Written evidence from University of Edinburgh (ENB0037)

The University of Edinburgh (www.ed.ac.uk) is an internationally leading research-intensive university, ranked 4th in the UK for the quality and breadth of our research (REF2021), and 5th in the world for Industry, Innovation & Infrastructure (Times Higher Education). We employ over 4,400 independent researchers and train over 6,000 PhD researchers, across the natural sciences and engineering, medical and life sciences, social sciences, arts and humanities. Particular research strengths include our UK-leading research in AI and Engineering Biology, both of which are UK Government Critical Technologies.

The Centre for Engineering Biology is a university-wide community of more than 50 research groups and 200 researchers spanning biology, chemistry, physics, mathematics, engineering, informatics, medicine and social sciences. Research carried out is broad and deep, addressing a diversity of scientific questions with wide ranging impacts for society, industry, the economy and the planet. Researchers explore fundamental biological questions about living cells and systems and apply these insights – often in collaboration with industry – to create innovations for many markets including industrial biotechnology (including bioremediation and biofuels), agriculture, the environment, and medicine and healthcare.

1. What are the UK's key strengths in the area of engineering biology?
A key strength of engineering biology is that it has a diverse reach, with significant impact across a range of application spaces e.g., the pharma industry, advanced therapeutics industry, sustainability and net zero, waste remediation and valorisation; this covers essentially the whole bioeconomy so impact will be enormous.
Edinburgh is an epicentre for Engineering Biology in the UK. The ecosystem is underpinned by the research powerhouse of the University of Edinburgh (UoE) which is the only UK university to secure progressive strategic engineering biology investment from UKRI at every strategic call: from the foundational Centre for Systems Biology at Edinburgh (2007), through the UK Mammalian Synthetic Biology Research Centre (2014), the Edinburgh Genome Foundry (2014 & 2019), Engineering Biology Transition Awards (2021) and finally the recent Engineering Biology Mission Hub (2024) this totals over £70M. The UK's combination of huge strength in the pharmaceutical and therapeutics industries with this mammalian engineering biology being undertaken at the University of Edinburgh is a key strategic USP.

Key engineering biology research areas at UoE are:
(1) Cell and gene therapies focusing on the ability to control the expression of genes at specific levels, in specific places at a specific time (e.g., EngBio Mission hub award led by Prof Susan Rosser and spin outs Trogenix and Concinnity Genetics)
(2) The combination of synthetic biology and synthetic chemistry to create biobased solutions to produce industrially relevant molecules and materials (Prof Stephen Wallace). Stephen has won multiple international awards recognising this work including the prestigious Colworth Medal of the Biochemical Society (2023) and the Royal Society of Chemistry's Norman Heatley Award (2023) and works with multiple companies across the whole supply chain, including global users.
(3) Biological recovery and upcycling of those metals which are essential but of limited worldwide supply (led by Prof Louise Horsfall). Her work has recently been identified as a key innovation in sustainability, winning the Global Trends Forum Grand Prize 2024 from 2050Now La Maision (a global observatory linked to UNESCO), which identifies and recognises the most promising and exciting innovations globally.

The UK is also extremely strong in the combination of engineering biology with informatics, AI and ML. UoE has been leading AI and Computer Science research for over 60 years (being the 2^{nd} University globally to establish AI research and an academic department in the area). The School of Informatics is the largest in the UK and one of the largest in Europe, and is currently ranked amongst the best in the world. UoE is world-leading in the combination of AI & engineering biology, e.g., Prof Filippo Menolascina, Prof Giovanni Stracquadanio and Prof Diego Oyarzun
The long-term funding of the IBioIC (Industrial Biology Innovation Centre) and the recent award of Innovate UK Launchpad funding for biobased manufacturing (2023) underscores the strong biobased manufacturing cluster (including innovation focussed SMEs, see below) centred in the Edinburgh region and across the central belt of Scotland.
The Roslin Institute is globally leading for engineering of livestock with unique combinations of capabilities and facilities.
The UK has key strengths in engineering in vitro alternatives to animal testing, spanning genetic engineering, organ-on-a-chip technologies, creating tissues from human stem cells, and engineering 'lower' organisms (e.g., flies) to become better models for humans. UKRI hosts the NC3Rs, which does an excellent job of coordination and some funding, but NC3Rs is often missing from the Engineering Biology table. This is a mistake – the UK and Netherlands lead the world in this area and there is massive potential for markets as regulators drop their requirement for animal testing (as the FDA has just done) or restrict it (through various EU directives). The UK government could usefully help UK-based industry to make the switch (Contract Research Organizations particularly). It is important to note that testing of agrichemicals, consumer chemicals etc. is just as relevant.
The software being developed for engineering biology from the Edinburgh Genome Foundry is world leading and globally recognised. It is being used by international biofoundries and small and large companies. We are currently leaders in automation for biology in Europe, but EU countries are beginning to invest heavily. Recent investments in the US, Canada, Australia and China also mean that to maintain our competitiveness more serious investment is needed.

Edinburgh and the Central Belt of Scotland has a strong track record and a growing ecosystem of start-up and spin out companies with Edinburgh recognised as the UK's top start up hub outside London (Beauhurst, 2024). There are a number of notable innovative companies in the area e.g., AskBio based in Edinburgh which makes synthetic promoters – it was initially a start-up called Synpromics which was bought by an American company called AskBio which in turn was bought by Bayer. The company is still based in Edinburgh but not UK owned. miAlgae grow omega 3 producing algae on waste from the whisky industry and turn it into fish food for the aquaculture industry.

2. What are the key applications for engineering biology?

Engineering biology is being developed to control cell and gene therapies to switch genes on in the right tissue, at the right time and at the right level for therapeutics to be safe and effective. These applications could be realised within the next 5-10 years. Research aimed at using engineering biology to enhance biologic drug production could have impact within 5 years. There is a lot of activity using engineering biology to enhance sustainability by (1) recycling waste materials and valorising waste (2) using sustainable feedstocks instead of fossil fuels to produce chemicals and fuels. In addition, there is exciting engineering biology work being undertaken in the area of biomaterials. The alternative protein area has become a popular area of engineering biology research. The challenge with all of these areas is scale up. Processes that work at the lab bench do not necessarily work at large commercial scale. In the UK, utilisation of waste streams is a more viable commercial proposition than using sugar-based feedstocks. For many of these processes to become economically viable there would need to be the application of some form of carbon tax to motivate industry to move away from fossil-fuel based processes which are currently cheaper.

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

A £2 billion investment in engineering biology over 10 years would be very welcome. However, there are questions that need to be addressed for this to be effective. (1) is this 'new' investment to be spent in addition to the standard research grant spend? The DSIT response to this question has not been clear. (2) Will this take the form of new, specific engineering biology funding calls – or will it involve standard grant applicants simply indicating their proposal relates to engineering biology (often for projects that are not appropriate) on the expectation the project is more likely to get funded? While it appears to be a significant amount of money over the 10-year duration it is still far short of the level of funding that competitor countries are investing. Support for facilities, skills and research projects are all important because without this diverse funding it will not be possible to grow research in this area.
UKRI has a vital role in supporting engineering biology. It can tap a community of researchers with the expertise to evaluate which projects are viable, novel and could provide a step change. The BBSRC has led in the area closely followed by the EPSRC. There has been less engagement by the MRC and NERC to date. To maximise the impact of engineering biology it is vital to ensure specific engineering biology funding calls, and that projects are for a longer duration (up to 10 yrs.) to allow the research to become mature enough to be translated. Using the standard responsive mode grant panels will not provide an adequate or appropriate multidisciplinary reviewing panel. A scheme that worked well previously was the IB Catalyst scheme for biotechnology which was extremely popular with both academics and industry – the scheme had different funding models going up the TRL levels. UKRI Impact Acceleration Accounts also support a broad range of impact activities, strengthening engagement with users in order to accelerate the translation of research outputs into impacts
In addition, it is essential that we train more people in engineering biology. We need more doctoral training centres to train the next generation of scientists to participate in the new bioeconomy.
The UK is not getting the best value out of the biofoundries because the funding model imposed on them makes them too expensive to be competitive and to be used by start-ups, SMEs and academics. The equipment in the biofoundries was funded by UKRI, but lacks funding for either staff to run them, or consumables to enable them to be set up initially or to innovate. This means that the biofoundries have to be supported by their host institution (apart from the London foundry which is supported by a philanthropic donation). The Edinburgh Genome Foundry is underwritten by the School of Biological Sciences at the University of Edinburgh and we have to recover staff costs and all basic costs associated with running a biofoundry and lab over and above the experimental consumables to provide a service. This makes us extremely expensive and not competitive on price with other foundries globally – e.g., we lost an industry project to a Canadian biofoundry because they were cheaper. We would strongly suggest that when there is capital spend on large complex pieces of equipment that there is associated funding for staff to run the equipment for reasonable duration (e.g., 5yrs). Having such staff on a patchwork of short-term grant funded positions is no substitute because it doesn't provide stability for the

highly skilled staff and it makes them more likely to move on (frequently to industry in competitor countries). In addition, it should be noted that the UK was at the forefront of biofoundry development and made strategic investments in 2014. That was 10yrs ago so the equipment bought is now old and other countries are making very large investments in biofoundries. If the UK wants to remain at the cutting edge, or even just be competitive, in the automation of biology then there is an urgent need for new investment. Edinburgh is engaging with major industrial partners in the sector globally from Fujifilm Diosynth Biosciences, Ginkgo, Twist, Givaudan to name but some. Funding agencies such as DARPA have catalysed companies such as Gingko to collaborate on major initiatives in the US. While there is recognition of the expertise and capability offered by the UK research landscape particularly in Edinburgh greater incentive to engage in driving the field in the UK would be welcomed.

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

VC firms and angel investors are investing in engineering biology in the UK. The scale of investment in an individual company is relatively small compared to investments in equivalent companies in the US and elsewhere. The UK also tends to be more risk averse. It is relatively easy to get a seed investment of £2-3M (in the US you could get 10X that for a similar stage company) but very challenging to get significant funding for growth and scaling of companies to the next stage. In the UK there simply isn't the large pool of investors with large enough funds to enable scaling growth. As a result, companies look outside the UK to scale or very commonly are bought by overseas companies when they are still small and haven't reached their full potential, resulting in lost opportunities for the UK economy. Given the lack of private capital there needs to be governmental support for companies to scale here or inducements for inward investment into the UK rather than companies being bought and the technology leaving the UK. Compared to tech, engineering biology is expensive requiring significant investment in people and lab infrastructure and it is relatively slow so there needs to be patient capital investment.

Some facilities that are lacking are (1) GMP production facilities for small scale production of cell and gene therapies for clinical trials. (2) small and medium scale fermentation facilities enabling testing of scale up.

In Scotland, Scottish Enterprise have a high growth spin out and company creation grant scheme providing up to £270K equity free grant funding for spin outs from Scottish universities. However, there is a serious lack of lab space for companies to move into once out of the universities. This is extremely damaging for attempts to build a Scottish engineering biology company ecosystem. Despite the excellent existing Scottish talent pool many Scottish companies are being forced to move to the south east of England simply to access appropriate lab space.

5. What are the risks posed to society by engineering biology?

There are 2 areas of concern – bad actors and accidental release or harm.

Engineering biology requires a certain level of expertise and facilities particularly if working with pathogens. There is an international sequence screening system in place that commercial DNA synthesis companies and many of the biofoundries (the Edinburgh Genome Foundry was the first academic foundry to participate) sign up to screen DNA orders for sequences from pathogens and flag them up as potentially problematic. The DNA would not be made and shipped without further clarification. The risk assessment is not necessarily simply which sequences are being synthesised, but who is placing the order. For example, a researcher who works on the mechanism of disease caused by a specific pathogen in a legitimate UK research organisation is a different risk prospect compared to someone in an organisation or country of national security concern or someone doing DIY bio in their garage.

Accidental release can occur, but engineered organisms tend to be less able to survive outside the lab than environmental organisms. In addition, they can be engineered to require a nutrient or chemical that is only provided in the lab or production facility without which they cannot survive if they escape into the environment.

Any therapeutics made using engineering biology would have to go through all the standard, and highly rigorous, approvals and safety tests that all therapeutics go through.

6. How should engineering biology be regulated?

The United Kingdom has been a world leader in the development of responsible innovation (RI) (sometimes called responsible research and innovation or RRI) as a crucial component of the wider science governance ecosystem. Responsible innovation recognises that technical expertise alone is not sufficient to introduce engineering biology into new social and commercial contexts, but requires complementary expertise in society, ethics and governance. It also acknowledges that building a culture of responsibility, rather than relying on regulation alone, is necessary. The UK Synthetic Biology Roadmap (2012) highlighted the importance of responsible innovation, and prominent frameworks for its implementation, including the EPSRC's Anticipate, Reflect, Engage, Act (AREA) framework and the BBSRC's Agenda for Responsible Innovation in Biotechnology (see Smith et al. 2019), have proven influential beyond our borders.

The UK's leadership in responsible innovation will slip without dedicated investment. To date, funding has been piecemeal and/or tied to other larger engineering biology initiatives that serve to reduce responsible innovation to an optional 'add-on' with limited influence or legacy beyond specific research projects. While investment in responsible innovation in AI balloons on the back of public and political attention (see e.g., Responsible AI UK), there exists no similar funding for responsible research in engineering biology despite it being identified as one of the five 'Critical Technologies' in the Government's Science and Technology Framework. This compounds a lack of co-ordination in this area across the National Engineering Biology Programme, resulting in a lost opportunity for integrating capacity for responsible innovation across the engineering biology innovation system. Dedicated and co-ordinated funding would enable the UK to maintain and enhance its position in this field through the creation of a workforce with the skills and capacity to participate in the collaborative, interdisciplinary culture required to deliver responsible innovation. Moreover, it would allow more diverse groups to contribute to developing engineering biology that meets the needs of the public as well as signals that the public interest is a policy priority.

Engineering Biology is currently regulated under existing regulations e.g., those that cover genetic modification of crops. Consumer products that are produced via engineering biology are regulated in the same way as consumer products produced via traditional methods. In addition, engineered therapeutics are governed via the same standard mechanisms as govern all medicines including advanced therapies such as cell and gene therapies. To date there has not been a need to develop specific new regulations. The one exception is the opportunity afforded by gene edited crops. The bioscience community warmly welcome the Precision Breeding Act for the potential to provide sustainable solutions in agriculture, however there are delays in its implementation: we need the government to implement the Genetic Technology (Precision Breeding) Act as soon as possible.

Engineering Biology is still not a mature discipline and is yet to be widely taken up uniformly across industry sectors. We should be careful not to impose standardisation too early which could stifle innovation.

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

Public Understanding and Acceptability: The public acceptability of engineering biology-based technologies in the UK is less dependent on 'public understanding' of them than it is on public trust in the institutions that create, promote and govern them. It is well established in the scholarly literature that trust and legitimacy in technological innovation is not achieved through communication aimed at reassuring the public about the safety of new technologies. Such an approach falsely assumes that a lack of technical expertise is the primary source of resistance to technology, and conversely that high levels of technical expertise produce interest/acceptance (the so-called "deficit model", see Marris 2015). However, practical experience shows appetite from the public and a variety of stakeholders (including patients, schools, other non-experts) for clear, accurate, accessible digital information - co-created with scientists - on the science of and underpinning new technologies and treatments, to facilitate more equal engagement and inform decision-making. Recent large-scale surveys establish academic scientists as the most trusted source of such information (Eurobarometer 2021). Activities aimed at such information provision should be supported.

Responsible innovation is also a requisite part of a fruitful approach to legitimate public concerns. Developed in response to emerging technologies including synthetic biology, it holds that building technologies in the public interest that address genuine societal needs is the surest way of addressing questions of acceptability and trust. This requires taking questions like sustainability, public/private value and safety seriously (see e.g., Wilsdon and Willis 2004; Macnaghten 2020; Public trust in science-for-policymaking (British Academy) 2024). Moreover, responsible innovation provides methods to reflect on the goals of engineering biology, anticipate its potential consequences, and create opportunities for stakeholders to shape the development of technologies (Owen et al. 2012). Responsible research is therefore not just about ensuring public acceptance but also about improving the quality and usefulness of innovation itself in the longer term through being responsive to the needs of a diverse and changing society.

Skills Base: The UK does not have a sufficient skills base for engineering biology. The National Vision for Engineering Biology proposes to 'grow and retain a diverse talent pool within the UK to match demand from academia and industry'. For this vision to be realised, funding is needed to establish new Engineering Biology training centres, so industry, academic institutions and their attached facilities can recruit from specialised cohorts. New doctoral training centres (CDTs) are needed, as well as technical research or vocational programmes (Masters, Colleges) to train skilled research assistants and technicians. Another issue is the governments restrictions on legal immigration which negatively impacts on the recruitment of skilled overseas scientists and researchers.

Barriers to Manufacture: Two of the key issues are that many manufacturers trained as chemical or process engineers and don't have any background in biology or using biological processes. A second issue is that to change from an essentially chemical process to an (engineering) biological process often requires a significant change in infrastructure with associated additional implementation costs.

Feedstocks: Globally, feedstocks are primarily based on sugar production from sugar cane or corn. The UK cannot realistically produce these feedstocks for large scale production of products such as biofuels. Much research has been done on developing lignocellulosic materials as feedstocks but to date no commercially viable, scalable process has resulted. Some work was undertaken by the IBioIC in Scotland looking at the opportunity for using sugar beet as a feedstock crop in the UK. There is an opportunity for the UK through government investment in the valorisation of waste and for small volume high value processes. In the UK we do not have sufficient and appropriate research scale-up facilities to demonstrate processes at a commercial scale. The government should look at current provision, examine the cost recovery model (some existing facilities are too expensive to use) and invest in a new network of fermentation facilities. These facilities would also function as training providers for the skilled workers required for the future UK bioeconomy.

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