



ROYAL
ACADEMY OF
ENGINEERING

ENGINEERING BIOLOGY A PRIORITY FOR GROWTH



ENGINEERING BIOLOGY
A PRIORITY FOR GROWTH

CONTENTS

| | |
|--|----|
| FOREWORD | 2 |
| EXECUTIVE SUMMARY | 3 |
| SUMMARY OF RECOMMENDATIONS | 5 |
| OVERVIEW OF ENGINEERING BIOLOGY | 6 |
| THE STATE OF PLAY AND WINDOW OF OPPORTUNITY | 9 |
| ACTION PLAN - RECOMMENDATIONS | 13 |
| METHODOLOGY | 19 |
| STEERING GROUP | 19 |
| REFERENCES | 20 |



FOREWORD

Supporting the development of emerging technology areas with the potential to deliver economic and social benefit to the UK is a priority of the Royal Academy of Engineering. Engineering biology – building upon more than a decade of rapid progress in synthetic biology – is one such technology. At present the UK demonstrates a competitive advantage in engineering biology, but action is needed to accelerate commercialisation and translation to ensure the UK captures both economic and societal value from it.

Engineering biology presents a suite of opportunities to solve the problems people and the planet face, now and tomorrow. As well as bringing cheaper, greener and custom-designed products to market, engineering biology can dramatically transform the processes that underpin existing industries, such as helping to lessen the impacts fossil fuels have while they are still an embedded component of our lives.

Engineering biology sits at the convergence of genomics, data science and other disciplines, benefitting from major increases in computing power and drawing on growing capabilities of machine learning and AI, as well as the decreasing costs and improvements in DNA synthesis, pushing the boundaries of what can be achieved.

The UK has a strength in engineering biology, and has built up considerable momentum since the Academy's landmark 2009 study *Synthetic Biology: scope, applications and implications*. We now stand at a crossroads. There is an opportunity for explosive growth in the commercialisation and application of this rapidly developing field. However, momentum is easily lost, and with other countries investing heavily, standing still runs a high risk of losing hard won gains as industry and researchers go elsewhere. This report sets out what needs to be done to accelerate commercialisation and truly capture value from our great national expertise in this field.



Ian Shott CBE FEng, Steering Group Chair

Engineering biology encompasses a plethora of applications, and therefore this report is intended for a range of audiences. For policymakers, it should act as a guide to how we might support a technology with wide social application. It forms one strand of a strategy to develop a high-skill, knowledge-based economy in the UK. We hope it will provide information and insights to investors, both in the public and private sectors. It is also addressed to practitioners, encouraging greater collaboration between different disciplines and industries that can achieve vastly more together, building on the precedent set by the government's Bioeconomy strategy. Greater communication and collaboration, and a heightened focus on real-world applications, combined with more sophisticated and intelligent marketing will drive progress in engineering biology.

We hope to have practiced what we preach, and have worked to bring together a range of different perspectives in the development of the report. This report can in part be read as an act of self-reflection; of individuals, groups and communities getting together and thinking deeply about what they truly need to thrive, and what they need from, and can offer, each other, rather than simply a wish list for a sector. The report reveals aspects of engineering biology that are unique, but also many factors that are familiar from other areas of innovation. This is reflected in some of the themes of the report: urgency and the importance of timing; good and bad approaches to risk; the need for agility; the skillset needed not only to do great research but to make great things come of it; and the balance of breaking new ground while building on what already exists. The study itself can be taken as a case study of one large emerging field attempting to come together to grasp enormous potential. In doing so, it reiterates and grapples with challenges that are observed in many innovative sectors across the UK.

Of all the themes that arose, urgency is perhaps the one that was repeated most. Other countries are ramping up support for their own engineering biology sectors, and it is critical that the UK acts now in order to take our companies to the next level of commercial success, stimulate further private investment and secure the exponential growth engineering biology can deliver.

EXECUTIVE SUMMARY

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 to the societal challenges faced in food, chemicals, materials, water, energy, health and environmental protection. Harnessing the capabilities of organisms, processes and mechanisms that exist in nature, and combining this with the incredible advances in areas such as processing power and machine learning presents solutions to problems of all scales – most pertinently in the need for sustainability and reducing emissions.

This is an area of global interest, with countries around the world vying to dominate and capitalise on what engineering biology can deliver. The UK is currently an engineering biology leader, with a strong academic base, established infrastructure and a thriving community of SMEs – but action is needed to accelerate commercialisation and industrialisation if this position is to be improved, or at the very least maintained against very active global competition.

The environment is fragmented, with pockets of good practice and activity in different disciplines and industries. Bringing a complex and fast-moving area together is essential if the UK is to realise the full potential of the engineering biology base it has nurtured, and deliver the benefits it can provide. This can be achieved by taking a holistic view of the entire innovation ecosystem, and working to bring together disciplines, businesses and different industries. Understanding needs to be built between them, alongside awareness of the support that already exists.

There are five themes running throughout the report and the recommendations it contains: urgency, risk, agility, people and skills, and building on what already exists.

- **Urgency:** With immense global appetite for engineering biology, the time to act is now in order to prevent a loss of the progress made in the UK.
- **Risk:** Taking risks is essential to reap the benefits of engineering biology. Government has a role in supporting risk-taking and facilitating companies to realise their full potential.
- **Agility:** Agile and flexible funding mechanisms and attitudes that mirror the nature of engineering biology itself will ensure that the UK can stay ahead and respond rapidly to changes and new challenges.
- **People and skills:** Supporting and valuing people who can and do work across disciplines, and increasing cross-boundary working at all levels will drive progress.
- **Building on what already exists:** a multitude of successes already exist across all the areas this report examines, and fortifying existing strengths, forging connections and bridging gaps are key, rather than creating new initiatives, bodies and processes.



© This is Engineering

The recommendations in this report are actionable and community-created, with each stemming from identified issues, outlined below.

The vast majority of the UK's dynamic community of engineering biology SMEs are small or micro businesses, at the early stages of development - growing these businesses is key.

- Engineering biology often features long development cycles, which can be a less appealing investment prospect. To help counter this and support these businesses to prove their technologies, funding is needed to support these risky endeavours. Funding would also help address the historic under-investment in innovation and draw in private sector investment.
- Businesses must identify appropriate customers and markets, and demonstrate and scale their technology. Help to access expert guidance and translational infrastructure would assist in addressing this.
- Navigating innovation support is a longstanding challenge and remains so. Increased awareness of existing support and simplifying the routes to existing provision would aid growth of companies in all sectors, not just engineering biology companies. *(See recommendation 1)*

Collaborations between businesses and universities are known to provide benefits to businesses of all sizes, and as engineering biology is an inherently interdisciplinary endeavour it is of even greater importance to companies in this space.

- UK business-university collaboration has many strengths, but increased agility and speed are needed. This will allow the quick de-risking and testing of ideas, necessary to accelerate commercialisation in a fast-advancing global interest like engineering biology.
- Increasing the links between industry and the academic research base at a variety of scales should increase the opportunities for collaboration. *(See recommendation 2)*

Engineering biology is a complex technology providing benefits and applications for a wide-range of industries. Improving communication and ensuring that businesses, policymakers and the public are equipped to understand and engage with the opportunities engineering biology provides are key to supporting growth of companies.

- Reframing communications to focus on the applications and solutions engineering biology can provide will help with wider engagement. Communication is also a key component in breaking down silos between the disciplines that comprise engineering biology, and in helping to forge a collective identity.
- Increased joint working between the Synthetic Biology Leadership Council, Industrial Biotechnology Leadership Forum and other sector groups will increase exchange and understanding. *(See recommendation 3)*

The UK's networks and government-funded infrastructure have reached maturity, but the head start the UK's strategic public investment has achieved is at risk, at a time when other nations are racing to establish and out-compete them.

- While industry interest and funding continue to increase, there is still a need for a plan to ensure sustainability of the key translational infrastructure and the research base. This will ensure that these established networks and infrastructure, and the momentum they have catalysed, can continue to grow. The focus of any support should be on translation and partnerships with industry, with funding awarded on a competitive basis for existing facilities and that also permits new players to compete. *(See recommendation 4)*

This publication is not an end point, rather a stepping stone towards what needs to be achieved. Action is needed both from outside and within the sector to support, consolidate and unify engineering biology, to ensure it can return benefits to the UK and that the researchers, ideas and companies that have emerged to date, and those emerging now or in the future, are not lost to competitors. The recommendations set out in this report aim to achieve this.

SUMMARY OF RECOMMENDATIONS

1

Act now to improve the UK's capability to grow engineering biology businesses [UKRI/BEIS/Relevant sector groups]*

- a Grow risk funding for development, commercialisation and scaling [UKRI/IUK/BEIS/HMT]
- b Support companies to access expert guidance and translational infrastructure [UKRI/IUK/BEIS/Research base/Innovation Centres/KTN]
- c Increase awareness and simplicity of navigating innovation support [UKRI/IUK/BEIS/Innovation Centres/KTN]

2

Stimulate and incentivise businesses and universities to work together efficiently and with agility [Research base/Businesses/UKRI]

- a Increase flexible small-scale, short-term funding to support projects to test ideas [UKRI/IUK/Innovation Centres]
- b Increase links between industry and the engineering biology academic research base [Academics/Businesses/Research base/Innovation Centres]

3

Make engineering biology more easily accessible to ensure businesses, policymakers and the public understand the opportunities it provides [Academics/Businesses/Research base/SBLC/IBLF]

- a Communicate and promote the applications of engineering biology and the solutions it offers [Academics/Businesses/SBLC/IBLF]
- b Increase joint working between the Synthetic Biology Leadership Council and Industrial Biotechnology Leadership Forum [SBLC/IBLF/Relevant sector groups]

4

Act now to sustain the UK's position as a global leader in engineering biology by committing to long-term investment [BEIS/UKRI/HMT]

- a Agree a sustainable plan to support the synthetic biology research base and, crucially, other key translational infrastructures [BEIS/UKRI/IUK/KTN/Research base/Innovation Centres]

* Organisation categories in square brackets indicate primary target(s) of recommendation: UKRI (UK Research and Innovation); IUK (Innovate UK); BEIS (Government Department for Business, Energy and Industrial Strategy); KTN (Knowledge Transfer Network); SBLC (Synthetic Biology Leadership Council); IBLF (Industrial Biotechnology Leadership Forum); Innovation Centres (encompasses Catapults, SynbiCITE and IBioC).

OVERVIEW OF ENGINEERING BIOLOGY

There is a window of opportunity for the UK to accelerate the commercialisation of **engineering biology** - which includes a broad and deep base of biotechnology across a spectrum of companies - to finally generate explosive growth and reap the resulting economic and societal benefits. This study has sought to understand the current barriers that are preventing the UK from fully exploiting this opportunity and suggest potential solutions, considering the balance between market pull and technology push.

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 to the societal challenges faced in food, chemicals, materials, water, energy, health and environmental protection.

Royal Academy of Engineering 2019



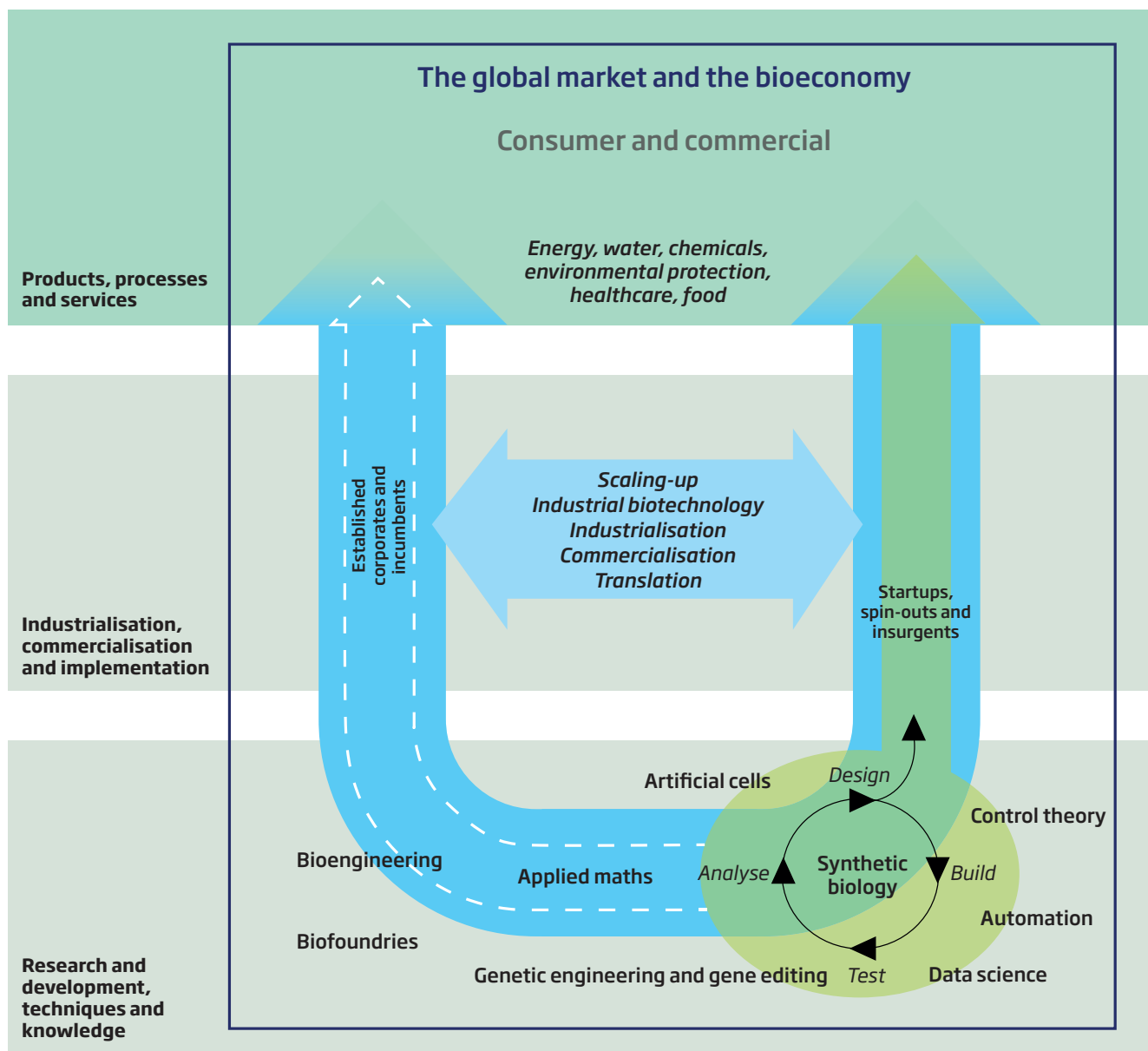
Engineering biology

The discovery of the structure of DNA in 1953 heralded a revolution in molecular biology, which set the stage for the initial sequencing of the human genome in 2001. This was made possible by technology developments in our ability to read the sequence of bases in DNA relatively rapidly and accurately. In parallel, it became possible to write the bases in DNA chemically, a process known as DNA synthesis. For the first time, it was possible to manipulate DNA and instruct cells to produce and function according to human design. This was followed by commercialisation and scale-up of early biotechnology approaches, which established the broad-based sector of **industrial biotechnology**. Over the past two decades the convergence of engineering, biology, physical sciences and more recently data science has focused on applying the rigorous engineering principles of design, modularity, characterisation and standardisation to the process of DNA manipulation, with the emergence of the academic discipline of **synthetic biology** and its commercialisation by innovative spin-out companies.

This recent convergence of engineering, biology, data science and physical sciences could now produce sustainable and resource-efficient commercial solutions to the rapidly changing challenges faced in food, chemicals, materials, water, energy, health and environmental protection. Some commercial applications have already emerged in recent years. Accelerating this commercialisation involves transitioning from proof of concept activities to delivering full-scale successful applications. This involves a broad set of challenges, including the creation of new scalable production and processing capabilities and harnessing the technologies and processes of industrial biotechnology to produce products and processes from biological resources.

This study's definition of engineering biology captures the entire innovation ecosystem, including advances in research and development, specifically in synthetic biology, through industrial biotechnology channels to ultimately deliver new commercially viable solutions, including those that respond to societal demands and challenges. In this context, engineering biology has the potential to underpin and transform bioeconomies worldwide. Figure 1 presents a schematic of what is captured by engineering biology in the context of this study.

Figure 1
Engineering Biology in the context of this study



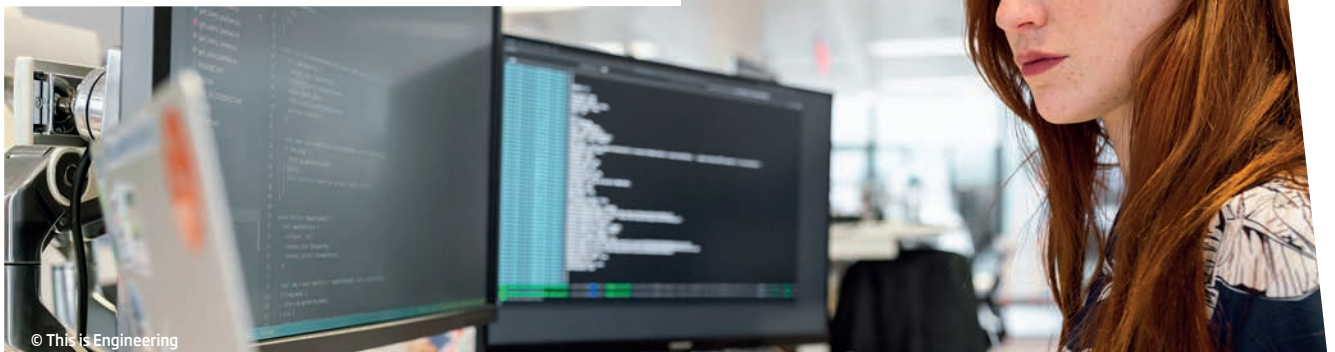
This schematic represents engineering biology in the context of this study. The study has taken a holistic view of engineering biology. The focus is not solely on the fundamental knowledge that underpins a technique or a product, nor solely on the final product or processes. The processes, mechanisms and communities that an idea flows through to become a valuable and successful end-product are also important. There are a wide range of routes companies can take in the engineering biology space, and a whole host of mechanisms to facilitate these - the diagram aims to display a snapshot. Currently there is a growing community of startups and spin-outs arising from the academic research base represented by the green arrow. However, there is still much more scope for synthetic biology to be embraced by the established corporates and incumbents, represented by the dashed white arrow.



BOX 1

Responsible Research and Innovation (RRI)

RRI is an approach that anticipates and assesses potential implications and societal expectations regarding research and innovation, fostering the design of inclusive and sustainable research and innovation, and facilitating societal approval. RRI is understandably pivotal in the growth and commercialisation of engineering biology. Although the wording and descriptors vary between sectors and organisations, with RRI a well-recognised label in academia, the fundamental components and values are observed to be embedded in both academia and industry across engineering biology.



CASE STUDY

Cleaning up the textiles and fashion industries

The textiles and fashion industries use vast quantities of resources and have a number of negative effects on the environment. The processes and by-products involved in dyeing fabrics are particularly resource-intensive, especially in their use of water. They are also harmful to workers involved as well as the environment when chemicals are washed away. Norwich-based **Colorifix** have engineered microorganisms to produce, deposit and fix naturally-occurring pigments to fabrics. Their process uses ten times less water than traditional dyeing methods, and does not rely on non-renewable petrochemicals.¹ In December 2018, the company raised \$3 million to scale its UK team and facilities and launch pilots with several leading players in the international fashion industry.² Any efforts to improve the resource-efficiency of the industry have the potential to have huge positive environmental impacts, while meeting the public's growing desire for more ethical and environmentally-friendly clothing options.



© Colorifix

THE STATE OF PLAY AND WINDOW OF OPPORTUNITY

The UK is well-placed to benefit economically and societally from engineering biology. There are already more than 1,800 UK businesses undertaking Industrial Biotechnology-related activity. These employ over 14,000 people, generating £3.7 billion in revenue, and contributing £1.2 billion in gross value added.³ The UK has an excellent and broad biosciences research base with impressive growth seen for synthetic biology. For example, the UK is second only to the US in synthetic biology research excellence and investment, and is home to a growing community of young companies spinning out of the synthetic biology research base.⁴ However, there is a consensus that there is significant unrealised potential in the commercialisation of engineering biology in the UK.⁵ Against a backdrop of increasing international competition, there is a window of opportunity for the UK to understand what is required to accelerate the commercialisation of engineering biology, to generate explosive growth and reap the resulting benefits.

Public sector investment into the research base has been substantial and significant, with the UK establishing a world-leading synthetic biology research infrastructure, attracting skilled people, building successful partnerships, and underpinned by Responsible Research and Innovation (see *box 1*). However, support and focus on translation and commercialisation has been widely recognised as being underpowered and intermittent. With the foundations of engineering biology in the UK strong, now is the time to ensure their longevity, and build on their success to accelerate translation, demonstrate commercial scale, and secure the value from such activities in the UK.

Multiple reviews, publications and strategies relevant to engineering biology in the UK have been published over the last ten years, as highlighted by *box 2* and *figure 2*. Reviewing the progress of the implementation of the recommendations from the three key reports on synthetic biology in the UK



© This is Engineering

BOX 2

Synthetic biology: scope, applications and implications, Royal Academy of Engineering, 2009

In 2009, the Royal Academy of Engineering authored one of the world's first comprehensive reports on the then new discipline of synthetic biology. The report identified the UK as being well-placed to become a synthetic biology world leader. It made a compelling and successful case for the UK government to begin the groundwork that would lead to a national strategy for synthetic biology. Within four years of the report's publication, synthetic biology was one of the government's 'eight great technologies', the Synthetic Biology Leadership Council was established and a synthetic biology UK roadmap published. The roadmap was accompanied by additional investment from government to complement ongoing research commitments. UK public sector investment in synthetic biology totalled approximately £300 million, including £102 million of government funding for the Synthetic Biology for Growth Programme. This investment has resulted in the creation of an additional six multidisciplinary research centres (at the universities of Bristol, Nottingham, Cambridge, Edinburgh, Manchester and Warwick, in addition to Imperial College London, collectively termed here the Synthetic Biology Research Centres 'SBRCs'), DNA synthesis facilities ('DNA foundries'), training centres and a seed fund for innovative companies. Taken together, these activities have established the UK as a leader in synthetic biology research, resulting in the creation of centres of excellence at other universities and a growing community of startups and spin-outs.



CASE STUDY

The scale of potential

Engineering biology companies have great potential to grow to scale, and those abroad offer an excellent window into what is possible. US-based **Ginkgo Bioworks**, founded in 2009 by a small group of Massachusetts Institute of Technology scientists, has grown from a university spin-out to an organisation with over 200 employees in the space of a decade.⁶ The company specialises in the creation of custom organisms for producing cultured ingredients, improving these strains, and the design of enzymes.⁷ This range of tools have applications in producing flavours, fragrances, food ingredients and cosmetics, as well as in pharmaceutical production and clothing manufacture. The company gained venture capital funding in the summer of 2014, being supported by multiple grants from the US government prior to this. In December 2017, the company secured \$275 million in Series D funding, leading to valuations of over \$1 billion.⁸

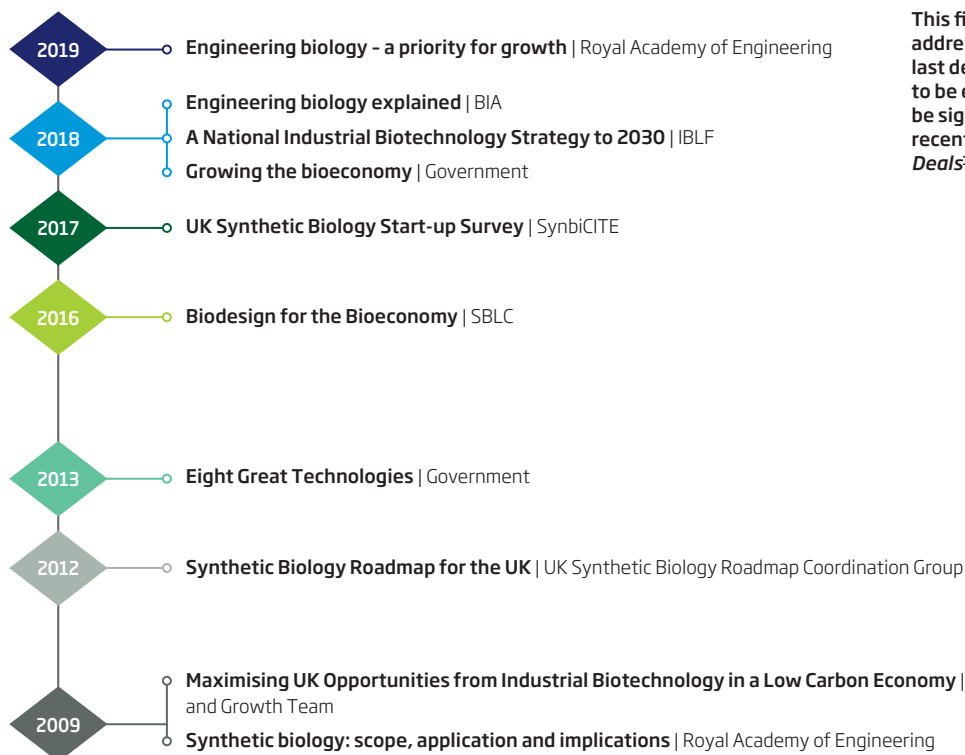
revealed that commercialisation, innovation and adoption are areas where progress has lagged and significant work is still required.⁹

This report is the most recent contribution to the corpus.

This report focuses on what is needed now to accelerate the growth and commercialisation of engineering biology in the UK. During the 18 months from January 2018 to June 2019 evidence was gathered from a wide range of relevant stakeholders, building on previously published reports documenting progress on this subject.¹⁰ In May 2019, the evidence gathered was shared at a workshop with over 40 participants from across industry, academia and government.¹¹ The purpose of the workshop was for the community to input into the design of actionable, community-created recommendations.

This report presents four overarching recommendations setting out the action that is now needed to capitalise on the UK's strong position in engineering biology to accelerate translation and realise the economic and societal benefits. Five themes run throughout the recommendations: urgency, risk, agility, skills and building on what already exists.

Figure 2
Reviews addressing UK engineering biology over the last decade



This figure presents a selection of reviews addressing UK engineering biology over the last decade. The selection is not intended to be exhaustive. In particular, there will be significant overlap with elements of the recently published *Life Sciences Sector Deals*¹² and strategy.¹³

Themes

Urgency

- Engineering biology expertise and facilities have been built up in the UK, enabled by significant public investment. This momentum takes time to build. Establishing new facilities, recruiting staff and students, designing programmes, training and building partnerships all takes time, with lags from initiation until full operational capacity. In parallel, there is a growing community of young engineering biology companies, including 146 synthetic biology startup and spin-out companies created between 2000 and 2016, many of which have also benefited from public investment¹⁴, that are ready to grow.
- However, as the initial public investment begins to taper off, this momentum is at risk, potentially damaging both what has already been built and our future trajectory. This uncertainty is exacerbated by a broader concern that the UK

demonstrates short-termism, including in its funding cycles, strategic approaches and policy levers. In the meantime, other countries are investing heavily in engineering biology and are beginning to reap the rewards, proving that the UK's leadership position is not guaranteed in the long-term. For example, US synthetic biology startups attracted over USD\$1.9 billion in venture funding in 2018¹⁵, and Singapore announced investment of SD\$ 25 million over a five-year period into synthetic biology R&D projects in January 2018¹⁶. We are now at a decision point for engineering biology in the UK. It needs to be decided whether to act now to accelerate the translation and commercialisation of engineering biology, or risk losing the momentum to other countries, thus eroding the foundations that have been laid. What is important now is collaboration, engagement and commercialisation.

Risk

- For the UK to reap the rewards of engineering biology, taking calculated and measured risks is essential. Engineering biology has the potential to completely reimagine the products and processes involved in many existing industries, making it a highly disruptive technology. Without taking risks, only incremental changes will be achieved. Companies can sometimes perceive risk as a radical departure from business as usual. The culture change, the interdisciplinary skillsets and the facilities required, are often unfamiliar to them. It is vital that companies take a mature approach to risk, balancing the attraction of hanging back until the technology has been demonstrated at scale, with the rewards of being successful early adopters, while factoring in the risk of being left behind.
- Government has a pivotal role in supporting balanced risk-taking. This can be done by directly reducing the risks involved, mitigating the risk for others and accepting occasional failures as inevitable. All of the recommendations made in this report encourage companies to see beyond 'business as usual' and embrace the opportunities presented by engineering biology.

Agility

- Engineering biology is a fast-paced and constantly developing field. To fully realise the potential of engineering biology, flexible approaches are required to embrace new opportunities and respond rapidly to challenges posed. This applies across all facets of engineering biology, from reactive funding mechanisms that respond proportionally to opportunities, through to agile attitudes by those in academia and industry to identify new opportunities, to overcome the fear of failure, and to work in new partnerships.



CASE STUDY

DNA synthesis

DNA is life's information carrier, and DNA synthesis is the process by which chains of DNA are created. This happens within cells as part of their lifecycle as they divide, and it is carried out by design as part of the research, development and production processes of many engineering biology applications.¹⁷ If DNA synthesis is 'writing' DNA, then the flipside is 'reading' DNA with DNA sequencing technologies. Following the development of next-generation sequencing and large-scale research programs - including the Human Genome Project and 100,000 Genomes Project - the cost and time taken to sequence and 'read' DNA have dramatically decreased. However, improvements in the cost and capability to synthesise and 'write' DNA have not yet developed to the same extent. The current methods for DNA synthesis use environmentally hazardous chemicals, and cannot consistently achieve longer DNA sequences with the required accuracy. In Cambridge, **Evonetix** and **Nuclera** have both secured private investment and government grants to develop their DNA synthesis technologies and scale their operations. A key breakthrough is the use of enzymes - nature's catalysts - to achieve synthesis, rather than relying on traditional chemical approaches.¹⁸ Enzymatic approaches are poised to increase the scale, speed, and accuracy of DNA synthesis, while reducing its environmental impact.

People and skills

Skilled people, especially those who can thrive in multi-disciplinary environments, are essential to the success of engineering biology. As engineering biology extends beyond traditional discipline boundaries, drawing from engineering, biology, data science, and physical sciences, it requires individuals who can communicate across these boundaries.¹⁹ Universities need to employ skilled individuals who can spot the commercial opportunities and facilitate connections with business. Increasing the flow of people and partnerships between academia and industry should promote mutual understanding and identify opportunities for new ideas to develop and grow. As engineering biology can operate across different industrial sectors and divisions within companies, similar efforts to working across boundaries and effective communication are needed, mirroring those required within academia. Cultural as well as technical differences must be embraced and overcome.

Build on what already exists

Effective infrastructure, skilled people and successful relationships have been built up in the UK over the past five years thanks to significant public investment – not least the £300 million UK public sector investment in synthetic biology, including £102 million of government funding for the Synthetic Biology for Growth Programme.²⁰ Private investment is also on the rise, with startups identifying as part of the UK's synthetic biology community raising over £620 million of public (£56 million) and private (£564 million) investment in the UK between 2010 and 2016.²¹ It is crucial that every opportunity is taken to build on these existing successful initiatives, institutions and infrastructures. Government will maximise returns on previous investments by ensuring the continued operation of successful activities, as well as spreading best practice and learning derived from them. Stability and continuity are critical for leveraging private investment, giving business and others the confidence to make investments over the long term and to accrue the benefits from a wide range of policies that impact engineering biology.

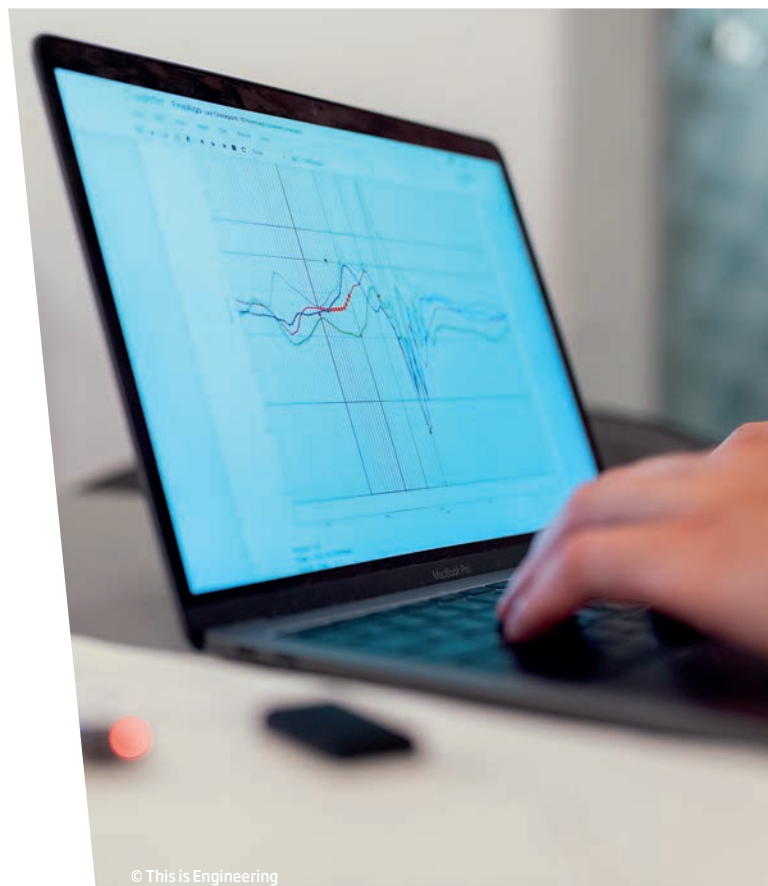
The reviews have been done, the evidence gathered, now is the time for action.



CASE STUDY

DNA sequencing

The ability to quickly and accurately read the information encoded within DNA is integral to engineering biology. Faster, cheaper and easier genome sequencing has applications not only in research, but also in medical diagnosis, agriculture, food and water surveillance, education and more. Additionally, DNA sequencing plays a vital role in the development of other technologies, such as those mentioned throughout this report. As well as breaking ground in commercial applications that arise out of DNA sequencing, the UK is leading in the development of underpinning equipment and processes that can support and facilitate innovations across many sectors. **Oxford Nanopore**, an Oxford-based 'unicorn' spinout, has developed a range of high performance, portable DNA sequencing devices. The technology is based on nanopore science, using single-molecule sensing to read strings of DNA highly accurately, molecule by molecule. Since being founded in 2005, the company has raised over £500 million, most recently securing a £50 million equity investment in October 2018 from American biotechnology company Amgen.²²



© This is Engineering

ACTION PLAN - RECOMMENDATIONS

1. Act now to improve the UK's capability to grow engineering biology businesses [UKRI/BEIS/Relevant sector groups]

Now is the time for engineering biology to demonstrate commercial scale and secure value from its activities in the UK. UK engineering biology companies need to progress to the next level of commercialisation and success, with increased focus on translation and stimulating private investment. The UK has a young, dynamic and growing community of engineering biology startups and spin-outs, including 146 synthetic biology startup and spin-out companies created between 2000 and 2016.²³ With few exceptions, these companies are classified as SMEs, but this masks the reality that the vast majority are small (11 to 50 employees) or micro (10 employees or fewer) enterprises. Many of these companies are still at the early stages of development and are not yet generating revenue. To accelerate their growth, they will need to prove their technologies, identify appropriate customers and markets, attract private investment and grow to scale independently or via assimilation with existing large companies.

a) Grow risk funding for development, commercialisation and scaling [UKRI/IUK/BEIS/HMT]

- The UK has historically under-invested in innovation and the 'D' of R&D. For engineering biology, funding mechanisms targeted at supporting the translation stage, such as the Industrial Biotechnology Catalyst, have been intermittent, creating uncertainty and impacting the confidence of businesses to participate and invest. Government support for innovation and development is critical for reducing the risk to investors and for bridging a funding gap when private investors, especially in the case of disruptive technologies, are not ready to invest. Innovate UK's budget should be increased to help address the UK's historic under-investment in innovation and the 'D' of R&D, with specific schemes building on previous successes, available for engineering biology.
- Engineering biology companies need to demonstrate their technology through to a later stage of development to persuade a business, customer or investor to collaborate or invest compared to a company with a non-disruptive technology. In addition, the development cycles of



engineering biology applications are, by their very nature, longer than for other technologies, such as digital. This can make them less appealing to investors. Consequently, the match-funding requirements required by Innovate UK can often be unachievable and out-of-reach for engineering biology companies. Innovate UK should explore if it can reduce the barrier posed by match-funding requirements to companies with disruptive technologies that have longer lead times to get to market, and provide adequately prolonged funding options.

Private sector investment is essential to help companies grow to scale. The government has a number of powerful levers at its disposal to stimulate private investment, including highly effective mechanisms for influencing investors' behaviours. The Seed Enterprise Investment Scheme (SEIS) and Enterprise Investment Scheme (EIS) have made significant contributions to improving access to equity investment. The government has been perceived as having a significant role in articulating the aspiration and narrative that led to the formation of the independent Business Growth Fund (BGF). These successful precedents should be built on and government should maximise its ability to leverage private investment.

b) Support companies to access expert guidance and translational infrastructure [UKRI/IUK/BEIS/Research base/Innovation Centres/KTN]

Support and guidance for technology development and technical scaling is important for companies. This needs to be considered early on during technology development and company growth in order to be effective. However, companies often underestimate the time, cost and changes that their technology might need for commercial success.

Facilities to support translation and the testing of technical scaling activities, including access to technical expertise and guidance as well as access to equipment, are essential for companies to demonstrate and prove the concept of their technology in a risk-reduced way. Such facilities can also provide commercial guidance. Significant investment has been made in the UK to establish facilities such as the CPI (The Centre for Process Innovation). However, accessing these facilities can be challenging for time- and money- poor companies, especially smaller SMEs.

The value proposition of engaging early with translation infrastructures should be communicated clearly by the SBRCs and other research centres and leadership councils, with the KTN playing a clear role and mobilising other parties. To make it easier for engineering biology companies to grow to scale they should be supported so that they are able to access expert guidance, both commercial and technical, and translational infrastructure. An incentive scheme, such as innovation vouchers, could be used to encourage and facilitate SMEs to access translational infrastructures.

c) Increase awareness and simplicity of navigating innovation support [UKRI/IUK/BEIS/Innovation Centres/KTN]

The UK offers a range of innovation support mechanisms for companies. Innovate UK is the primary source; however, many other public sector organisations also offer support, including Research Councils, individual government departments, LEPs and Growth Hubs. This has resulted in a complex innovation support ecosystem. Innovation is a complex non-linear process, so the complexity of the ecosystem is not surprising and to some extent may be inevitable. Complexity, navigation and awareness are all well-recognised challenges of the UK system.²⁴ But the complexity and the challenges of navigating the ecosystem poses a barrier to engagement with companies.²⁵ The challenge of navigating the ecosystem is exacerbated by lack of clear communication tools. These are needed in order to reach companies and academic stakeholders beyond those already familiar with the UK's innovation support offer. The complexity of the system also makes it difficult for government to take a systems' view of its innovation support, although the creation of UKRI offers the opportunity for a more strategic and systems view to be taken.



© This is Engineering

Reducing complexity, simplifying the navigation of the system, and reaching out to companies and entrepreneurial academics that could benefit from innovation support but are not already doing so, should increase the likelihood of engineering biology succeeding. To do this UKRI should 'hide the wiring' and offer a simple single user-interface that directs companies to the innovation support across the whole of government that is most useful to them. It might also make use of data analytics. To increase awareness of what the UK has to offer, a coherent communication package used by all parties involved in provision of innovation support should be developed. Finally, Innovate UK should work with the leadership councils and KTN to target companies who could most benefit from innovation support.

2. Stimulate and incentivise businesses and universities to work together effectively and with agility [Research base/Businesses/UKRI]

Industry-academia partnerships are crucial to accelerating the commercialisation of engineering biology. Collaborations with academia are important for businesses of all sizes and the benefits have been well articulated.²⁶ Collaborations can help identify market pull opportunities and pathways for commercialisation for academic research. They can also provide access to expert skills for both businesses and academics while sharing and reducing the risk of trying new approaches for businesses. The UK environment for business-university collaborations is good, but there is scope for further improvements, including some specific to engineering biology.

a) Increase flexible small-scale, short-term funding to support projects to test ideas [UKRI/IUK/Innovation Centres]

For engineering biology, relatively small amounts of flexible funding to allow universities and businesses to respond rapidly to business needs are invaluable, allowing ideas to be quickly de-risked and tested. This is necessary to determine if a larger-scale collaboration is warranted, and, crucially, if funds can be deployed rapidly ideas can keep pace with industry timelines. Such funding can be deployed to fund researchers to work on short-term projects to address a business need, provide proof-of-concept funding, enable university staff to take short secondments in industry and employ staff to focus on facilitating industry access to research. Such activities could de-risk and pump-prime partnerships that later go on to seek funding from established mechanisms to support larger-scale collaborations.

The Research Councils' Impact Acceleration Accounts (IAA), and in England the Higher Education Innovation Fund (HEIF), have both been highlighted as important sources of generic flexible funding²⁷ to pursue such activities. Specific to engineering biology, SynbiCITE, provides proof of concept funding which, for successful projects can lead to

longer, larger funded projects through their Development of Prototype awards. The Industrial Biotechnology Innovation Centre (IBioIC) also provides project funding and facilitates referrals to other funding bodies and is currently supporting over 130 companies. Sustaining and increasing the availability of flexible small-scale, short-term funding for engineering biology is essential to ensure new ideas are tested for their commercial potential.

b) Increase links between industry and the engineering biology academic research base [Academics/Businesses/Research base/Innovation Centres]

Increasing industry links with the engineering biology research base would increase the opportunities for the commercialisation of engineering biology. Increased links should take a variety of different forms. From academic staff and students having the opportunities to acquire skills relevant to industry, to universities increasing meaningful and effective engagement with companies that have the potential to grow to scale.

As a UK-wide network, the SBRCs, working with the other centres of synthetic biology research excellence, could take a strategic approach to increasing industry links across the whole network, learning from each other and ensuring no opportunities go unmissed. SynbiCITE, the national centre for the commercialisation of synthetic biology, already plays an important role here, but there is opportunity



CASE STUDY

IBioIC

Launched in 2014 and located in Glasgow, the Industrial Biotechnology Innovation Centre (IBioIC) is one of eight Innovation Centres in Scotland, funded by the Scottish Funding Council with support from Scottish Enterprise and Highlands and Islands Enterprise. The ambition of IBioIC is to stimulate the growth of the industrial biotechnology sector in Scotland to £900 million by 2025, with strategic areas of focus on industry-academia collaboration, de-risking scale-up, developing competitive opportunities and providing a skilled workforce. It does this by offering scale-up facilities, talent development, funding provision and networking opportunities. Organisations can become members of IBioIC which gives them access to these provisions and provides a platform for collaboration, connecting expertise in industrial biotechnology with the problems it can help solve. The Centre currently supports over 130 companies, 50 research projects, and works with 18 Scottish universities and research institutes.²⁸

for more to be done. While the SBRCs need continued sustainable support to further increase the UK's capacity and capability in research, they are now at a stage where a joint commercialisation strategy could be designed.

3. Make engineering biology more easily accessible to ensure businesses, policymakers and the public understand the opportunities it provides [Academics/Businesses/Research base/SBLC/IBLF]

Communication has been the thread running through every aspect of this study. From how engineering biology is defined, the way different sectors communicate with each other, to awareness of existing incentives and initiatives to support engineering biology. Improvements in communication, with a focus on simplicity and solutions, could have a positive impact on the acceleration of the commercialisation of engineering biology.

Defining engineering biology is not easy. As a rapidly emerging technology with involvement and interest from many different industries and academic disciplines, the language used to describe engineering biology differs. However, for businesses, definitions are not a concern, instead, the emphasis is on what the technology can do for their company.



CASE STUDY

SynbiCITE

The UK's National Industrial Translation Centre for Synthetic Biology (SynbiCITE) is based at Imperial College London. SynbiCITE accelerates and promotes the commercial exploitation of synthetic biology research and engineering biology applications. This is achieved by supporting companies through access to business and technical resources, including business education and training, funding for proof of concept and prototype development projects, and access to facilities including the London Biofoundry. SynbiCITE was established in 2013 to nucleate, incubate and accelerate company growth in the sector. The centre was funded by EPSRC, BBSRC and Innovate UK through to September 2018.²⁹ Following this, it has secured a further £5 million grant from UKRI and other sources to underpin a new five-year strategy.³⁰ Since 2014 SynbiCITE has supported over 50 start-up companies, which have attracted over £5 million in investment from a range of public and private sources.³¹

a) Communicate and promote the applications of engineering biology and the solutions it offers [Academics/Businesses/SBLC/IBLF]

Focusing on the applications of engineering biology and the industrial problems it can solve is a more meaningful approach when communicating with business, end-users and policymakers. Doing this will increase the reach beyond communities already familiar with engineering biology. Selling solutions, rather than a complex technology, will require a shift in messaging. It will need to be in a language not so tied to terms commonly used in academia. Similarly, communicating the role engineering biology and its applications can play in addressing political and societal challenges should also gain traction with the public and policymakers.

b) Increase joint working between the Synthetic Biology Leadership Council and Industrial Biotechnology Leadership Forum [SBLC/IBLF/Relevant sector groups]

There are many different academic disciplines and industry sectors that are involved with engineering biology. Many more will need to be involved for its full commercial potential to be realised. There is a need to break down the boundaries that exist between these different silos in order to build a collective identity. Effective communication and resourcing will be central to this. For different communities to understand each other and work together effectively they need to 'speak each other's language' and understand each other's cultures.

Bridging the gap between the synthetic biology and industrial biotechnology communities will maximise the growth and application of engineering biology and if done effectively could lead to a sum greater than its parts. For



© This is Engineering

example, the industrial biotechnology community could apply engineering biology approaches and pull technologies through to the market, while the synthetic biology community will challenge the industrial biotechnology community to innovate and may find customers for their products, processes and services. Although some synthetic biology companies are already finding their own routes to grow to scale, such as UK company Green Biologics and US company Amyris.

Each community has clear leadership infrastructures via leadership councils, networks - including through the KTN - and defined community ambitions by way of strategies and roadmaps. However, increased interaction at all levels is needed. The IBLF and SBLC should be supported to engage more purposefully with each other, and in turn also with other relevant sector groups, including the Medicines Manufacturing Industry Partnership (MMIP), the Chemistry Council, and the Food and Drink Sector Council, as well as the agri-tech sector. There are already excellent precedents of cross-working, most notably for the Bioeconomy Strategy³² (see Box 3), and that success can be built on. The *Life Sciences Sector Deals* demonstrate the action and join-up across communities that can result from a coordinated strategy - and as that strategy acknowledges, this is also an area where engineering biology will have significant impact.³³



CASE STUDY

Future of mobility: greener fuels

The UK is headed towards a huge shift in the demographics of our road vehicles, with the numbers of electric cars projected to significantly increase as it implements its decarbonisation targets. Some forms of transport are taking longer to electrify than others, such as heavy goods vehicles and air travel. There are still further ways that the environmental impact of these forms of transport can be reduced while these electric replacements are developed. **C3 BIOTECH** is a University of Manchester spin-out which has developed a microbial biosynthetic pathway to produce renewable propane from waste materials. This offers the potential to reduce the amount derived from natural gas and crude oil. In 2018 the company received grants from both Innovate UK³⁴ and Horizon 2020³⁵ to develop various aspects of their activities. The gases produced via this new process can feed into the existing supply and distribution chains of liquid petroleum gas, which can, in turn, be used in vehicles, cooking equipment and heating.³⁶

4. Act now to sustain the UK's position as a global leader in engineering biology by committing to long-term investment [BEIS/UKRI/HMT]

Strategic government investment has grown the UK's world-class research capability, established infrastructure, attracted talent and resulted in a growing community of companies. This thriving research base underpins much of the translation taking place in the UK and thus plays a role in leveraging private investment. However, other countries are investing heavily and are beginning to reap the rewards, and the UK's leadership position is not guaranteed in the long-term. If the UK stands still, the momentum will transfer to other countries.

a) Agree a sustainable plan to support the synthetic biology research base, including the SBRCs and, crucially, other key translational infrastructures [BEIS/UKRI/IUK/KTN/Research base/Innovation Centres]

It takes time for new infrastructures and facilities to get to full operational capacity. In the last six years, the majority of key infrastructures in synthetic biology have been established, including seven SBRCs, five DNA foundries, a Knowledge and Innovation Centre (SynbiCITE) and Centres for Doctoral Training, as well as other centres of excellence. These infrastructures have completed their establishment and initiation phase, and are fully operational. Now, a plan is needed to ensure their sustainability and continued operation and growth. The focus should be on translation and partnerships with industry, with funding awarded on a competitive basis for existing facilities that also permits new players to compete.

BOX 3

The Bioeconomy Strategy

There are precedents of the leadership councils working together successful to generate impact. In December 2018 the UK government published *Growing the Bioeconomy*, its National Bioeconomy Strategy to 2030.³⁷ The five most relevant leadership organisations worked jointly to create the strategy:

- Synthetic Biology Leadership Council
- Industrial Biotechnology Leadership Forum
- Food and Drink Sector Council
- Chemistry Council
- Medicines Manufacturing Industry Partnership

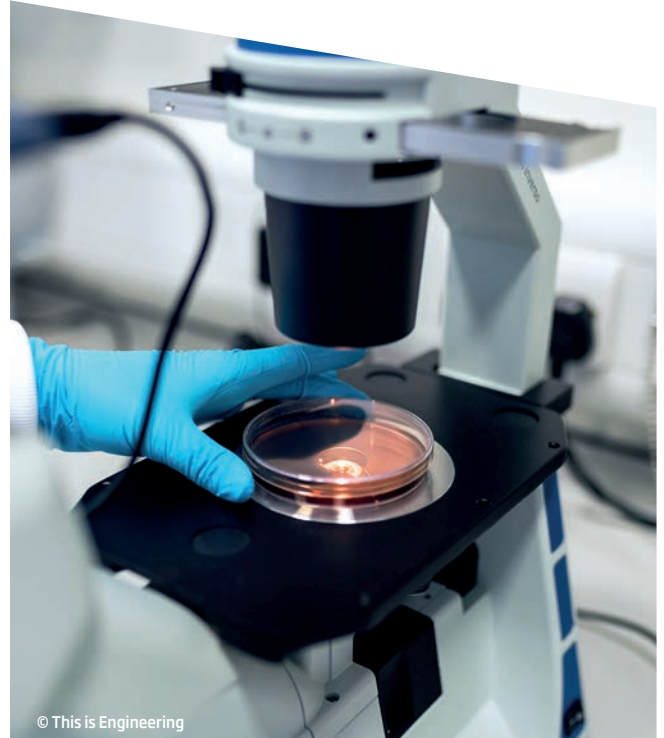
By working together, they were able to unlock further value by linking to wider goals and actions within their respective industries.



CASE STUDY

Capturing pollutants in water

A key component of clean growth is having the capability to remove undesirable compounds from resources we could otherwise use, or to clean them from a contaminated environment. Micropollutants, such as certain pesticides, high performance chemicals and pharmaceuticals, are particularly difficult to remove from water. London-based startup **CustomMem** has developed genetically engineered microbes to produce a cellulose-based material. This material can be tailored to selectively capture particular micropollutants, with applications in wastewater processing and ecosystem clean-up. In January 2018, the company secured £1.2 million in Horizon 2020 SME Instrument funding from the EU Commission.³⁸ In July 2019 the company secured £2.8 million in an oversubscribed seed round, and is now rebranding and changing its name to **Puraffinity**.³⁹



© This is Engineering



© This is Engineering



METHODOLOGY

For the evidence-gathering process this study engaged with relevant stakeholders to understand the state of play in engineering biology in the UK and what is needed to accelerate its growth. This study was informed by companies with relevance to engineering biology, ranging in size, sectoral focus and stage of growth. Individual semi-structured interviews were conducted with 24 companies, and a roundtable focussing on the experiences of 12 SMEs was held in 2018, primarily attended by small and micro-SMEs. In May 2019 the evidence gathered to date was shared at a workshop with over 40 participants from across industry, academia and government. The purpose of the workshop was for the community to input into the design of actionable, community-created recommendations.

To support the evidence-gathering, a broad range of literature was read. In addition, a systematic gap analysis of three key reports was undertaken: *Synthetic Biology: scope, applications and implications*, Royal Academy of Engineering, 2009; *A Synthetic Biology Roadmap for the UK*, UK Synthetic Biology Roadmap Coordination Group, 2012; and *Biodesign for the Bioeconomy*, Synthetic Biology Leadership Council, 2016.

STEERING GROUP

Ian Shott CBE FEng (Chair)

Professor Lionel Clarke OBE

Professor Alicia El Haj FEng

Professor Richard Kitney OBE FEng FRSE

Professor Chris Lowe OBE FEng

Professor Alison Noble OBE FEng FRS

Professor Nilay Shah FEng

REFERENCES

1. *About us*, Colorifix [accessed 2019].
2. *Synthetic biology start-up Colorifix raises \$3m to scale its textile dyeing solution*, Cambridge Network, December 2018.
3. *A National Industrial Biotechnology Strategy to 2030*, Industrial Biotechnology Leadership Forum, 2018.
4. *Biodesign for the Bioeconomy*, Synthetic Biology Leadership Council, 2016; *Engineering Biology Explained*, BIA, 2018 and *UK Synthetic Biology Start up Survey 2017*, SynbiCITE, 2017.
5. *Biodesign for the Bioeconomy*, Synthetic Biology Leadership Council, 2016; *Synthetic Biology Roadmap for the UK*, UK Synthetic Biology Roadmap Coordination Group, 2012; and *Developing standards to support the synthetic biology value chain*, Rand Europe, 2017.
6. *Team Directory*, Ginkgo Bioworks [accessed 2019].
7. *About us*, Ginkgo Bioworks [accessed 2019].
8. *Ginkgo Bioworks secures \$275 million in Series D valuing the company at over \$1 billion*, Sarah Buhr, TechCrunch, December 2017.
9. As part of this study a systematic gap analysis was undertaken of the recommendations from the following reports: *Synthetic Biology: scope, applications and implications*, Royal Academy of Engineering, 2009; *A synthetic biology roadmap for the UK*, UK Synthetic Biology Roadmap Coordination Group, 2012; and *Biodesign for the Bioeconomy*, Synthetic Biology Leadership Council, 2016.
10. *Synthetic Biology: scope, applications and implications*, Royal Academy of Engineering, 2009; *A synthetic biology roadmap for the UK*, UK Synthetic Biology Roadmap Coordination Group, 2012; and *Biodesign for the Bioeconomy*, Synthetic Biology Leadership Council, 2016.
11. *Engineering Biology Observatory shared prior to workshop*, Royal Academy of Engineering, May 2019.
12. *Life Sciences Sector Deal 1*, Government, 2017; and *Life Sciences Sector Deal 2*, Government, 2018.
13. *Life Sciences Industrial Strategy*, Sir John Bell GBE FRS FMedSci, 2017.
14. *Synthetic Biology Start-up Survey 2017*, SynbiCITE, 2017.
15. *Synthetic Biology Annual Investment Report (2018)*, SynBioBeta, 2018.
16. *Synthetic Biology R&D Programme*, National Research Foundation of Singapore [accessed 2019].
17. *Applications*, Evonetix [accessed 2019].
18. *Enzyme-mediated DNA writing*, Nuclera [accessed 2019].
19. *Biodesign for the Bioeconomy*, Synthetic Biology Leadership Council, 2016.
20. *Synthetic Biology for Growth Programme*, BBSRC [accessed 2019].
21. *Synthetic Biology Start-up Survey 2017*, SynbiCITE, 2017.
22. *About us: Biology for anyone, anywhere*, Oxford Nanopore [accessed 2019]; and *Amgen invests £50 million (\$66 million) in Oxford Nanopore Technologies*, Oxford Nanopore [accessed 2019].
23. *Synthetic Biology Start-up Survey 2017*, SynbiCITE, 2017.
24. *The Dowling Review of Business-University Research Collaborations*, Royal Academy of Engineering, 2015; and *The Changing Nature of R&D*, CBI, 2019.
25. *The Dowling Review of Business-University Research Collaborations*, Royal Academy of Engineering, 2015.
26. *The Dowling Review of Business-University Research Collaborations*, Royal Academy of Engineering, 2015.
27. *The Dowling Review of Business-University Research Collaborations*, Royal Academy of Engineering, 2015.
28. *About IBioIC*, IBioIC [accessed 2019].
29. *About us*, SynbiCITE [accessed 2019].
30. *SynbiCITE launches new five-year strategy*, SynbiCITE, October 2018.
31. *Start-ups*, SynbiCITE [accessed 2019].
32. *Growing the Bioeconomy*, Government, December 2018.
33. *Life Sciences Industrial Strategy*, Sir John Bell GBE FRS FMedSci, 2017; *Life Sciences Sector Deal 1*, Government, 2017; and *Life Sciences Sector Deal 2*, Government, 2018.
34. *Gateway to Research - Newton Bhabha Industrial Waste: Integrated biorefinery for converting paper mill waste into chemical wealth (waste-2-wealth)*, UK Research and Innovation [accessed 2019].
35. *CORDIS EU Research Result - Horizon 2020: Fuels from electricity: de novo metabolic conversion of electrochemically produced formate into hydrocarbons*, European Commission [accessed 2019].
36. *Solutions*, C3 BIOTECH [accessed 2019].
37. *Growing the Bioeconomy*, Government, December 2018.
38. *CORDIS EU Research Result - Horizon 2020: A next generation nano media tailored to capture and recycle hazardous micropollutants in contaminated industrial wastewater*, European Commission [accessed 2019].
39. *Puraffinity's \$3.55M Seed*, Puraffinity, July 2019.

ENGINEERING BIOLOGY A PRIORITY FOR GROWTH



ROYAL
ACADEMY OF
ENGINEERING

Royal Academy of Engineering
Prince Philip House
3 Carlton House Terrace
London SW1Y 5DG

020 7766 0600
www.raeng.org.uk