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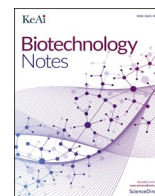
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Synthetic biology landscape in the UK

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ABSTRACT

The UK is home to a vibrant and diverse synthetic biology community. Many of its successes in research innovation and technological commercialisation can be attributed to a strong base of dedicated academics, investors, industrial leadership, and policymakers. Here, we give an overview of the organisations making up the network that have been key to these successes and the roles that they play within the different levels of the community. We start with a brief history of synthetic biology in the UK and continue by describing the progression of the societies and institutions that were set up, with particular focus on the UK's active student and entrepreneurship scene, as well as centres of research. We then contextualise the UK's growing bioeconomy, detailing government trajectories of planned innovation and how these coincide with research translation. The path to commercialisation for researchers is put into comparison to that of the US, the world leader in synthetic biology and its translation, highlighting aspects that differentiate the UK globally. Finally, we conclude with a bright outlook on the current velocity of progress and the state of the community.

1. Introduction

Over the last 20 years, synthetic biology - and by extension the synthetic biology community - has matured from infancy to a flourishing field. Its beginnings can roughly be traced back to the year 2000, where two seminal papers proposed that biology could be engineered in predictable ways using reusable building blocks.^{1,2} This excited scientists and engineers alike, which lead to the formation of the early synthetic biology community through the inception of the international Genetically Engineered Machine competition (iGEM) and the first international meeting on synthetic biology (SB1.0) at MIT in 2004. Since, the global synthetic biology community has spawned several hubs around the world, which facilitate education, knowledge exchange, and commercialisation. These include independent national hubs and communities such as SynBioUK, which helps bring together the student-led synthetic biology societies for specific universities (for example SynBio Imperial College, UCL BeakerSoc, SynBio Society University of Edinburgh,

Oxford University Biotech Society, etc.), and students from academic centres for doctoral training (e.g. BioDesign Engineering CDT). The greater researcher community is tight-knit as well, and researchers often move between the now numerous research centres that have been set up in the UK, for example the Imperial College Centre for Synthetic Biology, OpenPlant Cambridge, Warwick Integrative Synthetic Biology Centre (WISB), BrisSynBio (BBSRC /EPSRC funded Synthetic Biology Research Centre), UK Centre for Mammalian Synthetic Biology (SynthSys Edinburgh), Synthetic Biology Research Centre Nottingham, and SYN-BIOCHEM Manchester. Additionally, a joint initiative between several research councils including the BBSRC and EPSRC helped establish seven research networks across the UK with funding of ca. £970k, each focusing on a different technological or societal aspect of synthetic biology.³ The pressing need for research translation is also addressed on several fronts, including by global synthetic biology and biotech-oriented accelerators (e.g. Nucleate, Entrepreneur First, ConceptionX, GapSummit), synthetic biology-focused venture funds (e.g.

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Petri, NfX Bio, Nucleus Capital), academic commercialisation hubs and incubators (e.g. SynBiCITE), independent research spaces (e.g. We Are Pioneers Group, OpenCell BioHotel, Industrial Biotechnology IBioIC), genome foundries (e.g. Edinburgh Genome Foundry, Earlham Biofoundry, SynbiCITE London DNA Foundry), and many more. Leading figures in these groups also serve as representatives in the UKRI constituent Engineering Biology Leadership Council (EBLC) - formerly known as the Synthetic Biology Leadership Council (SBLC) - which is the chief body interfacing with the UK government on synthetic biology policy and national roadmaps.^{4,5} Because of the interdisciplinary nature of synthetic biology that is borne out of applying engineering principles to molecular biology the UK's strong synthetic biology community has arguably been essential to the success of synthetic biology and its impact on the wider bioeconomy in the UK. Over the course of this article, we will describe the synthetic biology landscape of the UK, focusing on synthetic biology hubs and societies, the bioentrepreneurial state and potential of the UK, and the legal and regulatory framework in the UK. These will also be put in comparative context to the US, the world leader in the field in both academic and commercial output.^{6,7}

2. Synthetic biology community in the UK

To map out a timeline of synthetic biology, most reviews and opinion pieces point towards two seminal papers that got published in the year 2000: The "Repressilator",² that aimed to engineer a stable limit cycle in *E. coli*, and the "Toggle Switch",¹ that described how to engineer bistability in *E. coli*. Similarly, when speaking about the beginnings of a synthetic biology community, people point towards the inception of iGEM and the first international synthetic biology meetup (SB1.0) at MIT in 2004.⁸ The UK was very early to engage with this community, and the University of Cambridge was amongst the first international teams to ever compete in iGEM in 2005.⁹ The first time a UK team was placed in the top 3 was the following year, where Imperial College London was placed as runner-up (2nd place).¹⁰ This illustrates the early adoption of synthetic biology in the UK, and demonstrates the beginnings of a strong community amongst students. In 2008, the founding of the Centre for Synthetic Biology at Imperial College marked the beginning of a national effort to foster a base of academic leadership and connect professors. This £8 M investment also marks the beginnings of significant national funding in synthetic biology in the UK. Additionally, £970,000 were distributed amongst seven research networks at different institutions.³ By 2012, these national efforts culminated in the publication of the UK Synthetic Biology Roadmap through the SBLC.¹¹ Apart from mapping out technical trends, the document stresses the importance of translational research in synthetic biology.

Over the next decade, a host of student societies were founded, typically by iGEM teams or alumni.^{12,13} With synthetic biology becoming increasingly popular all over the UK, the need for a nationally coordinating society arose. SynBioUK was thus founded in 2017 by PhD students at the University of Oxford to meet that demand. In the first few years of the society, the focus was on connecting undergraduate students through organising iGEM meetups, talks, and conference panels. In 2020, the society shifted its focus more towards serving the graduate student community and therefore towards entrepreneurship, subsequently setting up the *Catalyse* programme - an educational accelerator teaching synthetic biologists all over the UK the fundamentals of biotech entrepreneurship. Within two years of its founding, the SynBioUK *Catalyse* cohort grew to ca. 300 participants and spawned >20 teams (with a number of them spinning out into start-ups), making it the largest synthetic biology accelerator in the UK.

Starting in 2022, SynBioUK leadership are partnering with Nucleate, a student-led founder-first biotech accelerator in the US that is expanding worldwide. Nucleate has a partnership with Petri to offer 1.5 M USD in uncapped, non-discounted SAFE notes to up to 8 teams. With 3 new Nucleate Chapters opening in London, Oxford and Cambridge, SynBioUK growing to almost 1000 members, and other hubs founded

across the country (Fig. 2), the next-generation synthetic biology community in the UK is now larger and better connected than ever before.

3. The UK's bioeconomy in context

In the past decade, the UK has recognised the innovative potential of biotechnology and emphasised greater focus on investing in its bioeconomy to address food security, improved healthcare, and sustainability,¹⁴ all of which synthetic biology is projected to make a great impact in Ref. 15. The UK's research community also hosts several projects that rely on international cooperation, and are indicators of the strong ties UK researchers have with the global synthetic biology community. A prominent example of this is the Yeast 2.0 effort, which involves academics from over a dozen different institutions based in the US, Europe, Australia and Asia.^{16,17} Several government agencies are set up to coordinate national strategies for synthetic biology (BEIS, OGDs, BBSRC, I-UK, KTN) and collaborate with industry (IBLF, MMIP, EBLC) [see Table 2 for acronyms]. Plans for expansion include doubling the size of the UK bioeconomy by 2030 to become a world leader in bio-based solutions.¹⁸ To this end, capitalising on the UK's world-class knowledge base is key, yet this is one area where the UK still lags behind the US and other European countries. In terms of scientific output, the UK leads in Europe¹⁹ with around 10.1% of synthetic biology publications between 2000 and 2015 stemming from UK-based authors and the 3rd greatest global publication impact after the US and China between 2016-2020,⁶ closely followed overall by Germany, arguably the biggest EU synthetic biology player.⁶ There is also more biotech funding in the UK compared to other European countries,⁶ yet there are fewer patents filed relative to these resources in the UK.⁷

Nevertheless, there are multiple avenues in the UK for synthetic biology researchers to translate their ideas commercially that are designed to be easily accessible. In fact, much support is built around the popularised idea of founder-led tech ventures. Spin-out support can come through general programmes like the Catapult Network (I-UK), Innovation to Commercialisation of University Research (ICURE), YES competitions, and other student-oriented university competitions, such as the University of Sheffield Biodigester Hackathon.²⁰ Independent accelerators like Entrepreneur First and US-based YCombinator select their cohort largely by the potential founder's ability to execute but still emphasising a strong technological background. Conversely, in-house university accelerators like the Francis Crick Institute's KQ Labs and Imperial College SynbiCITE have the luxury of having access by design to a base of science-heavy backgrounds and thus tend to emphasise business and company-building skills in their training. The idea of the tech founder having more skin in the game compared to a CEO with a purely business background is an attractive proposition for investors - the tech founder cannot take a backseat in commercial thinking and rabbit-hole into developing solutions that are not aligned with the company's business success criteria. In biotech, many universities now also have facilities for academics and early-stage spinouts to test their concepts, like communal labs and offices.²¹ Such cheap lab space is especially competitive to rent even in major hubs like London, where science universities and independent lab spaces receive overwhelming numbers of applications by startups. Much investment has therefore gone into setting up biotech foundries to provide services such as strain engineering and DNA synthesis. There are currently 5 such foundries in the UK, summarised in Table 1. There are also alliance programs and centres focusing on broader biotechnology translation, such as the BiopilotsUK program, UK's CPI, the Future BRH facilities, BEACON, Biorenewables Development Centre, the Biorefinery Centre, and the Industrial Biotechnology Innovation Centre (IBioIC), which is a Scotland-focused centre that in addition to translation offers support through funding and training.²²⁻²⁵ The Imperial College White City incubator, the Oxford BioEscalator, and Cambridge's Start Codon provide a combination of such facilities and services for early stage startups, in some cases restricting such facilities away from companies beyond the

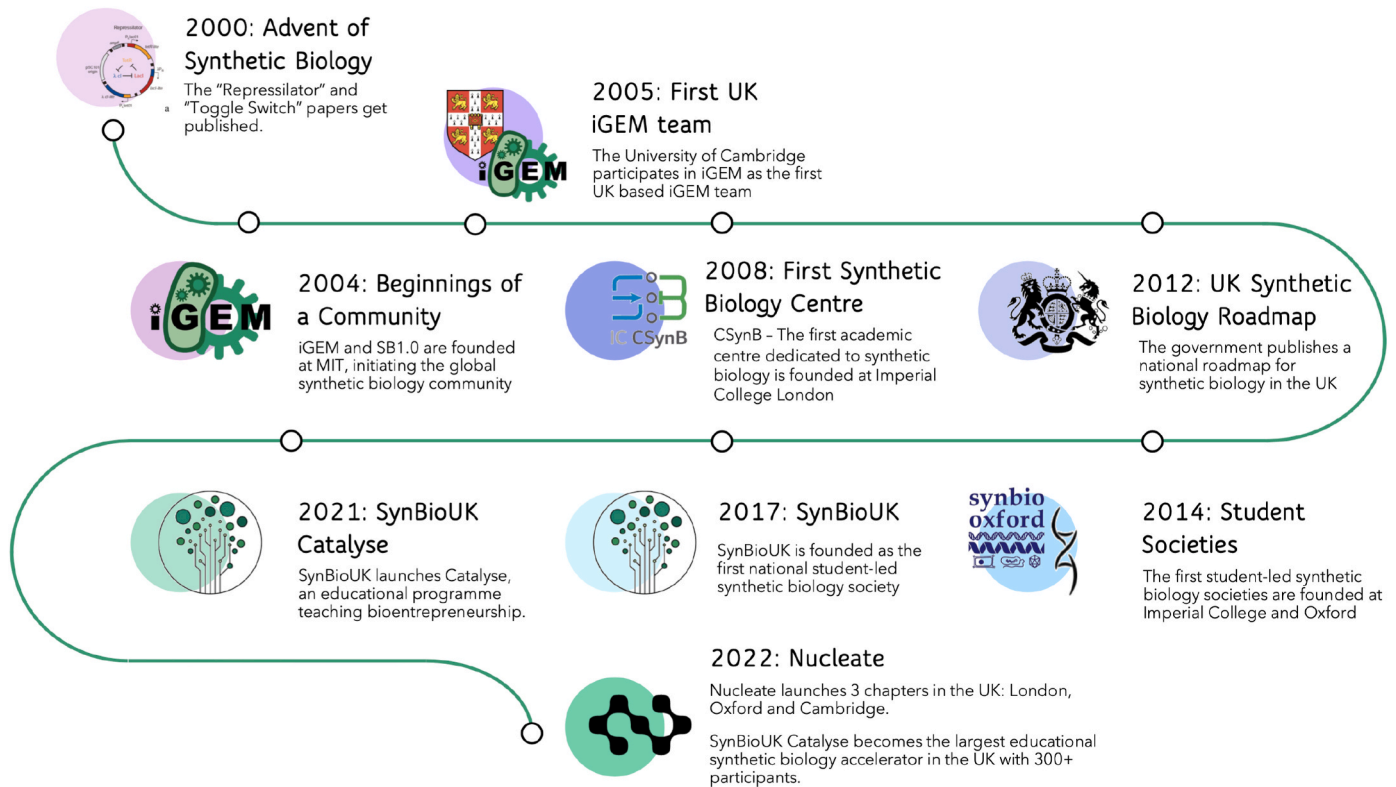


Fig. 1. The evolution of the synthetic biology community in the UK.



Fig. 2. Geographical distribution of some major synthetic biology Hubs in the UK.

Table 1
Overview of major UK biotech foundries by city.

City	Facility
Edinburgh	Edinburgh Genome Foundry
Glasgow	IBioIC
London	SynbiCITE London DNA Foundry
Norwich	Earlham Biofoundry
Manchester	SYNBIOCHEM Biofoundry

Table 2
Summary of major acronyms used for groups and institutions.

Acronym	Full name
Government Agencies	
BEIS	Business, Energy and Industrial Strategy
OGDs	Other government departments
BBSRC	Biotechnology and Biological Sciences Research Council
I-UK	Innovate UK
KTN	Knowledge Transfer Network
Industry Leadership	
IBLF	Industrial Biotechnology Leadership Forum
MMIP	Medicines Manufacturing Industry Partnership
SBLC	Synthetic Biology Leadership Council
EBLC	Engineering Biology Leadership Council

early stage. Alternatively, independent rentable lab spaces such as London's OpenCell (BioHotel), Scale Space, and BioCity Nottingham & Glasgow are also at affordable rates and growing in number, for example with the plans to build the largest commercial lab work space in Europe in London's Canary Wharf.²⁶ Failing fast is therefore a Silicon Valley paradigm that can translate into UK biotech thanks to such infrastructure.

Similarly to the US, funding for UK biotech startups typically starts at the venture capital or angel investment level. The UK BioIndustry Association (BIA) represents interests of the biotech industry in UK government and frequently compiles biotech business data, finding that the majority of capital invested in biotech companies in the UK comes from venture capital funds and has increased over the last couple of years to over £2.5 billion.^{27,28} IPOs have also increased in magnitude, with total life sciences investment in 2021 reaching £4.5 billion.²⁸ Venture capital funds increasingly have a biotech focus (eg. Abingworth, Amadeus Capital, Hummingbird Ventures), with investor subteams that have a scientific background and are headquartered both in the US and the UK. It is therefore not uncommon for UK founders to also turn to US investors during funding rounds, in addition to the fact that there is more investment capital in the US, before building their base in the UK. The time after which these funds expect to get a return on their investment typically operates between 5 and 10 years, which is just about compatible with biotech development timelines.

Such pressure to deliver can be difficult to keep up with in the world of biotech however, so the numerous governmental institutions set up to support budding biotech businesses can help bridge the barrier to a proof of concept. For example, the UK Innovation and Science Seed (UKI2S) Fund received a £10 million investment to start the Synthetic Biology Seed Fund for new businesses to apply to Ref. 29. The Industrial Biotechnology (IB) Catalyst also funded over £76 million worth of projects with a biomufacturing focus.³⁰ Indirectly, translational research in the form of a proof of concept comes more easily through the type of specific projects that UK synthetic biology research centres have received funding for, springboarding the launch of new ventures.³¹ While these funds are built to support synthetic biology, there is an active revision in nomenclature due to perceived negative associations by the public with the term "synthetic biology" itself. It has become more of a key phrase for people within the synthetic biology community to identify each other with, find collaborators and establish a shared vision, which makes finding directed funding straightforward. The UK

government for example is shifting away from using "synthetic biology" to the more general "engineering biology" (e.g. Engineering Biology Leadership Council), a trend mirrored in some of the international community. For example, when "synthetic biology" was named in the 2015 UK government document describing the "eight great technologies", the term was substituted out for "engineering biology" in the 2017 iteration (published as the "seven technology families").^{32,33} While it is unclear due to insufficient public perception of synthetic biology how this trend will evolve, this reflects a deeper understanding within policy and government-adjacent entities and a real engagement with the future prospects of the UK as a synthetic biology leader, which bodes well for further allocation of public funding.

While government and VC funding is crucial to the early stages of a business, it quickly becomes insufficient for the capital-hungry entity that is the medium-size biotech startup. Angel investors are in highest demand at this stage and their limited availability marks the dissolution of many companies. To incentivise angel investment, the UK government offers tax relief through several different schemes, including the Enterprise Investment Scheme (EIS), the Seed Enterprise Investment Scheme (SEIS), the Social Investment Tax Relief (SITR), and the Venture Capital Trust (VCT).³⁴ The levels of income tax and capital gains tax relief differs for each scheme and depends on the amount invested, as well as the duration of the investment. SEIS for example supports smaller businesses by capping the amount of capital for which relief can be claimed (at the time of writing this is at £100,000 with 50% income tax relief³⁴). Founders nevertheless still travel internationally to seek investment, especially to the USA.

As the world-leaders in the biotech industry, the USA should provide a source of inspiration for countries seeking to improve their bio-economies. A comparison highlights differences in approaches to intellectual property within academia and rates of company spin-outs. Although the UK outputs 4x more publications based on GDP than the US, the US dominates the patenting rate with 54 patents per 1000 publications, compared to just 8 patents per 1000 publications in the UK.⁷ This stark difference already emphasises one major advantage US universities have.

4. Discussion

Synthetic biology has a strong community and infrastructure in the UK. Additionally, the UK is positioned as an exceptionally founder-friendly environment, with tax breaks for angel investors, and 40% of European VC funding getting invested in the UK. This is in part because the regulation for founding a company in the UK is comparatively easy.

4.1. Technology transfer in the UK

Despite a strong community in synthetic biology and opportunity to commercialise, very few patents are filed when compared to the UK's research output.⁷ This may be due to the historical burden on founders who want to start a university spin-out. Most commonly, the institution still receives 20–50% of the founding equity of university spin-outs, for example at Imperial College London, the University of Oxford, and the University of Cambridge. Apart from demotivating founders, this limits opportunities for investment, as VCs cannot get a satisfactory stake in the company to justify buying in. When comparing this to the most entrepreneurial institutions in the US (e.g. MIT or Stanford), the university licenses out the technology, and may even take no equity at all in some cases. Apart from incentivising venture creation, this gives founders more negotiating power when engaging with VCs and makes them a more attractive investment. Over the last 5 years, founder friendly options have emerged in entrepreneurial institutions across the UK, revitalising their startup infrastructure. For example: In 2017, Imperial College launched an 18-month pilot founder-driven route to venture creation, where founders retained up to 95% of company equity. During that period, the majority of participating founders opted for this more

hands-off style instead of the co-driven route, where the institution retained 50% of the founding equity. The founder-driven route is now a permanent option for those spinning out from Imperial College London.³⁵ A similar shift occurred at Oxford in 2021. Founders now typically retain 80% of equity rather than the previous 50%, with the level of university involvement again positively correlating with its stake in the company. With TTOs now slowly following suit to the otherwise already founder-friendly ecosystem, the UK will continue to remain a competitive location for synthetic biology venture creation.³⁵ (See Fig. 1).

5. Conclusion and outlook

On the fronts of community, entrepreneurship, and funding availability for synthetic biology, the UK performs strongly. A vibrant research community underpins global leadership in synthetic biology innovation and industrial venture creation. The landscape of accelerators and student-focused entrepreneurship programs promises to continue fostering translation of research, enabled by increasingly accessible facilities that make new businesses competitive even at an early stage to secure funding. The accompanying trend of increasing investment is similarly projected to continue, though there are still challenges for this growth to match that of synthetic biology in the US and China. Examination of the differences between the UK and these leading countries highlights university cultures geared better towards founder-first entrepreneurship, especially in terms of patent writing and equity agreements, along with high availability of capital.

The next key challenges to solidifying its standing as an early leader for engineering biology include attracting top international talent and investment through world-class training, an innovation-enabling spin-out culture and supportive government policy, and integration of synthetic biology into greater industries. Continued funding of the inception points of the current community - university courses, doctoral training programs, fellowships, and research centres geared towards engineering biology - provides the basis for solidifying a strong bioeconomy and should remain a priority. Enriching such programs with international exchanges would broaden research perspectives and encourage the flow of new ideas that could potentially be commercialised better in the UK. Following on that, continued investment into throughput capabilities and manufacturing capacity would not only serve as a testbed for such new ideas and accelerate notoriously slow biotech time-scales, but also enable the UK to access otherwise uneconomical industries and handle challenges of scale and emergency in a unified fashion. While these challenges are all roughly addressable through money, one of the most important cultural shifts for UK engineering biology remains learning to fully recognise the value of an idea, to be protective of it, and to better manage its maturation into a tool or intellectual property - this is what differentiates synthetic biology as an engineering discipline.

Credit author statement

The listed authors participated in the creation of this study in the following ways: Georg Wachter: Conceptualisation, Writing, Fig. 1, Editing Olivia Gallup: Conceptualisation, Writing, Editing James Bayne: Conceptualisation, Fig. 2, Editing Louise Horsfall: Conceptualisation, Editing.

Declaration of competing interest

The authors declare no competing interests.

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