Written evidence from Norwich Research Park (ENB0046)

1. What are the UK's key strengths in the area of engineering biology?

The UK excels in the fundamental sciences that underpin Engineering Biology including engineering, computational modelling, genomics, microbiology, molecular sciences and genetics.

The early investment into Synthetic Biology, including the 'Synthetic Biology for Growth' program and the 'Synthetic Biology Road Map', established the UK as a global lead in Synthetic Biology. This investment resulted in a new generation of scientists - the first to describe themselves as Synthetic Biologists. This program established centres of excellence, including the plant-focussed OpenPlant Centre, that trained many graduate students and postdoctoral scientists and helped to establish new interdisciplinary research groups, focussed on synthetic biology approaches. This augmented the UK's already exceptional reputation for producing high-quality graduates and post-graduates in life-sciences and engineering.

The Genetic Technology (Precision Breeding) Act 2023 represents a significant breakthrough for some biotechnologies, mainly those related to agriculture. It is enabling scientists working in these areas to validate the value of their innovations and providing a pathway to market for new products. This supportive regulatory framework, combined with the exceptional expertise of UK researchers, presents a timely opportunity to explore the full potential of genetic technologies in crops and animals.

1.1 Are there any notable research institutes or groups or key projects? Are there innovative companies, start-ups, or spin-outs that you think are of particular promise or significance using engineering biology in the UK today?

The Norwich Research Park is a cluster of independent, non-profit research organisations - the Earlham Institute, John Innes Centre, Quadram Institute and The Sainsbury Laboratory, co-located with the University of East Anglia and the Norfolk and Norwich University Hospital, and around 40 commercial organisations, start-up and spin-out companies. The Park harbours expertise in genomics, computational modelling, chemistry, biochemistry, pharmacology, and molecular genetics, all of which are critical to engineering biology and which we apply across biomedical, microbial, plant and animal biotechnology.

2. What are the key applications for engineering biology?

The UK has shown the power of synthetic biology through many proof-of-concept projects, and the development of engineering biology allows these to be taken to the next technology readiness level. There is breadth of skill across the UK that incorporates metabolic engineering with recombineering to address greener commodity and speciality chemical production, improved crops with increased nutrient density and disease resistance, gene therapy and regenerative medicine, diagnostics (for both agriculture and health), and bioremediation and metal recovery.

2.5 How does the UK compare to other countries, such as Germany, the US, or China, in terms of investment and policy activity, as well as areas of specialism?

A key investment of the UK SynBio for Growth program was the establishment of UK Biofoundries. The UK Biofoundries were established with a one-off £2 million capital-only investment and no ongoing operational costs, including no funding for the recruitment of staff to run these facilities. Despite this, the UK Biofoundries led the Global Biofoundry community to work together, and have worked to support numerous projects with academics and Industry across the UK. The Earlham Biofoundry, based on the Norwich Research Park has worked collaboratively to help support a number of start-ups in Engineering Biology.

However, despite an early and strong start, the UK has now lost its competitive edge in this area. Due to the scarcity of funding after the initial investment, the UK Biofoundries have been eclipsed by those established in Asia, the USA, the EU and Australia with significantly larger investments and commitments. The UK biofoundries need investment, particularly to enable engagement with start-ups and SMEs, if they are to support the growth of the UK's bioeconomy.

2.6 Which applications for waste biorefining and the circular economy merit particular attention?

The ELEMENTAL project brings together specialists from various UK institutions, led by the Quadram Institute and the University of Kent and including researchers from the University of East Anglia, to establish an open knowledge hub focused on bio-extraction and bio-recovery of metals. The hub aims to enhance ongoing projects related to mineral extraction, urban mining, industrial waste, and nuclear waste by leveraging engineering biology tools and approaches.
For example, bioleaching uses microorganisms to recover metals from various sources, while bioremediation employs micro-organisms or plants to remove metals from polluted water and land. The project also explores the potential of phyto-mining, where certain plants naturally accumulate metals from the soil.

3. How can Government policy support the development of engineering biology?

The current Government has been supportive of Engineering Biology and has recognised the role of this area of research in the growth of the bioeconomy. It is important that any subsequent government:

- Ensures that educational programs remain cutting edge and produce interdisciplinary graduates with training in computational biology, engineering, maths, biology and chemistry;
- Funds early-stage translation projects to enable progression from the earliest Translational Research Levels (TRL1-3). Many great ideas fail at this stage because proofs-of-concepts are insufficiently advanced to establish industry collaborations, but too applied for current UKRI Responsive Mode Panels;
- Ensures that the UK is attractive to leading scientists in the field. Recruitment has been threatened by visa restrictions in the post-Brexit era, economic challenges of immigrating to the UK and international non-competitive wages in academia;
- Establishes and expands the key infrastructures required for the scale-up of biomanufacturing including Biofoundries for strain engineering, and Engineering Biology Hubs and Missions for microbial strain engineering as well as facilities for fermentation and bioprocessing.

3.2 Which are the key enabling technologies that have developed in recent years that have enabled wider applications for engineering biology?

Public Biofoundries such as the Earlham Biofoundry can support the development of pilots, which can benefit start-ups/SMEs seeking data to support scale-up. Biofoundries can accelerate the generation of combinatorial libraries to create multiple variants, for example of biosynthetic pathways, to allow for rapid optimisation of bioproduction strains, accelerating timelines and testing cycles.
The ability to biomanufacture small molecules and biologics, including new-to-nature and designer molecules has been critical: For example, the GlycoCell Engineering Biology Hub, led by the University of Nottingham with the Quadram Institute, is designed to transforming the biomanufacture of glycans for health by developing platform technology to produce glycans, glycoconjugates, and glycoproteins in micro-organisms. There is a range of applications for vaccines, diagnostics and therapeutics for medicine, pandemic preparation and as alternatives to antibiotics.
Engineering Biology can be used to introduce new pathways into production hosts, including plant and microbial expression systems, for the sustainable and scalable production of valuable chemicals currently obtained from petrochemicals and from fragile environments or rare plants. Such technologies are transforming the way we manufacture some of the world’s most valuable chemical products for applications across pharma, agri-science and other sectors.

Engineering plants for agriculture: Genome editing in agricultural species has made remarkable progress in the past five years. UK academic institutes have driven these innovations and are actively engaged in advancing the technology readiness levels of the resulting plants and farmed animals. The first generation of genome-edited crops are based on simple disruptions of single genes, yet confer improved nutritional, sustainability and resilience traits.

Similarly, the technologies behind the development of GM (transgenic) crops continue to improve in precision. It should be noted that important agricultural traits such as resistance to disease that can reduce or eliminate the need for pesticides and fungicides, as well as the biofortification of plants with vitamins, will at times be best achieved using cis-genic and trans-genic technologies where genes from closely or distantly related species, respectively, are transferred into a new species. Such strategies are progressing rapidly outside of the UK and EU, where crops have been safely grown for over twenty years.

Predictive tools that harness machine-learning and AI (artificial intelligence) are critical: AI-driven technologies provide the opportunity to improve the predictability of engineering biological systems. In particular, advances in sequencing technologies have provided rapid and low-cost access to sequencing data, and innovations in Biofoundries and transposon-based technologies such as TraDIS enable the production of very large datasets.

New computational methods are allowing us to analyse these data in ways that were not possible just a few years ago. The availability of large and growing numbers of sequenced genomes (~400,000 microbial and ~1,000 plant genomes) also makes it possible to elucidate individual biosynthetic pathways for target natural products and to discover entirely new chemistries using advanced genome mining approaches.

3.6 Is the UK getting the best value out of its existing facilities, such as the biofoundaries? If not, why not?

The initial investment into the Synthetic Biology Research Centres (SBRCs) and Biofoundries was allowed to expire with no communication of future plans. This resulted in loss of talent and dispersion of expertise. The subsequent 'Transition' and 'Breakthrough' funding calls were last-minute and, as expertise had already been lost from most scientific teams, these new projects required the recruitment and training of new staff. This made it impossible to maximise success from these very short projects, which particularly impacted projects that use organisms with longer life-cycles, including plants and animals.

A key challenge is retaining highly skilled technical staff when they rely on temporary contracts, where security is limited. Such timelines also negatively impact the ability of academics to engage with industry as they do not allow sufficient time for agreement on intellectual property etc.

There is also insufficient diversity in the types of funding available. To date there have been either short (12-24 months) awards (e.g. Breakthrough/ Transition/ Mission Awards) or a very small number of awards for very large centres (SynBioResearch Centres/Mission Hubs). While short, low-cost projects (1-2 years) are helpful for early-stage, high-risk high-reward projects, as well as for translation projects, they are insufficient for most projects.

What is most needed are regular (>1 year) calls for 3-4 year projects that fund teams of 2-4 principal investigators (from different disciplines). While, for example, BBSRC Responsive Mode grants fund projects of this length, the amount of funding available per project is insufficient for the collaborative, multidisciplinary teams of, for example, computational, biological, chemical experts required for engineering biology projects.

4. How can the UK maximise the economic potential of developments in engineering biology?

4.2 How should the Government best support engineering biology startups to scale-up in the UK? Are there specific facilities that it would be helpful to invest in? Are the financial support mechanisms for start-ups and scale-ups appropriate and sufficient, or could they be reformed?

The UK lacks a unified voice that brings together academics with expertise in engineering biology with industry so that they can effectively engage with the UK Government. We need a coordinated approach to technological innovations to allow us to consolidate expertise and foster the creation and exchange of knowledge among researchers, and stakeholders including policy makers. A successful model is the US-based non-profit public-private partnership Engineering Biology Research Consortium (EBRC).

4.10 How does the UK's approach to engineering biology, commercialisation and translation compare to other nations, such as Germany, China and the US? Are there specific areas the UK should look to focus on in order to gain or maintain a competitive advantage?

Incentives are needed to attract longer-term investment in Engineering Biology for new spin-out companies. A key reason why the UK lags behind the USA in major biotechnology companies is often the restricted investment provided at the outset. More incentives to capitalise on new developments would allow for greater investment and longer-term funding of new companies.

4.11 Is there a danger that engineering biology advances developed in the UK are exploited overseas?

In several areas where the UK has excellent academic research, there isn't the industry available to take products to market. As a result of the previous GM regulation in the EU, many UK seed and breeding companies moved their breeding activities to the US, put off by the additional cost and time for product development. The new Genetic Technology (Precision Breeding) Act could increase innovation across the sector and diversify the global market, helping put the UK at the forefront of crop science. However, this Act does not apply to transgenic (GM) crops, meaning that UK innovations such as the high-anthocyanin Purple Tomatoes developed at the John Innes Centre are only available to US customers albeit very successfully, selling 13,000 seed packets in their first launch. The fully blight-resistant potatoes developed by The

Sainsbury Laboratory is currently more commercially feasible in the US than in the UK, even though potato late blight is the most significant potato disease in Britain.

6. How should engineering biology be regulated?

Material Transfer Agreements are limiting collaborations with industry partners. The use of the Uniform Biological Material Transfer Agreements (UB-MTAs) for DNA vectors and strains is required by universities, even in case of material for which patents have expired and/or where they have decided to not protect intellectual property. The UB-MTA also includes clauses restricting redistribution. Material transfer is often time-consuming and effort-intensive, leading to sometimes extreme project delays.

UB-MTAs are extensively used by academic institutions, even though there is very little evidence of legal enforcement. Scientists at the Norwich Research Park, co-developed an alternative, the Open MTA https://www.openplant.org/openmta) of which use has already been demonstrated to foster innovation in industry via the exchange of underpinning materials with industry partners to enable collaboration. The use of UB-MTAs for DNA and strains not protected by intellectual property needs to be addressed.

7. What are the possible barriers and limitations to good and effective use of engineering biology?

7.1 What is already known about the likely limitations of engineering biology due to limits in our scientific understanding? Are there areas that would benefit from more fundamental research before those limitations might be understood? Are some suggested applications implausible?

Microbes and plants are chemical engineers par excellence and are a rich source of medicines, agrochemicals, and other bioactive molecules. However, there remain substantial challenges in relating a gene sequence to a function in a cell, particularly the predominance of convergence in the evolution of specialised metabolism in plants.

Technical advances are needed to decrease error rates in DNA synthesis, which are particularly noticeable in large-scale synthesis, and to address the ability to synthesise challenging sequences, such as those with high 'CG' content or repetitive sequences.

Improving the predictability of engineering is critical: for organisms with long-lifecycles and those that are difficult to engineer, the ability to conduct a large number of experiments to optimise engineering design is time-consuming and costly. This particularly impacts work in complex multicellular systems (animals and plants). Modelling approaches are helpful, but in many cases, particularly plants, we lack the systems level data, which is expensive to generate. It is currently difficult to cover the costs of such data-generation within the sizes of available grants.

7.2 What more can the Government do to foster public understanding of engineering biology? Is public acceptability of these technologies a barrier to deployment in the UK?

Effective communication with stakeholders, including the public, is critical, and we develop public engagement strategies for all projects. We achieve this through various methods, such as: posting explainer videos and informative blog posts on websites and social media; hosting and participating in local events for direct dialogue; using local and national print and broadcast media to communicate the goals and outcomes of Engineering Biology projects; and including social scientists in project teams to identify key areas for public discussion.

At the Norwich Research Park, we take into consideration that the technical/scientific background of the public can be limited; that religious beliefs can influence opinions about the use of technology and should be respected; that many of the potential products of biotechnology (particularly medical products and diagnostic methods) may be high-cost, privately-owned, or will not be sold directly to the public and that these factors will directly influence opinion.

We believe the Government should continue to seek evidence from a wide array of stakeholders and ensure public access to this evidence for informed policymaking. Additionally, it's crucial that the UK's regulatory bodies are well-supported to recruit technical experts for horizon scanning and to collaborate effectively with academia and industry on emerging technologies. Regulatory agencies must be transparent, trustworthy, and functional, prioritizing social and environmental health and welfare. If public trust in essential services such as waterway regulation is compromised, as seen by the ongoing sewage crisis, this could diminish trust in the regulation of more complex technologies.

7.3 Does the UK have a sufficient skills base to harness the potential of engineering biology?

Engineering biology, particularly Biofoundry work, requires trained and experienced technicians and these skills are in short supply here in the UK. As research institutes focussed on PhD and post-PhD post-doctoral training, we require undergraduates and MSc graduates. Training in bioinformatics and computational skills at these levels has improved, enabling more students to work at the intersection of engineering and biology. However, advanced statistics, computational modelling, machine learning and AI, and biochemical modelling are lacking from many MSc level courses.

We also need highly trained technical specialists/technicians in our laboratories. Many of the workflows we use such as routine tissue culture, media prep etc., would be well suited to T-levels, apprenticeships, or degree apprenticeships. Both the Earlham Institute and The Sainsbury Laboratory have successfully hosted T-Level students and we are committed to becoming more involved in developing the skills pipeline within our local workforce. Improved access to apprenticeship training providers for laboratory technician would enable laboratories at the Norwich Research Park to bridge the gap between training and employment and provide more local incentive to pursue this profession.

Where the UK lacks the skills required for engineering biology, talent from outside the UK must be attracted. Recruitment in this area of science is already globally competitive but the Government's immigration policy is adding an unnecessary burden of restrictions and additional cost and bureaucracy to that challenge. Most researchers looking for international career development opportunities cannot afford to pay for visa fees as well as the Immigration Health Surcharge before they take up a new post here. It is a major disincentive particularly to those with dependants. Our experience is that we are receiving fewer applications from international researchers now than in previous years.

Potential further restrictions to the graduate visa route risk deterring even more international students from choosing the UK for their higher education and subsequent career development. We have anecdotal evidence that the Government's anti-immigration rhetoric is as damaging to the UK's talent recruitment as the new immigration restrictions and increased costs themselves. Early career researchers are no longer considering the UK as an attractive career destination.

UK science has always benefitted from the diversity of its multinational workforce. The Government cannot achieve its science superpower ambitions without international collaboration, facilitated by a multinational workforce.

7.4 What barriers are there to incumbent manufacturers making use of engineering biology techniques? Is there anything the Government can do to address these?

Biofoundries: As noted above, the UK Biofoundries provide access to the equipment and expertise to industry scientists who are interested in developing proof-of-concept data and engineered organisms at pilot scales. We would particularly welcome an increase in funding that specifically enables the UK Biofoundries to work with start-ups and SMEs in order to support the delivery of early-stage work and to provide expertise and training. The Australian Biofoundry and the US-based Agile Biofoundry have both been awarded funds specifically for industry collaborations. These have advanced their technical capacity and achievements and have led to rapid growth in the US bioeconomy.

Transgenic crops: Innovations developed by academics and SMEs have effectively been blocked from reaching consumers in Europe as only multinationals have been able to afford the process. The US has opened a path to SMEs to deregulate crop traits that have no adverse environmental effects for subsequent commercialisation, within a reasonable time frame for review. This path enabled the successful commercialization of the Purple Tomato in the US, developed in the UK at the John Innes Centre in 2008.

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