Written evidence from Manchester Institute of Biotechnology, The University of Manchester (ENG0019)

Introduction

The Manchester Institute of Biotechnology (MIB) is an interdisciplinary biocentre based within The University of Manchester, and a forms major part of the University's strategic Biotechnology Beacon. MIB hosted the Manchester Synthetic Biology Research Centre (SYNBIOCHEM), that in turn established the Manchester Biofoundry capability, which together with state-of-the-art technical platforms now supports diverse engineering biology programmes. It is also a partner in the BioDesign Engineering CDT in engineering biology and has a large cohort of PhD students and post-doctoral researchers working in the field.

While the MIB has a large portfolio of fundamental engineering biology research programmes, with cross-campus, national and international academic collaborations, it also works closely with industry to ensure application and translation across diverse sectors.

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

There are significant strengths across Engineering Biology at **The University of Manchester**, from the development of enabling technologies through to their application and translation. Particular strengths exist in the engineering of enzymes, parts, pathways, and microbial systems for the sustainable bio-based production of chemicals, materials, pharmaceuticals, and fuels. This includes the directed evolution of bio-parts, including enzymes, and the development of synthetic bio-mimics[1] and bio-bricks[2] for chemical transformations and construction of advanced materials.
In addition, there are emerging strengths in microbiome engineering and environmental biotechnology.
We are beginning to see a transition towards application of these technologies, with the potential to grow the biomanufacture of sustainable chemicals, which will bring associated economic impact in terms of business growth and jobs in the region.

Across the UK:

- Growing strengths and connectivity across the biomedical/health, environmental, food, sustainable chemicals, and materials sectors (clean growth).
- Strong underpinning technology and research base providing platforms and cross-cutting capabilities.
- The translational landscape is *beginning* to realise that it needs to grow and level-up across the UK.

Innovative companies: There are a growing number of start-up and spin out companies in the North West. A few examples from The University of Manchester:

[1] studying natural biological processes and using this knowledge to develop innovative solutions to human problems
[2] DNA sequences that serve a defined biological function and can be readily assembled with any other BioBrick parts to create new BioBricks with novel properties

C3 Biotechnologies is a Manchester based company that is transforming waste into high performance synthetic fuels using biology and engineering, helping to pave the way towards net zero, with pilot scale facilities now in operation. **Holiferm** is a university spin-out that develops processes for manufacturing biochemicals in eco-friendly and sustainable ways. **Manchester BIOGEL**, a start-up company from UoM, used directed evolution to fabricate biologically relevant scaffolds for use within cell culture, bioprinting and drug discovery. It grew to a team of 10 people, and generated revenues from a global distribution network over a 10-year period, with technology now transferred to **Cell Guidance Systems**.

Economic impact: Much of the early translational focus in engineering biology has been around the health sector and development of therapeutics. However, the bio-based manufacture of chemicals and materials is an area with major potential to generate significant economic growth particularly with the need to transition away from use of petrochemical feedstocks.

2. What are the key applications for engineering biology?

Opportunities: The clean growth space is a key area of opportunity, specifically in the de-fossilisation of carbon-based chemicals/materials production sectors.

- **Chemicals industry** (including materials and fuels): engineering biology has the potential to deliver more sustainable solutions to current industrial processes and bring access to novel chemical diversity with diverse applications.
- **Valorisation[3] of waste** (biorefining): perhaps localised at waste source, and production of new materials with built-in functionality for ease of end-of-life deconstruction (e.g., plastics).
- The easiest and earliest opportunities are likely to be in the chemicals/materials sector, as significant barriers may remain in the adoption/application in other areas.
- Direct application of biotechnology in the environment for bioremediation[4] of pollutants (e.g., organic pollutants during wastewater treatment, recovery of metals), and to achieve sustainable food production (e.g., RNA pesticides, functionalised microbiome deployment[5]).

Timeline: The need for investment is now if we are to realise this vision within the next 5-10 years.

Comparison with other countries: Other countries – such as the US, China, South Korea, Singapore, Australia, Canada, and the EU – are currently putting major investments into research and infrastructure.

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

[3] the process of reusing, recycling or composting waste materials and converting them into more useful products including materials, chemicals, fuels, or other sources of energy

[4] the use of living organisms, like microbes and bacteria to decontaminate affected areas

[5] the use of modified microbial communities in the field (e.g., in agriculture).

Infrastructure investment: The 2023 National Vision for Engineering Biology addresses key priorities, and in particular, highlights the need for infrastructure investment to ease/de-risk the transition from lab to pilot-scale delivery to realise engineering biology applications.

- **Biofoundries:** Existing facilities (e.g., Manchester Biofoundry) are well utilised but would benefit significantly from sustained investment (both capital and running costs) to build on the infrastructure, ensure continuity, and provide the opportunity to expand towards scaled delivery. This would support wider community-use access to Proof-of-Concept platforms, and development of collaborations to drive translation and accelerate innovation.
- **Build** on this to establish **Innovation/Acceleration Hubs** close to the academic base, with access to pilot scale facilities, entrepreneurship training, and the right sector-focussed ecosystem development to deliver impact from the fundamental science base.
- **Industrialisation:** Building on the discovery scale, we need to ease the transition towards the industrialisation of biotechnology, with agile access to the skills and pilot scale infrastructure required for delivery. Regional investment will also need to include funding/subsidies/tax incentives for companies to invest in local skills development to train the technical and production teams needed for biotechnology at scale.
- Ideally **scalability hubs** should be integrated and located close to the academic research base where possible with a mechanism to support engagement with large-scale production.
- **Enabling technologies**: Support for fast accurate sequencing facilities and computational design.
- The development of AI technologies and computational workflows will further enhance our understanding and predictability of systems used in engineering biology.
- Training and retention of core technical staff in academia will be challenging as the industrial base grows, with a recommendation for long term funding for research technical professionals alongside infrastructure investments.

Companies and sector trade bodies alike have made ambitious commitments, i.e., beyond use of low-carbon manufacturing plants/processes. There is high quality data from the Nova-institute on the scale of the challenges ahead in the next 25 years to transition away from fossil-based feedstocks for 'embedded-carbon' that ends up in the products.

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

Facilities to invest in:

- **Regional biorefineries/pilot/demo-scale facilities for bioprocessing/fermentation etc.** To bridge the current difficulties in moving from lab small-scale volumes to pilot-scale and provide the industrialisation ecosystem.
- **Spin-out space** close to state-of-the-art academic facilities to de-risk the transition towards independence at the early stage. Distributed scale-up facilities close to the lab-scale infrastructure with easy access

cost model (currently some companies are using EU sites due to a lack of UK access).

- **Innovation ecosystem** development to help academic spin-outs/start-ups to thrive and grow, not only with access to suitable infrastructure, but also with the entrepreneurial training and support to enable acceleration.
- **A UK version of BioMade**, as per the US-based PPI in this EngBio/biomanufacturing space, would help bring the HEI, SMEs, and industry together. The engineering biology ecosystem needs a connected network from feedstocks (including waste), to intermediaries, and through to final suppliers – a connected infrastructure of capabilities.

Also need to invest in:

- The appropriate **translational ecosystem** to facilitate transition towards industrial application accompanied with easy affordable access to scale up infrastructure and support.
- **Skills and training** to ensure a pipeline of talent within the UK for both academic and industrial workforces, including training for re-skilling and up-skilling the current workforce across all levels (operator through to C-suite level).
- **Knowledge exchange** activities to ensure take up of new academic findings within the current industrial base.

Consideration:

- Large companies are happy for the de-risking to be undertaken at the academic/spin-out/SME level rather than support this directly (and will then take in-house according to business needs).
- Major industrial players (e.g., chemicals / fuels sector) are beginning to look towards sustainability and to consider investment in Engineering Biology – Government encouragement may be required to drive the investment.
- Engineering Biology across the globe is a major focus for academic and industrial investment, with significant sums committed particularly in US and China but also in other places including Singapore, Korea, Canada, Australia, and EU.
- Alongside the range of infrastructure needed to deliver on engineering biology-derived products, companies need access to computational and robotics platforms to enable high-throughput production and automation.

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

Engineering biology research at The University of Manchester has embedded Responsible Research and Innovation (RRI) activities in order to anticipate and consider the potential impacts of the technologies and their deployment in the wider context of society, economy and the environment.
Continued discussions are needed with diverse publics around security and control mechanisms and potential miss-use of engineering biology, and a biosecurity strategy is required to understand, react to, and anticipate biological threats.

Equally, clear public engagement is required to demonstrate the potential for engineering biology to help address societal grand challenges (particularly to move away from petrochemical based production).

6. How should engineering biology be regulated?

The regulation of engineering biology is needed at many levels, with clear guidelines and anticipation of where regulation will be required to ease the industrialisation of engineering biology solutions. For instance, the process of production may require regulation, but the final product may be treated in line with products produced by other means (e.g., synthetic chemistry). Similarly, deployment of engineered micro-organisms, or biomaterials beyond the industrial setting, will require clear regulatory routes.

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

Fundamental science base: Continued support for fundamental research is vital to ensure deep understanding of the benefits and risks of engineering biology. This is particularly important in the biomedical and environmental areas, where there are remaining gaps in the understanding of how the biotechnologies designed to be deployed in-situ will behave in the environment/human body.

Translational base: Support to enable impact creation from engineering biology covering incubation and pilot scale infrastructure, support, and skills to enable the fundamental science progress through the technology readiness levels and realise its potential impact.

Skills base: Training required at all levels, from bench scientists and core technical staff through to bioprocess engineers for scale-up delivery. There is a requirement for interdisciplinary skills and vision.

07 May 2024