive through specialisation: companies become expert in one part of the process. Ford assembles and markets cars, other companies supply parts and services aligned to their specific expertise. Synthetic biology is building the toolset to do this in biotechnology, and further support is needed in developing necessary governance models and frameworks such as technical standards to allow seamless integration between different organisations.

We must have innovation through start-ups, meaning funding and incubation. The increasing emphasis on start-ups and entrepreneurs for early-stage development is taking on the vertical integration model. The challenge here is scale. Significant innovation takes a lot of effort and the funding needed at an early stage can be large. However, the UK does not have the mindset to invest large at an early stage, especially compared to US. We need to develop investment and economic models to encourage that necessary investment early on, to deliver a step-change innovation.

There needs to be an informed dialogue regarding risk and reward. A key part of the governance model is the risk-reward balance and how the numerous stakeholders engage and understand both the benefits and issues of new biotechnology. We need to build on existing frameworks and approaches to establish mechanisms for good engagement and evaluating acceptability given the changing attitudes towards the status quo.

**Biotech has a bright future in the UK but there are still challenges ahead, says Zuzanna Brzosko, chief executive of Sixfold Bioscience**


# Testing times

Since the start of the unprecedented global Covid-19 pandemic and countrywide lockdowns, biotechnology has been at the centre of investor, political and wider public attention. Given its importance in the fight against the coronavirus and strong long-term fundamentals, investors and government continue to back the sector. However, in the context of the pandemic and political uncertainty, even our relatively well-capitalised industry may need additional support to prepare for the rocky road ahead and ensure it retains its leading position.

The UK biotechnology sector is larger and more vibrant than ever, with the number of research and development-intense companies soaring by 65 per cent between 2016 and 2019. The UK industry has a leading position in Europe, accounting for over a quarter of the continent's total venture capital funding. Built on the UK's unique assets – academic excellence; strong skills base; the largest single payer health system; and exemplary regulatory and ethical standards – the sector has been accelerating, thanks in no small part to the increasing support from the government to nurture biotechnology innovation.

Covid-19 has thrown the sector into sharp focus, with unparalleled pace of research and amount of funding directed at developing testing, vaccines and therapeutic approaches to combat the pandemic. Already back in March, a small Southampton-based company, Synairgen, announced that it received an expedited regulatory approval to conduct a Phase II clinical trial of its anti-Covid-19 drug. This is testament to the speed at which our ecosystem can move by connecting private and public stakeholders. The speed of funding decisions is also truly extraordinary for an industry that typically relies on stringent, but slow, peer-review processes. Whether this strategy proves successful, maintains high quality and, ultimately, leads to improved outcomes for patients, remains to be seen. Coronavirus research has further highlighted the strength of the UK's biotech position internationally. Five out of the eight recently announced EU coronavirus innovation projects, worth €117m, have a UK partner, and

**Biotech R&D firms have soared by 65%**

DANIEL ROLAND/AFP VIA GETTY IMAGES

two academic groups from Imperial College London and Oxford University are spearheading the research efforts for a vaccine, supported by the industry-led vaccine manufacturing group and a partnership with AstraZeneca.

Private biotech investment and fundraising has so far largely shrugged off the global pandemic. Data published by the UK BioIndustry Association (BIA) reveal that the sector raised a total of £894m in the first half of 2020, surpassing the £831m raised in the same period in 2018, a record-breaking year. Pharmaceutical companies also continue to pay to access biotech innovations. For example, Eli Lilly & Co, entered into a licensing and collaboration deal worth $830m with Oxford-based Sitryx. Meanwhile, certain UK biotechnology shares have provided some of the better returns in the market over the last few months.

## Home working has been a challenge

But just six well-established companies contributed 93 per cent of venture capital financing in March to May 2020, signalling early-stage biotech companies may be taking the hit, with deals abandoned or postponed by investors. The government's £500m Future Fund can help these ventures that do not qualify for emergency bank loans due to not being profitable. The government also showed they were prepared to listen, with some of the strict eligibility criteria loosened following an initiative from the 36 CEOs of top UK start-ups.

Many biotechs have not been able to adjust to remote working. Research and development productivity has suffered, and the suspension of academic research, which often underpins biotech output, has been costly to the universities and biotechs alike. Not as costly as the disruption of clinical trials though.

Over 1,400 trials were stopped because of Covid-19 since December 2019, including 200 cancer trials suspended from March to April alone. Valuable research, including clinical progress in life-threatening diseases that affect millions of patients, has been halted. It is important to ensure that the UK research ecosystem is back up and running as quickly as possible.

Looking beyond, the global recession that economists are predicting combined with the aftershocks of Brexit could mean a much longer-lasting disruption to the sector. A generous £1.25bn government support package for innovative firms has been welcomed by the industry and hopes are high that the sector has government backing also in the longer-term, with the updated Life Sciences Industrial Strategy confirming commitment to boost spending on R&D to 2.4 percent of GDP by 2027.

To date, there have been multiple well-designed and executed initiatives that have contributed to the sector's growth and functioning. To name a few, the R&D tax credits encourage companies to invest in innovation; the Patent box incentivises companies to keep and commercialise intellectual property in the UK; and the recently re-instated Biomedical Catalyst is a tried and tested funding scheme, shown to leverage up to £5 of private investment for every £1 of public money and increase employment. While there is a lot to be optimistic about, including our strengths in genomics and the cell and gene therapy space, there are areas for improvement.

Academic research and intellectual property are critical to the biomedical sector, with transfer technology offices (TTOs) playing an important role in connecting these two worlds. Unfortunately, the UK's TTOs are frequently perceived as barriers. We need processes that identify the best research in a timely and investable format, aligning incentives with those of the industry and placing higher value on the long-term benefits over short-term gains.

## Covid stopped over 1,400 clinical trials

Innovation must be taken forward by skilled management teams but the UK often struggles to build and retain sufficient commercial biotech talent. Both intellectual property and talent are mobile and facilitating their movement could be hugely beneficial to the sector. Top talent often follows the money to the US, in part because late stage funding remains relatively shallow in the UK. The London markets are also less favoured than New York's NASDAQ for biotech IPOs.

The constrained investment sometimes results in the premature exit of promising technology to global pharma, limiting the impact of our sector on the UK's economy. So we have a thriving ecosystem of small biotechs with good representation from large cap pharma but few strong mid cap companies.

It should be our ambition to create an environment in the UK, where successful biotech companies are not only founded but also grown and sustained.

# Engineering biology: A priority for growth

**Ian Shott CBE FREng**, Fellow of the Royal Academy of Engineering and engineering biology project chair, discusses the state of engineering biology today

The world we find ourselves in today is unrecognisable from how it was six months ago. We are asking big questions which go beyond working from home, reaching into decarbonisation, agriculture, and healthcare – with the latter understandably receiving particular attention at present.

These are all areas where engineering biology can have immense impact. Engineering biology is the application of rigorous engineering principles to the design of biological systems, with the objective of contributing to economic activity and sustainable and resource-efficient solutions. From companies like Colorifix engineering microorganisms to clean up the textile industry, to Puraffinity using customised biomaterials for water treatment, it's an exciting area to be in.

We have a world-leading engineering biology research base established through government investment, a vibrant community of start-ups, and substantial changes in the UK investor landscape in recent years reflecting the global interest and energy in this sector. Technological advances are propelling progress, and there are clear industrial, societal and environmental problems that, if solved, could give the UK an unmatched competitive edge. So much has happened in the past decade. This appears to be the perfect environment for the UK to become an engineering biology superpower, but instead we're seeing a real risk of research, talent, ideas and investment moving abroad. What can be done?

This is what we set out to explore at the Academy, conducting a policy project and publishing a report, *Engineering biology: A priority for growth*. We've engaged with government, industry, SMEs and academia to understand the issues. And we may be on the path to success.

The UK is at a crossroads: the engineering biology landscape is disjointed, with groups speaking different languages and too much focus on tools and platforms, which confuses government, industry and the public. We must ensure that government, universities and businesses are brought together to support the growth of engineering biology businesses, stimulate business-university collaborations, and connect those with problems to the problem-solvers. A shift to an applications focus, both in what is funded but also how researchers and SMEs talk about their work, will accelerate real-world products, processes, and changes.

As the world stands, we are now experiencing the perfect storm of drivers. What many are calling for is an overhaul of many of the systems framing our lives. Our use of fossil fuels and reliance on intensive agriculture are not givens. Harnessing biology and supporting ideas through to commercial solutions are better alternatives.

Even before this global overhaul, many across this space have been calling for change. We are now expecting sector groups for pharmaceuticals, chemicals, food and agritech to define how engineering biology can help overcome challenges and see the UK lead the world to a more sustainable future.

# Building the circular economy

Industrial biotechnology can help make the economy of the future a circular one, says **Mark Bustard**, chief executive officer, and **Ian Archer**, technical director of the Industrial Biotechnology Innovation Centre (IBioIC) in Scotland

The idea of a net-zero carbon emissions and zero waste economy isn't as far-fetched as some may think. The promise of a bio-based economy is that we can grow raw materials for everyday products. Industrial biotechnology (IB) is one of the many faces of innovation in the life sciences world. It offers sustainable solutions to the environmental challenges facing us all.

IBioIC has over 120 member organisations, working across the UK and Europe to find innovative solutions to modern problems. Our industry members range from medical biotechnology companies working on protein production through to those developing green solutions in bioenergy and biofuel. The projects IBioIC helps deliver are as diverse as taking waste from shellfish and using it to develop biodegradable packaging, to fermenting sugar in bioprocesses for the production of pharmaceuticals.

Our purpose goes beyond growing the bioeconomy – it is our role to raise awareness of the benefits of transitioning to a greener future. This is essential if we are to meet the ambitious net-zero carbon target for 2050. For this to be economically viable, government must be proactive.

Repurposing waste products is a great use of IB. Some of our members have developed technology that can repurpose waste from industrial and agricultural processes. The sources and uses are wide-ranging, such as salmon feed that can be made from algae from whisky co-products. One industry's waste is another's gold, helping the growth of a circular economy.

As we have recently learned, supply chains are complex and too often fragile. In some sectors there is an over-reliance on imports. Reshoring supply chains is something that IB can also support. Taking ethanol production for fuel as an example: Scotland imports over 50 million litres annually to blend into petrol to reduce emissions. That ethanol comes entirely from outside the UK to the benefit of European producers – and demand will more than double soon as we introduce E10 petrol containing 10 per cent ethanol. Post-pandemic, we need to build security into key supply chains as part of a sustainable future. The IBioIC is currently working with government, industry and academia to reintroduce sugar beet to Scotland. We can grow the crops, convert the sugar they contain, and ferment that sugar into ethanol all within 30 miles of Scotland's chemical industry in Grangemouth. A sugar supply is the foundation of a bio-based manufacturing cluster in Scotland. We can future-proof our manufacturing industries as part of the post-Covid-19 green recovery by embracing scalable biotechnology, which will be just the start of a journey creating economic opportunities, from agriculture to high-value manufacturing.

However, difficulty for companies often arises in the jump from R&D to manufacturing. If we are going to grow our industry and meet environmental targets we must incentivise companies to transition to manufacturing by supporting investment in manufacturing infrastructure.

With the right infrastructure, policy and funding environment, we can build a successful bio-based economy that will provide solutions for our clean, low-carbon agenda. IB has a lot to offer in creating a sustainable bioeconomy equipped for the future, and innovation is key.

IBioIC

Industrial Biotechnology Innovation Centre

# Industrial Biotechnology: Sustainable Living