

# Engineering biology: opportunities for the UK economy and national goals

## Annex A: Case Study: Engineering Biology for novel sustainable fuels

### Background

1. Liquid fuel is essential for a range of sectors and applications including transportation, defence, agriculture, and heating some homes. In 2020 the transport sector accounted for the largest share (24%) of domestic greenhouse gases<sup>1</sup> whilst the UK petroleum industry alliance estimates that some 46 billion litres of road transport fuel are used each year along with 14 billion litres of aviation fuel<sup>2</sup>.
2. The UK has committed to reaching net zero by 2050. Decarbonisation of the UK transport sector is underway but is challenging due to the comparatively low cost of fossil fuels, increasing demand for transport services, and subsectors that cannot be easily electrified (including aviation and shipping). The UK decarbonisation strategy for the transport sector and the Jet Zero strategy recognise the role of cleaner low carbon fuels in reducing emissions<sup>3,4</sup>. Globally there is likely to be ongoing demand for sustainable hydrocarbon-based fuels for a significant period and, even in countries pushing towards net zero, the transition to alternatives such as electrification and hydrogen could take longer than expected.

### The Opportunity

3. In contrast to other application areas for engineering biology, such as pharmaceuticals, fuel has historically been a relatively low-value but high-volume commodity. Overall, there is a huge potential global market on offer for sustainable fuels that is expected to grow over the next decade. For sustainable aviation fuel alone, the global market has been projected to reach ~\$15bn (USD) by 2030, from \$216m in 2021<sup>5</sup>, with another analysis projecting the broader renewable fuels market to reach ~\$1.7tn by 2030<sup>6</sup>. Long-term, a range of energy alternatives are being explored, including the use of hydrogen, which may limit the overall market share any one fuel solution could secure, depending on when and by how much these technologies penetrate the market.
4. Beyond the environmental benefits, potential advantages for sustainable fuels produced using engineering biology include:
  - Synthesis of highly specific hydrocarbon mixtures optimising energy density that are compatible with current infrastructure (drop-in fuels).
  - Reduced impurities which could extend engine life and reduce maintenance costs.
  - Reduced requirements for refining/processing increasing the productivity of manufacturing.
  - Improved air quality due to reduced particulates/pollutants in exhaust fumes.
  - Designed and efficient by-product generation and use.

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<sup>1</sup> Department for Transport. Supporting Recycled Carbon Fuels through the Renewable Transport Fuel Obligation. 2022. <https://www.gov.uk/government/consultations/supporting-recycled-carbon-fuels-through-the-renewable-transport-fuel-obligation>

<sup>2</sup> UK Petroleum Industry Association (UKPIA). Fuels. <https://www.ukpia.com/downstream-policy/fuels/>

<sup>3</sup> Department for Transport. Transport decarbonisation plan. 2021. <https://www.gov.uk/government/publications/transport-decarbonisation-plan>

<sup>4</sup> Department for Transport. Jet Zero strategy: delivering net zero aviation by 2050. 2022. <https://www.gov.uk/government/publications/jet-zero-strategy-delivering-net-zero-aviation-by-2050>

<sup>5</sup> The Brainy Insights. Sustainable Aviation Fuel Market. 2022. <https://www.thebrainyinsights.com/report/sustainable-aviation-fuel-market-12818>

<sup>6</sup> Precedence Research. Renewable Fuel Market Size to Worth Around US\$ 1,753.6 Bn by 2030. 2022. <https://www.globenewswire.com/en/news-release/2022/05/18/2446464/0/en/Renewable-Fuel-Market-Size-to-Worth-Around-US-1-753-6-Bn-by-2030.html>

5. 'Drop-in' sustainable fuels (which use existing infrastructure but are net-zero carbon emitters) will have a considerable economic and speed to market benefit over fuels which require new infrastructure if key price points can be reached.

### How it works

6. **Biomass to fuel.** Engineering biology offers possible productivity increases for current pathways from plant biomass (e.g. increasing lipid/energy content, enhancing degradation or growth through direct genetic modification or engineered soil microbiomes) and wholly new routes to fuels or precursors through direct production in engineered algae, bacteria, and yeast.
7. **Waste to fuel.** Waste gases from industrial processes as well as solid and liquid waste (e.g. food waste or cooking oil) can be processed by microbes to produce valuable chemicals, hydrogen, and liquid fuel/precursors. Waste to fuel routes that use only thermal and chemical reactions are already deployed at various sites in the UK<sup>7</sup>. Engineered microbes could process otherwise difficult and varied waste streams into liquid fuels and be optimised to produce valuable/specific by-products. The technology could be retrofitted to waste-generating sites to increase recycling of waste and generating a new revenue stream.
8. **Power to fuel.** Renewable electricity can be used to generate hydrogen via electrolysis (the splitting of water into oxygen and hydrogen) which can subsequently be reacted with carbon dioxide to produce liquid hydrocarbons for processing into fuels (e-fuels). Precision engineering of microorganisms presents an opportunity to optimise the reaction of carbon dioxide and hydrogen into drop-in fuels, minimising further processing. The EU Horizon 2020 programme has funded several projects (eForFuel<sup>8</sup> and Bactofuel<sup>9</sup>) to investigate this which involve UK companies (C3 Biotechnologies) and universities (Lancaster, Imperial).

### Challenges

#### *Economic Viability*

9. Every fuel must compete on performance, convenience, and price. Decarbonisation strategies may improve the economic feasibility of more sustainable alternative fuels (e.g. by raising the cost of jet fuel produced from crude oil) – but the exact technology, infrastructure, and economic, environmental, and regulatory context that would support this is unclear and may be sector-specific. The window of economic feasibility may also be limited with the progression of other energy sources and fuels (e.g., Hydrogen).

#### *Technology Readiness*

10. Many sustainable fuel technologies are already commercialised. However, applications of engineering biology to novel fuels are generally at a low technology readiness level (TRL) and have not been demonstrated at scale. These technologies will need time and resources to develop and there are likely multiple routes that have not been fully explored in the context of recent advances (e.g. optimising plant biomass growth through soil microbiome manipulation).
11. Low TRL routes such as algal biofuels require further understanding of the optimal biological chassis (species/strain), how to achieve optimal growth/characteristics via

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<sup>7</sup> For example, the Phillips 66 Humber refinery produces sustainable aviation fuel (SAF) from waste oil, with further SAF refinery sites using waste in development. Advanced Biofuels Solutions operate a plant in Swindon processing 8000 tonnes of household waste each year into biofuel and biohydrogen.

<sup>8</sup> eForFuel. [www.eforfuel.eu](http://www.eforfuel.eu)

<sup>9</sup> BactoFuel. <http://bactofuel.eu/>

gene editing and process management, how to effectively design by-product pathways to improve revenue potential, and how to increase sustainability by reducing energy and freshwater requirements. Routes will also need to develop pathways to higher molecular weight products with greater energy density.

#### *Manufacturing at Scale*

12. Fuels must be produced in extremely large volumes. Technologies can often be demonstrated at laboratory scale but struggle to find sufficient financing or facilities to demonstrate at a larger scale. Some routes may be more scalable than others, e.g. already established routes to produce bioethanol which could be enhanced through engineering biology in the short term.

#### *Biomass Availability and Biosecurity*

13. Access to biomass and waste material in the UK is limited and environmental conditions for growth of photosynthetic biomass (e.g. plants, algae) are likely better in temperate regions. Innovative farming or cultivation techniques (e.g. vertical farming, seawater farms<sup>10</sup>, macroalgae sea culture<sup>11</sup>) could be developed to mitigate this but cost, sustainability, and efficiency compared to other options should be considered. Importing biomass/waste or transportation from dispersed regions of the UK would have implications for the emissions profile of the resultant fuels. Any use of land to grow crops or other biomass for fuel production would have to be balanced against food security considerations.
14. Algal biofuel production may be limited to use in open waters considering the cost and energy requirements of closed photobioreactors. There is a biosecurity risk inherent to this, and the wider cultivation of genetically modified organisms in open systems for fuel or other applications.

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<sup>10</sup> Acre. The UK's first seawater farm that grows crops without freshwater. 2019. <https://www.acre.com/blog/2019/12/the-uks-first-seawater-farm-that-grows-crops-without-freshwater>

<sup>11</sup> The University of Manchester. Biofuels could be made from bacteria that grow in seawater rather than from crude oil. 2019. <https://www.manchester.ac.uk/discover/news/breakthrough-for-biofuels-that-could-be-made--from-seawater-rather-than-crude-oil/>

## Annex B: Case study: Materials

### Background

1. Engineering biology can be used to produce 'biomaterials' with novel properties. These have the potential to support a more sustainable future across a variety of industries by reducing waste and CO<sub>2</sub> emissions associated with manufacture, as well as improving product functionality. Widespread adoption of these materials will require significant investment in infrastructure to enable SMEs to scale up and improve the economic viability of product manufacture.

### The Opportunity

2. Biomaterials with bespoke qualities have been developed and utilised to create more resilient, flexible and biodegradable products, many of which have demonstrated early success across numerous sectors and are reaching commercialisation. However, despite the UK having a strong research base in the development of novel materials, a large proportion of the translation of this research is occurring abroad (e.g., BoltThreads (US), Spiber (Japan), and AMSilk (Germany)).
3. The UK's textile industry currently generates £20bn for the UK economy<sup>12</sup>, whilst the fashion industry, the UK's largest creative industry, is worth £26 billion and supports over 800,000 jobs<sup>13</sup>. Biomaterials present an opportunity to gain strategic advantage for economic growth, with the biotextile market projected to be worth \$2.2 billion by 2026<sup>14</sup>.
4. The UK textile industry is extremely polluting, producing 1.2 billion tonnes of CO<sub>2</sub> equivalent (CO<sub>2</sub>e) per year. Engineering biology can support the development of novel synthetic materials and sustainable dyes which aim to improve resource-efficiency in the industry, cut carbon emissions, and reduce chemical use. For instance, the British company Modern Synthesis Ltd have utilised microbial textile technology to develop a new class of textiles by microbial bioweaving to create high-strength biodegradable materials<sup>15</sup>. Colorifix, a Norwich-based biotechnology start-up, uses genetically engineered bacteria to dye fabrics, reducing the water consumption of conventional cotton dyeing steps by 48%<sup>16</sup>.
5. Within the construction industry, biomaterials can reduce expenses, fuel requirements, carbon footprints and increase product efficiency. HBBE Ltd have produced mycelium, which is a self-growing low-cost biomaterial which can be manufactured into a cheap insulation alternative. The 2021 Industrial Decarbonisation Strategy outlined how the government aims to decarbonise the construction industry to meet emissions goals in the coming decade<sup>17</sup>. The use of biomaterials could help to support this goal.
6. Novel peptide-based materials can also be created from bacteria to produce adhesives which have potential applications within the medical and defence industries. Pioneers of

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<sup>12</sup> UK Fashion and Textile Association (UKFT). Compendium of Industry Statistics and Analysis. 2020. <https://www.ukft.org/business-advice/industry-reports-and-stats/>

<sup>13</sup> British Council. The Power of Fashion. 2016. <https://www.britishcouncil.org/research-policy-insight/insight-articles/power-fashion>

<sup>14</sup> World Economic Forum. These materials are replacing animal-based products in the fashion industry. 2021. <https://www.weforum.org/agenda/2021/10/these-materials-are-replacing-animal-based-products-in-the-fashion-industry/>

<sup>15</sup> Modern Synthesis Ltd. <https://modern-synthesis.com/>

<sup>16</sup> Colorifix. <https://colorifix.com/why-colorifix/>

<sup>17</sup> HM Government, Minister of State for Business, Energy and Clean Growth. Industrial Decarbonisation Strategy. 2021. <https://www.gov.uk/government/publications/industrial-decarbonisation-strategy>

this technology, Zentraxa Ltd are establishing a new niche in the synthetic peptide market, which is projected to be worth over \$425 million by 2023.

## **Challenges**

### *Infrastructure*

7. The UK lacks the infrastructure required for the scaling of systems from small to medium and securing significant scale up investments. This prevents companies expanding manufacturing processes and commercialising products.

### *Economic viability*

8. A consistent theme of using biomaterials for manufacturing is the increased cost associated with the green premium for biobased products. These high costs make it increasingly difficult for emerging biomaterials to penetrate the market.
9. Research funding is often difficult to attain for novel areas of materials manufacture that are at low levels of technological readiness. Commercialisation is also difficult, with regulations required to incentivise and de-risk the pulling-through of marketable products.

## Annex C: Case Study: Engineering biology for alternative proteins

### Background

1. The poor accessibility and shortage of dietary protein, combined with our targets towards environmental sustainability, is driving a rapid interest in novel, alternative protein sources amongst consumers<sup>18</sup> (e.g., pea and soy protein). Engineering biology techniques to optimise these protein sources or create additional sources could fundamentally change the food system, help to meet protein demand, and provide resilience to the UK's food supply.
2. The alternative protein space is currently dominated by biomass fermentation-led meat alternatives, such as Quorn, which is derived from fungal mycoprotein. However, genetically engineered organisms (microbes, plants, or animals) could provide:
  - new biomass fermentation methods
  - precision fermented goods (e.g., the use of microbes to produce high-quality additives)
  - optimised crops designed for plant-based alternatives to meat
  - optimised livestock cell/tissue sources for cultured meat products.
3. The government has stated that it wishes to remain “at the front of this growing and innovative sector by supporting alternative protein research and innovation”<sup>19</sup>. Although the government has committed to investing over £120 million in food system innovation, which includes alternative protein sources, some experts consider the Netherlands, Singapore, and Israel to have already taken the lead ahead of the UK, resulting in some UK research being commercialised abroad.

### The Opportunity

4. The Food Standards Agency states that “plant-based proteins and microorganism-based proteins may reach price parity with meat by 2025, and cultured meat parity with animal meat by 2035”<sup>20</sup>.
5. The novel protein research space is highly interdisciplinary, and the UK has core strengths in almost all related fields (including microbiology, bioengineering, regenerative medicine, crop science, developmental biology and food manufacturing), priming the UK to lead globally in alternative proteins. However, routes to bring this expertise together is fundamental for unlocking this potential.

### Engineering Biology Pathways

6. Recent legislation to approve the use of gene editing in food sources could lead to the development of fermentation processes that are maintained on the use of non-traditional feedstocks. This could free up food sources for direct human consumption (e.g., sugar, water). Production could also utilise waste materials (e.g., CO<sub>2</sub>, food waste) to reduce the environmental impact of the food industry<sup>21</sup>.
7. Engineering biology could drive the development of engineered crops which are specifically designed for novel protein production. Plant-based meat alternatives can often struggle with off-flavours due to the innate biological attributes of the original plant

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<sup>18</sup> Boston Consulting Group; Blue Horizon. Food for Thought: The Protein Transformation. 2021. <https://www.bcg.com/publications/2021/the-benefits-of-plant-based-meats>

<sup>19</sup> HM Government, Secretary of State for Environment, Food and Rural Affairs. Government Food Strategy. 2022. <https://www.gov.uk/government/publications/government-food-strategy/government-food-strategy>

<sup>20</sup> Food Standards Agency. Alternative Proteins for Human Consumption. University of Cambridge, Cambridge, 2022. <https://doi.org/10.46756/sci.fsa.wdu243>

<sup>21</sup> Example found here: Marcellin, E; Angenet, L; Nielsen, L. & Molitor, B. Recycling carbon for sustainable protein production using gas fermentation. Current Opinions in Biotechnology 2022; volume 76. <https://doi.org/10.1016/j.copbio.2022.102723>

protein source, but these traits could be reduced or removed through the genetic engineering of source crops to create more palatable end products.

8. In the longer-term, engineered mammalian (or possibly insect-based<sup>22</sup>) protein sources will start to enter the market. The genetic editing of mammalian cell lines is likely to be used to precisely direct stem cell differentiation towards traditional meat cell types, creating unstructured (sausage, burger) and later structured (steak, fillet) cultured meat and seafood products. It may also be used to modify the characteristics of the starting cell populations, boosting the nutritional value of the end product (e.g., by containing higher levels of omega 3/6, or lower cholesterol).

## **Challenges**

### *Skills*

9. Engineering biology is a highly interdisciplinary and potentially disruptive research area. There is an unmet need for a focused pipeline for skills and talent in the alternative proteins space. However, there are currently no dedicated training programmes, doctoral training partnerships, or centres of excellence for scientists in this area, creating a large skills gap and a lack of co-ordination. This has led to many experts in this field going abroad for better opportunities, reducing the UK's talent pool.

### *Infrastructure*

10. There are challenges in how academia connects to the path of commercialisation, particularly at the earlier stages of research, due to a lack of infrastructure (e.g., pilot-stage fermentation facilities). This hinders the transfer of technology from pre-competitive research out to start-ups and creates a window for commercialisation abroad.

### *Public perception*

11. To encourage consumer acceptance of engineered protein sources, public concerns regarding safety issues will have to be addressed. Individual companies are largely unable to tackle this problem alone due to resourcing, meaning that public education on product safety, nutrition and labelling is needed from government, funders, and academia to ensure adoption. Additional encouragement for industry to help in communication would also be beneficial.

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<sup>22</sup> Rubio, N; Fish, D; Trimmer, B. & Kaplan, A. Possibilities for Engineered Insect Tissue as a Food Source. *Frontiers in Sustainable Food Systems* 2019: volume 3, article 24. <https://doi.org/10.3389/fsufs.2019.00024>

## Annex D: Case Study: Engineering Biology for data storage

### Background

1. Deoxyribonucleic acid (DNA) is the biological code which programmes life. The composition of the code determines the basis of our cells, tissues, and organs. Engineering biology makes it possible to create synthetic DNA strands which encode digital, rather than biological, information. Recently DNA-encoded data includes Shakespeare's full works<sup>23</sup> and the entirety of Wikipedia (amounting to 16 gigabytes)<sup>24</sup>. This synthesised DNA can be encapsulated for long-term data storage, often at low temperatures. Adoption of this technology at scale will require development of synthesis technologies.

### The Opportunity

2. The large, global increase in generated data (by 2025 this is expected to be 463 exabytes per day<sup>25</sup>) increases the need for new and robust storage methods<sup>26</sup>. Archival storage makes up a majority of newly generated data storage needs.
3. Currently, archival data storage primarily uses magnetic tapes which degrade after 10-15 years, requiring data to be migrated into new storage. In contrast, at low temperatures, DNA is far more durable<sup>27</sup>, takes up less space due to its higher data density<sup>28,29</sup>, and requires less energy to maintain. This makes DNA storage cheaper and less environmentally damaging than conventional methods. Although synthesis of long strands of DNA is currently expensive and impractical for large scale applications, sequencing software can piece together data from shorter DNA fragments and detect and correct any errors.
4. Data can be read and retrieved from DNA molecules via conventional DNA sequencing equipment, already widely used to sequence COVID-19 and human genomes in the NHS. Furthermore, DNA data can also be copied and amplified on standard PCR machines. Yet, whilst DNA sequencing machines are fairly cheap, the cost of DNA synthesis technology (to write and encode the DNA data) is high and presents a barrier for data storage applications.
5. Innovation in DNA sequencing capabilities (e.g., Oxford Nanopore) will make the DNA sequencing process higher throughput, cheaper and more portable, increasing the accessibility and affordability of technology adoption. New UK start-up companies (e.g., Evonetix, Nuclera) are innovating around new scalable DNA synthesis technologies.

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<sup>23</sup> Goldman, N and others. Towards practical, high-capacity, low-maintenance information storage in synthesized DNA. *Nature* 2013: volume 494, pages 77-80. <https://doi.org/10.1038/nature11875>

<sup>24</sup> CNET. Startup packs all 16GB of Wikipedia onto DNA strands to demonstrate new storage tech. 2019. <https://www.cnet.com/tech/computing/startup-packs-all-16gb-wikipedia-onto-dna-strands-demonstrate-new-storage-tech/>.

<sup>25</sup> Raconteur. 109379A Day in Data. <https://www.raconteur.net/infographics/a-day-in-data/>

<sup>26</sup> Furthur Market Research. The Escalating Challenge of Preserving Enterprise Data. 2022. [https://asset.fujifilm.com/master/americas/files/2022-08/5082fc03fc44d80b691c87a1a96febd5/Furthur\\_Market\\_Research\\_WP\\_080322\\_FINAL.pdf](https://asset.fujifilm.com/master/americas/files/2022-08/5082fc03fc44d80b691c87a1a96febd5/Furthur_Market_Research_WP_080322_FINAL.pdf)

<sup>27</sup> Kaplan, M. DNA has a 521-year half-life. *Nature* 2012. <https://doi.org/10.1038/nature.2012.11555>.

<sup>28</sup> Science. DNA could store all of the world's data in one room. 2017. <https://www.science.org/content/article/dna-could-store-all-worlds-data-one-room>.

<sup>29</sup> TechRadar. Watch out HDDs, the next generation of tape is here. 2019. <https://www.techradar.com/news/the-next-generation-of-tape-storage-is-finally-here-with-a-whopping-45tb-capacity>.

## How it works

6. Write – Creating DNA-format data begins with encoding digital data, normally stored in binary form, into a DNA representation (i.e., converting digital binary to DNA's four-letter system). This code is then synthesised from scratch into short DNA strands. Strands of approximately 300 DNA bases (letters) are the current commercial limit<sup>30</sup>, but data can be partitioned across several strands.
7. Store - Once synthesized, DNA can be encapsulated using methods to slow down degradation, some of which require drying or freezing. When the data needs to be accessed or duplicated, the sample is de-encapsulated and undergoes amplification and sequencing.
8. Retrieve - Once the raw DNA sequence is established, decoding software can detect and correct errors, and stitch the DNA sequence together to regenerate the original data file. However, it is crucial that the process happens quickly and with low computational intensity. There is also an opportunity to develop even cheaper DNA synthesis technologies that allow for sequence errors.
9. New approaches to storing digital data using nucleic acids (e.g., as fluorescent arrays<sup>31</sup>) could potentially provide an alternative means to read data without the use of conventional sequencers.

## Challenges

### *Read Latency*

10. Due to a high 'read latency' (delay in retrieving stored information), DNA storage is currently only considered feasible for archival storage. Opening this to broader applications would require high-speed data access and a reduction in latency down to potentially microseconds.

### *Parallel technologies*

11. To be adopted at scale, DNA data synthesis will need to be cheap, easy to use, high throughput (large amount of information can be stored and retrieved quickly) and environmentally sustainable. This will likely require the use of parallel microfluidic systems, which are still in development and currently expensive to operate, but costs could reduce if the technology is adopted at scale.
12. One of the key benefits of DNA data storage is its extremely high data density. However, many data storage scenarios that don't require this, potentially allowing alternative technologies, such as quartz glass storage<sup>32</sup>, to compete with DNA-based formats for archival storage.

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<sup>30</sup> Business Wire. Twist Bioscience Launches Long Oligos to Fuel Drug Development, DNA Data Storage and Gene Editing Research. 2019. <https://www.businesswire.com/news/home/20190729005200/en/Twist-Bioscience-Launches-Long-Oligos-to-Fuel-Drug-Development-DNA-Data-Storage-and-Gene-Editing-Research>

<sup>31</sup> Dickinson, G and others. An alternative approach to nucleic acid memory. Nature Communications 2021; volume 12, article number 2371. <https://doi.org/10.1038/s41467-021-22277-y>

<sup>32</sup> Microsoft. Project Silica proof of concept stores Warner Bros. 'Superman' movie on quartz glass. 2019. <https://news.microsoft.com/innovation-stories/ignite-project-silica-superman/>

## *Skills*

13. The adoption of biotechnology methods to encode data at scale will require people with skills in both computation/data science *and* molecular biology. This would involve the additional reskilling of existing workforces, or the training/recruitment of new workforces. A comprehensive approach to build skills for DNA data storage should be curated by government.

## Annex E: Capabilities underpinning Engineering Biology – Current situation in the UK

We do not yet know how to comprehensively write in the natural language of biology, DNA, to predictably engineer biology. We need to learn how to rapidly build the DNA of organisms and how to write DNA sequences that produce any desired function. Addressing these challenges will make biology truly engineerable, and support innovation and company growth across sectors.

### *Design*

1. The UK has a strong research base in **DNA sequencing and genomics**, led by the Wellcome Sanger Institute and the MRC Laboratory of Molecular Biology. The UK also hosts the European Bioinformatics Institute, one of the six major European Molecular Biology Laboratories, and is home to one of the world's largest concentrations of scientific and technical expertise in genomics.
2. The UK benefits from domestic enablers of engineering biology, such as Oxford Nanopore, which provides high throughput **DNA sequencing technology**. Globally, the UK ranks third for publications and investment activity within synthetic genomics but ninth for global patents filed by UK companies<sup>33</sup>.
3. The UK has led significant research projects to improve **understanding of biological systems** such as the Darwin Tree of Life Project, which explores the biology of organisms and evolution to aid conservation and provide new tools for medicine and biotechnology. The 100,000 Genome Project, led by Genomics England, sequenced 100,000 genomes from approximately 85,000 NHS patients affected by rare diseases to understand the role our genes have in health and disease<sup>34</sup>. The project led to new diagnoses for 25% of participants, 14% of which found variations of the genome that would have been missed by traditional testing methods.

### *Artificial intelligence (AI) and machine learning (ML) for engineering biology*

4. AI and ML methods can be used to resolve the complexity of engineering biology systems, increase the speed of problem solving and identify systems which lead to function in the Design-Build-Test-Learn process.
5. AI and ML techniques can be used to learn and detect patterns within a data set. This can support a wide scope of applications by enabling automated experimental data analysis and optimising the design of biological systems in silico. DeepMind launched the AI system AlphaFold<sup>35</sup> in 2016, which can accurately predict 3D models of proteins, highlighting how AI can be used to accelerate research within the field.
6. In May 2022, UKRI awarded £1.5m of funding to Imperial's Centre for Synthetic Biology to establish AI-4-EB, a collaboration with seven industrial partners and ten academic institutes aiming to leverage and combine key technologies in AI and engineering to enable

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<sup>33</sup> Synthetic Genomics, Rapid Technology Assessment. 2021.

<sup>34</sup> 100,000 Genomes Project. <https://www.genomicsengland.co.uk/initiatives/100000-genomes-project>

<sup>35</sup> AlphaFold. <https://alphafold.ebi.ac.uk/>

innovations<sup>36</sup>. This will significantly accelerate the translation of research into commercial and societal impacts by increasing capabilities for analysis, design and optimisation of engineered biosystems.

### *Data*

7. The availability, quality, and uniformity of data are core challenges in using AI and ML to model systems in silico. FAIR (Findable, Accessible, Interoperable and Reusable) and traceable data is needed for the effective exploration and exploitation of machine learning<sup>37,38</sup>. The hardware used to produce data within laboratories is diverse and fragmented, and research culture barriers to horde data.
8. Compared to other disciplines, there is also a lack of curated and standardised data sets in the life science field. Funding is targeted at end point applications rather than at platform technologies which could introduce the right standardisation, metrology, data gathering and processing.

### *DNA Synthesis*

9. DNA synthesis is the artificial creation of DNA molecules within a laboratory setting. It is an essential technique in molecular biology and has a broad spectrum of applications across disciplines including genetic engineering, clinical diagnosis/treatment and drug discovery. Modern DNA synthesis methods may offer a more sustainable pathway to access desired building blocks for engineering biology applications, in comparison to traditional strategies.
10. One innovation within DNA synthesis is DNA origami which involves folding DNA to create 2D and 3D shapes at nanoscale. These can be used for the construction of nanorobots which are structures used for studying enzyme-substrate interactions and drug delivery.
11. The UK is a world leader in DNA synthesis, however, the process has not significantly advanced since the 1980's. Techniques are limited by the size/length of the sequences and accuracy/error rates. Consequently, these approaches are currently not scalable enough to support the production of large genomes economically.
12. Despite innovations, DNA synthesis is often expensive. Competition with existing international supply chains can hold back the UK's development process. Many suppliers are situated outside the UK, with the most located in Germany (Genart @ Thermo Fisher), the US (IDT integrated DNA technologies, TWIST Biosciences) and China (SBS Genetech). These supply chains are well established but the UK should aim to expand capabilities and develop an improved supply chain for DNA synthesis, to protect against the supply chain issues which were experienced during the pandemic. This could also improve the UK's capacity for research.

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<sup>36</sup> Imperial College London. New UK-wide AI and engineering biology consortium. 2022. <https://www.imperial.ac.uk/news/236657/new-uk-wide-ai-engineering-biology-consortium/>

<sup>37</sup> Wilson, SL and others. Sharing biological data: why, when, and how. *FEBS Letters* 2021: volume 595, pages 847-863. <https://doi.org/10.1002/1873-3468.14067>

<sup>38</sup> Tellechea-Luzardo, J and others. Versioning biological cells for trustworthy cell engineering. *Nature Communications* 2022: volume 13, article number 765. <https://doi.org/10.1038/s41467-022-28350-4>