Written evidence from, Department of Biology, University of York (ENB0028)

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

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?

What is the current economic impact of engineering biology on the UK and what might its potential economic impact be?

UK strengths include in tools for the engineering of plant and microbial systems creating new tools for food production and agritech (e.g. high value chemicals and pharmaceuticals). Institutional strengths include York, Edinburgh, JIC

On engineering insects (insect synthetic biology), the UK is very strong by global comparison, only the US has comparable strength. This is particularly true for vectors (mosquitoes). The strength is both academic (relevant groups at York, Imperial, Liverpool, Keele) and industrial, e.g. Oxitec Ltd which has now been operating for >20 years in this space, and Biocentis Ltd, spinouts from Oxford and Imperial respectively. Economic impact will largely be through export, as insect issues are simply not big enough in the UK to require major commercial involvement – effectively no mosquito-borne disease, limited agricultural pest problems (agriculture is a relatively small part of the economy, also quite diverse so that no single pest has a huge economic impact). Insect farming is a separate area with considerable academic and industrial interest (e.g. York, Cambridge, Imperial, and companies Beta Bugs, Fera, Better Origin, etc); here there is space for domestic industry but knowledge-based export likely (in my view) to be much more valuable.

2. What are the key applications for engineering biology?

Can you give examples of particularly exciting or interesting applications? In particular, applications which could be taken forward or are being worked on in the UK?

Examples include:

Engineering plants (including marine algal systems) to capture carbon more efficiently, to reverse increases in atmospheric CO2.

Engineering plants to produce high value chemicals that have only been available as products of petrochemical industry. The potential is strong for the design of highly specific enzymatic capabilities into established plant chassis, as more sustainable sources of drug compounds, and building blocks for polymer

production. Examples include work on production of anti-malarial drug artemisinin, and alkaloids such as codeine.

Mosquito control: Such as self-spreading gene drive systems of Target Malaria, with additional exciting work (York, Liverpool, and elsewhere), the UK is leading the way in field use of engineered insects across a spectrum of applications. There's competition, of course, mostly from the US but also increasing interest in China, but (for example) the UK (Oxitec) conducted the first field releases of GM insects anywhere in the world, at least 10 years ahead of anyone else, and Target Malaria are leading the way on gene drives (though with competition from the US gaining ground).

On what timescales might the different applications for engineering biology be realised? Which applications are emerging now, and what is on the horizon in the next 5–10 years or further ahead?

A key aspect is regulation. "Contained use" applications may be able to reach market quite quickly. Field use of engineered biological organisms classified as GMOs (the definition of which varies somewhat by territory) is much more problematic, with longer timescales, higher costs and much more uncertainty. This will tend to limit commercial application to larger entities, i.e. large corporations, and large-scale use.

Widespread release of engineered plant is limited by the rate at which seed can be amplified to high enough amounts to make commercially valuable, even after all R&D and regulatory approvals have been met.

Are there areas of application for engineering biology where the hype exceeds the reality, or where significant barriers remain?

Engineering Biology approaches rely on working with understandable biological chassis. For example, use of microbial inocula to improve agricultural productivity is emerging as an important means of providing sustainable agricultural practices that are not reliant on petrochemicals. Engineering such microorganisms using synthetic bottom up approaches is unlikely to be successful, given the large amount of complexity inherent in any poorly understood system. Currently, engineering biology approaches are most likely to be successful with a narrow range of reasonably well understood organisms as the starting points - which may not be the ideal agents for success in real world applications.

Where does engineering biology have the potential to add value over processes that are currently used? What is the nature of this added value (e.g. throughput, sustainability, range of processes that are possible)? Which industries are most likely to be affected?

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?

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

Insect-based bioremediation (e.g. black soldier fly, mealworms, crickets). These can digest a wide range of organic waste and turn it into…insect.

Engineering of microorganisms for degradation of, for example, fabric waste to allow a circular economy in the fashion industry.

Systematic understanding for engineering of complex microbial consortia in e.g. waste for anaerobic digestion into usable energy.

Lignocellulosic waste is a potential game changer in terms of source of material for producing high value products, feedstocks and energy. Engineering of the organisms that carry out the degradation and the agricultural crops that compose the lignocellulose are both targets of importance.

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

Does the Government's "National Vision for Engineering Biology" set out the right priorities for government to develop the engineering biology field in the UK?

Was there anything missing from the strategy that should have been included? Does it build appropriately on earlier approaches to synthetic biology and life sciences?

Training. There is a low level of education and training on engineering biology in undergraduate curricula and in postgraduate training opportunities at Masters and doctoral levels. The government should seek to support postgraduate training through direct funding, and work with, for example, Royal Society of Biology to build up the knowledge base amongst bioscience students at University (and school age) in the concepts and practice of engineering biology. Incorporation of engineering biology principles into QAA Benchmarks for bioscience programmes would also help.

The Government has committed to spend £2 billion over the next 10 years on engineering biology. Is this scale of subsidy sufficient to be competitive? Where should this funding be focused to best support engineering biology in the UK? Is it more important to support facilities, skills, or flagship research projects? Which specific skills or facilities are most needed?

Opinions will differ but, on balance, flagship projects. The field needs high-profile projects and successes (technical, commercial); this will attract newcomers, and funding, to the field and correspondingly help with the other issues.

What should the role of UKRI be in supporting engineering biology? Which research councils are most involved in funding it? Are there areas where more could be done to support interdisciplinary research? What would the best mechanisms be for achieving this?

Problems of definition remain between different arms of UKRI (i.e. EPSRC and BBSRC seem to regard it differently).

Which Government departments, and non-departmental public bodies, are engaged or should be engaged with engineering biology?

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

CRISPR/Cas9, genome sequencing (and reducing cost of 'omics analysis generally). Cheap and rapid availability of nucleic acid synthesis. Ever increasing compute power. Artificial intelligence / machine learning methods underpin engineering biology approaches based on novel protein design.

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

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

Who is investing in engineering biology in the UK, and what is the scale of the investment activity right now? Where are the areas with significant economic and start-up activity?

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?

How well are Innovate UK, British Business Bank and British Infrastructure Bank supporting the commercialisation of engineering biology in the UK?

Are there any elements of UK taxation policy which could support engineering biology? How does it fit into efforts to increase investment in UK technology companies, such as the Mansion House reforms?

More investment in core technologies such as nucleic acid production to be UK based.

Are there opportunities for engineering biology to be used to improve public services, or opportunities for public procurement to support engineering biology, which the Government should consider?

Where could engineering biology improve productivity (GDP/capita) or provide value-added in the UK?

There is potentially considerable value in waste management, both in valorisation of organic waste and in avoided costs (financial and economic) of other disposal routes. While contained-use and biomedical applications may thrive, the political/regulatory environment in the UK is pretty hostile to field use of biological products (the Genetic Technology (Precision Breeding) Act should help for a small subset of products), so more likely knowledge-intensive export industry than UK-based end-users, though export can still contribute substantially to GDP/capita.

Does the UK need large companies in the field to help form the ecosystem in which spinouts and start-ups can thrive? If so, does it have the right ingredients for a healthy engineering biology ecosystem? Are major industrial players investing in engineering biology?

Given that the applications of engineering biology can include applications such as bulk materials or chemical production, are the right support mechanisms in place to support this type of investment in the UK? Or should the UK focus on high-value-add but relatively low through-put applications?

Need some examples of successful application of engineering biology to catalyse further engagement of commerce. These first gains will be in relatively low throughput, high value, socially impactful applications.

What can the Government do to encourage investors to invest in engineering biology and is there a need for investors with more scientific expertise?

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?

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

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

There are regulatory, ethical, and safety concerns that go along with any dual-use technology, particularly in the case of gene-editing. What are the major areas of concern?

Perhaps that extreme caution in this area will stifle commercial exploitation of a range of environmentally-friendly technologies? Need to embed socio-technical analysis of the engineered biology products early into the process of project development, to ensure that products are regarded as valuable by societal stakeholders, not just academics and corporations.

Does engineering biology pose national security risks and if so, what are they? Is the Government's 2023 Biosecurity Strategy sufficient to address these risks and, if not, what more does the Government need to do to?

What early warning systems are in place, both nationally and internationally, to monitor whether engineering biology is being misused? Are these sufficient, or is further regulation needed, for example setting out what DNA synthesis technology can be used for?

6. How should engineering biology be regulated?

Who regulates engineering biology in the UK and internationally?

Is the current regulatory framework adequate? Does it strike the right balance between encouraging innovation and ensuring safety? Where should any reforms be enacted?

How are the ethical, safety, and national security concerns raised in Q5 addressed under current regulations? Are regulators sufficiently independent from Government and from industry?

What implications would rapid progress in engineering biology have for existing regulatory structures, for example around intellectual property?

Industries with relatively short product-development cycles, such as software/IT, tend to prefer relatively short periods of IP protection. Conversely, industries with relatively long cycles, such as pharma, tend to prefer relatively long periods of protection, to provide exclusivity long enough to bring a product to market through a lengthy regulatory process and obtain adequate sales to fund that expensive product development process. At present field use of engineering biology looks very much more like the former than the latter, this probably applies also to biomedical applications, though not necessarily to all applications.

Has regulation in this area evolved quickly enough? Are regulators sufficiently resourced, in terms of expertise and budgets, to keep up with the pace of change of science? How does scientific evidence feed into regulation of engineering biology? What should the Government do to ensure the regulatory environment is able to keep up?

Internationally, regulators (EFSA, US regulators, for example) do an excellent job of keeping up with the science. Of course this is a constantly moving goal, but they do well. Also, most "breakthrough" innovations are not really fundamentally different

from everything that has come before, no matter the developer (or opponent) hype.

Is there a tension between the desire to support open-access science – for example in genome sequencing, genetic datasets, engineering biology platforms and techniques – and a risk that IP developed in the UK is exploited elsewhere?

It's difficult to keep underlying methods secret as regulators and publics understandably want transparency about science in general, and this seems to apply more strongly to genetics-based methods than some others. Hence the 'disclosure for limited monopoly' deal of patents (vs trade secrets).

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

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?

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?

Definitely ("Is public acceptability of these technologies a barrier to deployment in the UK?"). This varies considerably from one application to another, though. Field use of GMOs seems to remain highly problematic – we find ourselves in the bizarre situation where for years various GM crops/products can be sold in the UK, but not grown by UK farmers.

The underlying issue is, of course, a posited – and government-mandated – binary distinction between GMOs (bad, dangerous, highly regulated) and everything else (good, natural, presumed safe – or at least much more lightly regulated). This might possibly have been a justifiable position in the 1970's and 1980's when these technologies – and regulations – were being developed, but it certainly is not now. Of course engineering biology could perhaps be misused – but so can any technology, so that is not a strong argument. It seems to me that the Genetic Technology (Precision Breeding) Act was in some sense a missed opportunity in this regard; rather than try to tackle the issue it merely aimed to move a small fraction of applications/products from one side of the line to the other (indeed back to where, some years earlier, it had generally considered that they lay).

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

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

What are some of the key feedstocks and enabling technologies for engineering biology? Do these pose any risks to the supply chain for a bioeconomy that should be considered and addressed? Are there applications which are less viable in the UK due to a lack of feedstocks?

Does lack of land (e.g. for biofuels or growing GM crops) or dedicated lab space inhibit the growth of engineering biology? If so, what should the Government do to address this?

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