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Synthetic biology in Europe: current community landscape and future perspectives

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ABSTRACT

Synthetic biology has captivated scientists' imagination. It promises answers to some of the grand challenges society is facing: worsening climate crisis, insufficient food supplies for ever growing populations, and many persisting infectious and genetic diseases. While many challenges remain unaddressed, after almost two decades since its inception a number of products created by engineered biology are starting to reach the public. European scientists and entrepreneurs have been participating in delivering on the promises of synthetic biology. Associations like the European Synthetic Biology Society (EUSynBioS) play a key role in disseminating advances in the field, connecting like-minded people and promoting scientific development. In this perspective article, we review the current landscape of the synthetic biology community in Europe, discussing the state of related academic research and industry. We also discuss how EUSynBioS has helped to build bridges between professionals across the continent.

1. Introduction

Despite the concept being much older,^{1–3} synthetic biology only emerged as a discipline during the 2000s, thanks to the technical advances in the biotechnological and computational fields. Since then, the field has exploded as extensively reviewed elsewhere.^{4–6} While there is no universally accepted definition, synthetic biology is often characterised as the application of engineering principles to the design and development process of new biological functions or components.^{7,8} This is, in fact, the source of the term "synthetic": components and functions that can be designed, built, and operated according to known rules and models. The digital revolution was born from the use of this exact process to create circuit boards. In this context, synthetic biology is a transversal field that applies its principles and methodology to address challenges from different disciplines, ranging from agriculture to medicine, or from bioremediation to biomanufacturing.⁹ Due to its broad impact, synthetic biology is often said to be at the core and provide the fuel for the biorevolution, the process that seeks to transition current production paradigms towards a bioeconomy.¹⁰

Markets that support the biorevolution in areas like biomolecules, biosystems, biomachine interfaces and biocomputing are set for continued strong growth. Together they are estimated to reach an annual value of \$4 trillion within the next two decades, providing treatments to 45% of the world's current disease burden and 60% of the world's physical inputs according to a recent McKinsey report.¹¹ Such projections place the field amongst the most influential drivers of

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Abbreviations: EU, European Union; UK, United Kingdom; USA, United States of America; GBA, Global Biofoundries Alliance; GMO, Genetically modified organism; SC, Steering Committee; SME, Small and medium enterprises; EUSynBioS, The European Synthetic Biology Society; iGEM, International Genetically Engineered Machine.

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change for the 21st century, both from an economic and strategic standpoint. The global importance of synthetic biology is clear from governments long term program funding. Since 2017 the USA's Engineering Biology Research Consortium Roadmap has provided structure for federal investments in the bioeconomy and synthetic biology.¹² A similar rapid growth is seen in Asia thanks to governments' investments and private-public partnerships.¹³ In Europe (defined in this article according to its geographical definition), since its early days the UK has spearheaded the development of synthetic biology, releasing early governmental roadmaps by the Synthetic Biology Leadership Council in 2011 and 2016.¹⁴ At the same time, within the European Union (EU), multiple assessments and opinions were provided to the European Commission by different scientific committees. While many concerns and risks arose, a roadmap for the development of the synthetic biology field has not been officially released thus far and it is expected for O2 2023.¹⁵ The general interest of governmental bodies into the development of Synthetic Biology is clearly visible when examining the composition of the current members of the Global Biofoundries Alliance (GBA). The GBA is a network of non-profit laboratories willing "to share experiences and resources and work together to overcome shared challenges and unmet scientific and engineering needs".¹⁶ From the original 15 founding members in 2019, GBA has now grown to 32 members (Fig. 1) across four continents: three from Australia, nine from North America, eleven from Asia, and nine from Europe. Notably, out of the nine European members, five are based in the United Kingdom (UK), which has recently left the EU. In the rest of Europe, only Germany, Denmark and Finland have proposed similar initiatives, illustrating how the rest of the continent has been trailing behind the UK leadership in the field.

Despite the significant potential synthetic biology has, the field still retains political and ethical questions that need answers. Doubts from the initial 1990s public debates over GMOs have continued to linger.¹ Despite a continuous slow shift towards acceptance of biotechnology in EU countries,¹⁸ to this date a widespread scepticism permeates public opinion worldwide in regards to GMOs.¹⁹ This scepticism, which in Europe might be rooted in cultural elements,²⁰ has contributed to a slow down on regulatory innovation. In order to overcome these barriers, stakeholders in synthetic biology including scientists, policymakers and members of the public will have to work together to identify answers. To facilitate connections and discussions between these interest groups EUSynBioS was founded, along with a number of similar associations throughout the world.²¹ In this article, we review the current European synthetic biology ecosystem, highlighting achievement and challenges in academic research and industry. We then showcase how EUSynBioS has contributed to connect professionals through the continent, and

describe the overall performance of European iGEM teams.

2. Academic research ecosystem of synthetic biology in Europe

Academic scientific research is of key importance for the foundations of technological advancement. This is no different for synthetic biology, despite its applied nature. The recent development of synthetic biology can be tracked by the number of related publications, which started to emerge in the early 2000s.²² Nowadays, thousands of scientific papers are published worldwide on the topic every year (Fig. 2A). In this context, scientists from European countries have been playing an important role in progressing the field, as their contributions rival the amount of literature produced in the USA and other parts of the world (Fig. 2B). It should be noted that synthetic biology research in China, India, and Australia has steadily been increasing in the last five years.

In Europe, the UK and Germany have been spearheading efforts in the field with the highest publishing output, as they also account for the largest scientific communities in the continent (Fig. 2C). However, when normalising synthetic biology academic output by the overall absolute scientific production, smaller countries emerge as driving hubs in synthetic biology research, such as Denmark and Switzerland. It is important to note that the research described here may be underestimated, as it only takes into account explicit use of the term synthetic biology. Considering a broader definition of synthetic biology, i.e. including topics such as metabolic engineering or cell and gene therapies, these results could be significantly affected. A similar trend can be observed overall in European research and development (R&D), as these are countries that invest the highest fraction of their gross domestic product (GDP) into R&D.²³

In the early 2000s, the UK was one of the earliest adopters and promoters of synthetic biology research in Europe.²⁴ The rest of the continent followed with the EU continuing to increase funding for synthetic biology research, since it formally started in 2005. Investment was provided through the European Commission (EC) initiative on New and Emerging Technologies (NEST), within the 6th framework programme (FP6). This initial funding was intended to encourage synthetic biology research in Europe that later would be supported by local funding agencies.²⁴ Additional investments came as part of the Horizon 2020 Programme which ran from 2014 to 2020, offering a total of 21 grants focused on synthetic biology.²⁵ In parallel, the increasing interest in the discipline has led to the establishment of a number of European meetings and conferences. One of the most prominent of these is the Applied Synthetic Biology in Europe conference (ASBE), a conference organised by the European Federation of Biotechnology that has been held biennially since 2012.²

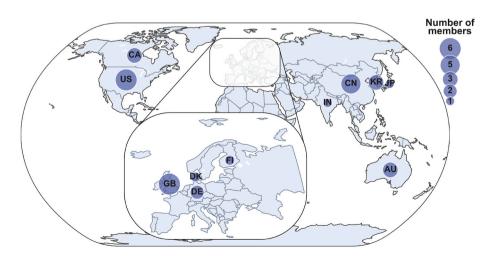


Fig. 1. Distribution of the current members of the Global Biofoundries Alliance (GBA). The size of the circle is proportional to the number of GBA members (also when the map is not in scale). Data retrieved from: https://biofoundries.org/.

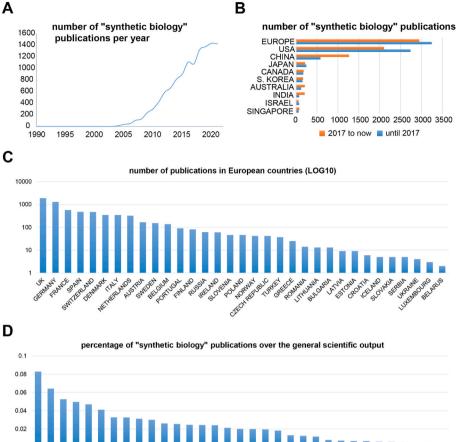


Fig. 2. Analysis of "synthetic biology" publications as an indicator of academic output. We refer as "Europe" to its geographical definition and to the countries comprised that way. A) Number of "synthetic biology" publications per year from 1985 to 2021. B) Number of publications based on geographical locations until 2017 and from 2018 until 2022. C) Total number of publications per European country between 2005 and 2022 D) Number of publications per European country, between 2005 and 2022, normalised to the number of scientific publications in the same time period. The data were obtained by querying Web of Science (www.webofscience.com) for scientific publications that include "synthetic biology" in their titles, abstracts or keywords.

National funding agencies continue to play an integral role in funding science in Europe. In those regards, funding agencies from the UK and Germany stand out compared to other countries (Table 1) due to the size of their economies and their research infrastructure. On the other hand, it appears that the EU is currently funding most synthetic biology research in the rest of the continent, importantly helping to even-out the gap between countries. In summary, the European academic research ecosystem in synthetic biology appears to be overall competitive at a global level, rivalling research efforts carried out in the

Table 1

Top funding bodies in Europe in the field of synthetic biology, based on acknowledgments of funding in publications to date. Data was obtained by querying Web of Science (www.webofscience.com) for scientific publications that include "synthetic biology" in their titles, abstracts or keywords.

Funding Agencies	Location	Publications
UK Research Innovation (UKRI)	UK	1100
European Commission	EU	994
Biotechnology And Biological Sciences Research Council (BBSRC)	UK	724
Engineering Physical Sciences Research Council (EPSRC)	UK	592
German Research Foundation (DFG)	Germany	329
European Research Council (ERC)	EU	325
Federal Ministry Of Education Research (BMBF)	Germany	175
Novo Nordisk Foundation	Denmark	169
Spanish Government	Spain	154
Swiss National Science Foundation (SNSF)	Switzerland	141
Max Planck Society	Germany	131
French National Research Agency (ANR)	France	107

USA or China.

3. Entrepreneurship and industry in Europe

The scientific and technological developments around synthetic biology - and life sciences in general - have led to the creation of many companies in Europe.^{23,27} In the last decade, we have seen a Cambrian explosion of company creation and funding in life sciences,^{27,28} which was also reflected in synthetic biology companies. There is a large potential for startup founding and growth due to a number of key factors: i) a large pool of talents and academic research on the continent²³; ii) increasing availability of private and public funding^{27,29}; iii) freedom of entrepreneurship and movement within countries part of the European Economic Area.³⁰

However, European synthetic biology companies, just like others in the life sciences, are facing many challenges. The European ecosystem is heterogeneous and scattered across different cities, regions, and countries, in opposition to more concentrated hubs in the USA (i.e., Boston, Silicon Valley) or China (i.e., Beijing, Shanghai, Shenzhen). The European synthetic biology ecosystem comprises companies concentrated mostly in the UK, France, Germany, Switzerland, the Netherlands, and Denmark.^{23,31,32} This is partly due to economic, institutional, technological and cultural factors.³³ The inherent challenges associated with a scattered ecosystem may be partially solved by leveraging software and lab-in-the-cloud technologies to allow startups and talents anywhere in Europe to access synthetic biology technologies.

The major challenge for European synthetic biology companies, beyond the creation of new startups, is continued growth and international independence. At the creation stage, most synthetic biology companies are academic spinouts, which involves Intellectual Property (IP) managed by universities' technology transfer offices (TTOs). When considering the number of awarded "synthetic biology" patents, Europe is again trailing in comparison to the USA. Already in 2010 the USA were accounting for almost half of the synthetic biology patents worldwide, with Japan following, and European countries altogether accounting for about a guarter of the patents.³⁴ In 2018 these numbers did not change substantially, and there were just some differences within European countries, with Switzerland notably increasing its share of synthetic biology patents.³⁵ Unfortunately, universities in Europe have taken the opposite initiative to those in the USA, and are known for capturing large equity in created spin-outs, severely blocking companies from growth and reducing the chances of becoming dominant players.³⁶ This has a tendency to encourage early company and technology acquisition, or licensing of IP, instead of growth.

A recent pattern of successful European companies becoming acquired by larger players, frequently based in the USA or China, has developed.^{37,38} Depending on the acquisition, this can lead to a gain or loss of know-how, but never leads to growth into a field leader. One factor is the availability of funding for the growth phase which is lagging behind the USA.²⁹ It has been highlighted that small and medium enterprises (SMEs) do not receive appropriate financial support,³⁹ with only 10% of European SMEs' external financing (e.g., venture capital) being significantly smaller than in the USA.⁴⁰ There are clear differences in commercial synthetic biology activities between Europe and the USA, particularly in hubs like the Bay Area and Boston, which are home to both established entities and an ever-growing number of startups. The disparity between the continents is frequently explained by the much larger size of investment made in the USA, estimated in 2019 by Syn-BioBeta as \$1.1 billion compared to a combined global total of \$147 million.⁴¹ The vast difference in investment combined with tighter European regulations on genetically engineered products has led to a significant difference in the entrepreneurial space.^{42,43} The EU is trying to put in place initiatives to bridge this gap by providing SMEs with better access to finance. The new SME strategy together with the European Investment Fund (EIF) is launching ESCALAR,44 a new investment approach aiming to boost the size of venture capital funds and encourage more private investment. Additionally, the new strategy aims to create an SME Initial Public Offering (IPO) Fund and a gender-smart finance initiative to stimulate funding for female-led companies.⁴⁵ An example of a promising initiative is the Bio-based Industries Consortium (BIC) and EU public-private partnership worth €3.7 billion called the Bio-based Industries Joint Undertaking.⁴⁶ This group invests in innovative technologies and biorefineries that aim to transform biological residue waste streams into green products. There is a positive trend with European and non-European funds that have been actively investing in European synthetic biology companies; for example, investors dedicated to synthetic biology have been now created in Europe, such as eureKARE.4

However, as already mentioned, in Europe there are not many major winners in the synthetic biology space yet. In fact, large actors are generally needed to grow a startup ecosystem by bringing specialised funding, support, and mentoring to the next generation of companies. In part, this lagging in ecosystem development could also be due to the efforts being focused on filling the digital gap with the USA,⁴⁸ with the risk of missing the coming synthetic biology-driven innovation wave. Further challenges for European synthetic biology companies are associated with restrictive European and national laws and regulations, and the generally adverse perception of the matter by the general public and policymakers.⁴⁹ Notably, these factors have a much higher impact on early-stage or small enterprises that - in contrast to large multinational groups - have reduced access to funding, lobbying power, foreign markets, and regulatory experts.

In order to foster the biotechnology industry and to advocate at the European institution level for a more competitive science-based market, in 1996, the major biotechnology companies founded EuropaBio, the European Association for Bioindustries. Among its members there are also some of the large actors involved in the European synthetic biology sector, ⁵⁰ as AB Enzymes, BASF, Corbion, DSM, Evonik, KeyGene, IFF, Merck, Novartis, and Novozymes. While these kinds of companies do not have a core business in synthetic biology, they are representative examples of enterprises that often apply synthetic biology principles and techniques, or provide synthetic biology services and products. This is also supported by the fact that some of these companies are among the top assignees of synthetic biology patents worldwide.³⁵ Notably, EuropaBio organises the European Biotech Week, a diffused event to explain and promote biotechnology among the general public.

Despite some challenges, the synthetic biology start-up ecosystem in Europe is very active and thriving in many fields. As an example, there are companies involved in the production of bioproducts both for industrial and food purposes, such as Biosyntia, AMSilk, Insempra, Mosa Meat, Meatable, Biocleave, EVbiotech, Gourmey, and many others. Another important sector is the one that evolved from the petrochemical industry, thus the production of bioplastics, biopolymers, and biofuels, as those being developed by: Carbios, Cambrium, and Avantium. With the development of the field and the necessity for better tools, an ecosystem of service providers has also emerged. They are mainly focused on two areas; providing DNA and protein material, such as Explora Biotech, DNAscript, Nuclera Nucleics, Evonetix, and Ribbon Biolabs; or software tools such as LabGenious, Algorithmiq, and Synthace. Arguably the largest part of the ecosystem in Europe is attributed to the health sector, with many companies directly or indirectly using synthetic biology to deliver medical solutions. The SARS-CoV2 pandemic led to the adoption of novel mRNA technology for vaccine applications, pharmaceutical companies like BioNTech and CureVac have used this synthetic biology innovation to provide medicines with global impact. Also companies in cell & gene therapies are growing across Europe, such as Cellectis, Genethon, Kiadis Therapeutics, Orchard Therapeutics, CRISPR Therapeutics, or TreeFrog Therapeutics. Moreover, microbiome engineering and living therapeutics companies, such as Eligo Bioscience, SNIPRBiome, EnteroBiotix and Prokarium, are also expanding the applications of synthetic biology in health and medicine through Europe.

For synthetic biology companies in Europe to reach their full potential, we need efficient markets, financing, and clear regulations. Additionally, it is important to connect the sparse European hubs to create an integrated ecosystem. This will allow all the companies involved to benefit from the advantages of a clustered hub. Connecting and promoting the different synthetic biology hubs in Europe is one of EUSynBioS' many missions. This has started with academics across Europe, and it is now naturally expanding toward early-stage and large companies, frequently founded by the same academics as part of this ecosystem.

4. The European Synthetic Biology Society

The European Synthetic Biology Society is a European non-profit association with the goal of promoting the Synthetic Biology discipline and its principles, as well as functioning as a reference point for the community of Europeans interested in the discipline.

4.1. History and organisation of the European Synthetic Biology Society

A few years after Synthetic Biology started to gain momentum in the USA, the lack of any dedicated organisation in Europe led to the founding, in 2014, of "The European Association of Synthetic Biology Students and Postdoc" (EUSynBioS), a student association based in Cambridge (UK).⁵¹ The association was initially strongly rooted in the UK due to the location of most founding members. After a few years, EUSynBioS organised its first Symposium at the Imperial College London (UK) in 2016.⁵² The event tried to offer scientific content as well as an

informal meeting-ground for people interested in Synthetic Biology. In the following years, the association increased its activities in continental Europe, expanding its Steering Committee (SC) with members located across all Europe and organising Symposia in Spain, France and Czech Republic. In 2019, EUSynBioS obtained a legal status as a non-profit association registered in France and renamed into "The European Synthetic Biology Society",⁵³ with the goal of bringing together all people interested in the field. The association is managed by its executive team, the Steering Committee (SC), formed by volunteers, either synthetic biology experts or enthusiasts are welcome. Every year, applications are open and new members are elected by the previous SC. Each member has an assigned function for 2 years, that is later revised or modified. Leaving SC members usually offer support to new members, ensuring a smooth transition and ensuring continued operations of the association. Throughout its 8 years of existence, 25 people based in 9 different countries and of 14 different nationalities have actively contributed to the cause of EUSynBioS, most of them early career researchers (ECRs). Moreover, the association relies on an Advisory Board composed by 15 leading experts in the field working in 9 different countries. The support of such a distinguished Advisory Board and uninterrupted operations of the association since 2014 to date have led EUSynBioS to become a reference point for European Synthetic Biology enthusiasts. At the present time, EUSynBioS can count on several thousands of people following its activities on social media platforms and on several hundreds people registered as community members (Fig. 3), of which around 41% are based in the United Kingdom. This over-representation can be explained by the large size of the UK research community in synthetic biology, and by its prevalence in the first years of the association. Financially, the association has operated strictly as a non-profit organisation. The volunteer-based nature of the SC and the mostly web-based presence of the association has enabled an agile management of resources, in which only basic operational costs need to be covered. In those regards, donations provided by sponsors have been crucial to support activities of the organisation.

4.2. Event organisation

EUSynBioS has relied on event organisation as one of the main tools for outreach. The main series of events so far has been the Symposia, which have taken place annually in up to 4 different European countries. The first EUSynBioS Symposium was held at the Imperial College in London in 2016, as a follow-up event to SynBioBeta London, a conference that brings together companies commercialising cutting edge research within the field of synthetic biology. The event consisted of different formats such as scientific talks and poster presentations, discussion panels and breakout sessions. The second Symposium took place

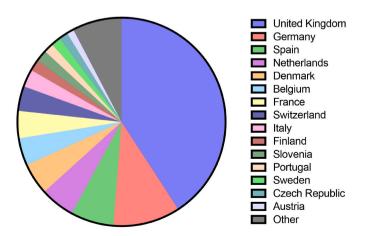


Fig. 3. country of residence of EUSynBioS community members. Under "Other" are included other countries as well as members that did not specify their place of residence.

in Madrid, at the National Center for Biotechnology (CNB–CSIC)⁵⁴ while the third Symposium was organised in Toulouse in collaboration with BioSynSys, the French Research Group on Synthetic Biology.^{55,56} The last in-person Symposium to-date took place at the Brno Planetarium (Czech Republic), in collaboration with the Biomania student association.⁵⁷ The following year EUSynBioS established a collaboration with the European Federation of Biotechnology, organising its Symposium as a joint meeting with the 5th Applied Synthetic Biology in Europe,⁵⁸ which was held online due to the COVID-19 pandemic.

4.3. Online presence

Due to the high internationalisation and decentralisation of its executive team, EUSynBioS has relied heavily on its internet presence. The official website has played a central role to communicate the vision and activities of the association. The website hosts a blog covering interviews with ECRs, iGEM teams, conference reports and opinion pieces. Social media have been used since the early days of the association to advertise its activities. In particular, EUSynBioS has been actively engaging its community on Twitter, expanding to LinkedIn and Instagram in recent years.

Apart from the Symposia, EUSynBioS organises a wide range of smaller online events. The EUSynBioSeminars series gives early career researchers the opportunity to present their research to the community with videos of the presentations published after online.⁵⁹ The EUSynBioS Entrepreneurship series, highlighted examples of technology generated with synthetic biology, and how the application of entrepreneurship could lead to startup creation.⁶⁰ In 2021 EUSynBioS hosted an event targeting the audience of a specific European country, by organising an online discussion panel on Biofoundries in Italy, an event part of the Italian Bioeconomy day.⁶¹ In particular, due to the onset of the COVID-19 pandemic, online seminars and online content have proven particularly successful in keeping the community active and engaged. Overall, EUSynBioS has been leveraging its online presence to connect people throughout Europe, producing original content and fostering discussions over synthetic biology.

4.4. Other associations and initiatives in Europe

Apart from EUSynBioS, other initiatives have started to emerge on the European scene in the last few years. National associations have successfully been founded to better represent the interest of stakeholders from specific European countries. The first national associations were founded in 2017, such as the German Association for Synthetic Biology (GASB),⁶² and Synthetic Biology UK (SynBioUK). GASB has proven particularly active organising, among others, public dissemination events in German language,63 the annual German Conference on Synthetic Biology (GCSB)⁶⁴ now in its 6th edition, an industry networking event (SynBio World Cafe) now in its 3rd edition and releasing content and publications.⁶² SynBioUK is also involved in coordinating the activities of the various clubs and initiatives across the country, such as SynBio Oxford, SynBIC, and others. The wealth of organisations present in the UK is a good testament to the scale of the synthetic biology community in the country. More recently, similar associations were founded, in France, Association Française de Biologie de Synthèse (AFSB), and in the Netherlands, the Synthetic Biology Associations of the Netherlands (SynBioNL). Interestingly, in many countries that host a considerable SynBio community such as Denmark, Switzerland, and Spain, similar widely known associations have not been founded yet.

The European Molecular Biology Organisation (EMBO) has also organised a series of activities aimed at disseminating the field of synthetic biology, such as the recurrent EMBO course "Synthetic biology in action"⁶⁵ and an EMBO Workshop "Creating is Understanding: Synthetic Biology Masters Complexity" in 2019.⁶⁶ Additionally, the European Synthetic Cell Initiative (SynCellEU)⁶⁷ has been active in connecting academic researchers and industry in the context of synthetic cells

research and applications.

5. iGEM in Europe

Another interesting proxy to evaluate the Synthetic Biology European landscape is the International Genetically Engineered Machine (iGEM) competition.^{68,69} It is a major and well-known event in synthetic biology where teams of students from all over the world compete in designing living systems. During the short period of the summer break, the participants get to know synthetic biology principles and tools with the aim to design and build a project for real-world application. Moreover, since its beginning, the iGEM organisation has encouraged all teams to share and educate the public about their projects and synthetic biology *via* local outreach activities. In a way, that makes iGEM one of the greatest platforms to showcase synthetic biology. In many different countries, the iGEM competition actually remains the only existing educational activity to learn about synthetic biology communities.^{62,72}

For its first edition in 2004, the iGEM competition counted 5 teams from North America; since then, it has encountered a phenomenal success leading to a continuously increasing number of teams joining the competition each year (with only one massive dropout in 2020, which can be linked to the COVID-19 outbreak). For its latest edition in 2021, 343 teams from all around the world participated, of which 82 teams from Europe (Fig. 4A). We can observe that European participation in the competition promptly but timidly started by two teams for the second edition (2005) and raised quickly until stabilising at around 25% of the total participation, corresponding to around 78 \pm 4 teams per year (for the last five years disregarding the 2020 dropout with 62 teams; Fig. 4A). This indicates that synthetic biology has become increasingly widespread and has attracted attention worldwide and across Europe.

The first two European teams to participate were from the UK and Switzerland (Fig. 4B) in 2005. This is probably because these countries already had, at the time, a strong academic background with the first synthetic biology studies conducted, and a synthetic biology ecosystem. Over the following years, the representation of European countries increased until reaching 20 ± 1 countries (Fig. 4C), of which most missing ones are from Eastern Europe. Unsurprisingly, the leading countries, in terms of participation and number of teams, are those with a strong academic infrastructure such as the UK, France, and Germany (Fig. 4B). However, the number of team participation is not completely correlated with the number of "Grand Prize" winners. Although, high participation countries have won the prize multiple times, such as Germany - six times -, UK - two times -, and France - two times-, smaller countries with less teams participation sometimes hit above their weight, such as the Netherlands - four times -, Slovenia - three times - and Lithuania - two times -. Finally, two other European teams, from Spain and Switzerland, were awarded in previous years.

Since 2009, teams attending iGEM started to compete in particular categories called tracks. The trend and popularity of the categories seems similar either in Europe or worldwide (Fig. 3D), but there are exceptions. The "high school" track refers to the category that high school teams compete in, and a clear difference between the world and Europe is observed in this category. 215 Chinese teams (~15 teams per 100 M) and 60 US teams (~18 teams per 100 M) competed in this track by 2022. On the other hand, in the diagnostic track, the attendance from European teams was 30% higher than for teams from the rest of the world, whereas, in the software track, the world's attendance doubled the one from Europe. The stronger synthetic biology infrastructures of European institutions might have led the teams to gain more wet-lab experience compared to the rest of the world, as similar trends are also seen in other similar tracks such as information processing.

In the early years of the competition, the participating teams were only from universities. Teams from USA high schools attended the competition for the first time in 2011. European countries were also represented at the high school level the following year. Since then, 41 teams from European high schools have participated in the iGEM competition. Turkey has been the leading country with 15 high school teams, and the UK followed with 9 teams. Also Spain, Hungary, Germany, and Greece sent high school teams to the competition multiple

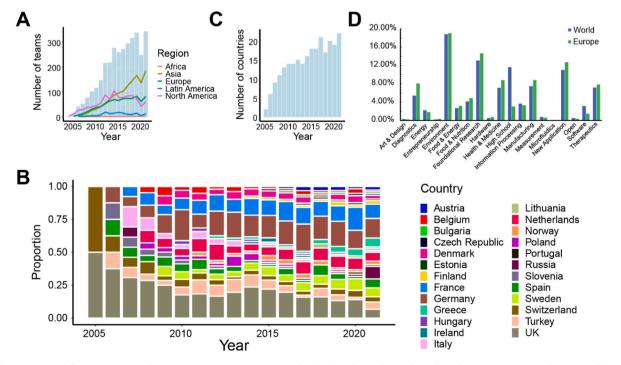


Fig. 4. The overview of the participation of European countries in iGEM. A) The bar plot shows the total number of teams participating by year and the different colored lines represent the team number participation by region. B) Proportion of European teams participation by country over the year. C) Number of different European countries that participated in iGEM over the years. D) Comparison of the proportions of the iGEM tracks between Europe and the world. The world's data also includes Europe. The commercial teams competing in high school tracks were not counted in this track. Data sourced from the iGEM website.⁷⁵

times. This suggests that synthetic biology has reached younger generations in many countries across Europe. In 2014, community labs were also encouraged to attend the competition, allowing amateur biologists and non-institutional scientists to compete in iGEM. Up to the present date, 22 community lab teams have taken part in the competition. However, only the UK and Russia sent two teams and one team, respectively, from Europe. Recently, iGEM announced that the commercial bodies that serve academic institutions or recruit members from these institutions should compete as commercial teams. Although only Asian teams attended in this category in 2021, more commercial teams from Europe are expected to participate in the contest. Still, expectedly, collegiate teams are dominating the attendance lists. Nevertheless, this variety also shows an increasing interest in synthetic biology from different segments of society.

The impact of iGEM in Europe can be seen beyond the competition, with iGEM projects that can sometimes contribute directly or indirectly to the creation of companies.⁷³ In Europe, many founders of successful synthetic biology startups have been part of an iGEM team. Some major ones were the Imperial College London 2014 team project that directly contributed to the creation of Puraffinity. Similarly, the University College London 2013 team created Bento Lab. The following teams had among their members future founders: DTU Denmark 2009 with Labster, Paris Liliane Bettencourt 2010 with Eligo Bioscience, Imperial College London 2011 with LabGenius, Cambridge 2009 with Colorifix, Paris 2007 and Evry 2012 with PILI and LA PAILLASSE, and Imperial College London 2009 with BioBright. The iGEM competition has created a unique worldwide network of alumni with founders, scientists, and many other people with a common interest in synthetic biology; this network is now starting to show an impact on the European startup ecosystem. This effect is likely to expand in Europe with the Grand Jamboree now organised in Paris in 2022 (Boston then remote before 2022). As the Grand Jamboree will be based in Europe, the easy access and lower price associated with travelling could make the competition more attractive for many smaller European teams, building an even larger European alumni base.

6. Conclusions and future perspectives

As the discipline of synthetic biology reaches its teenage years, the potential economic, environmental and health implications of the field are starting to be recognised by governments and importantly, by the global population. For example, during the COVID-19 pandemic, tools and technologies developed by synthetic biologists were used to combat the virus by providing treatments, vaccines, testing capacity and manufacturing processes.^{76,77} As for every emerging scientific field, fostering community, education and research is of prime importance. The iGEM competition has become one of the first cornerstones of synthetic biology and is one of the first instances in which students get exposed to the discipline before they start their scientific careers. Increasing participation from European countries in the iGEM competition draws attention and leads to a remarkable success, even though its popularity is relatively low at the high school level compared to other countries, such as the US and China. While European academic research on the topic seems to be highly competitive at a global level, this is not the case for the translation of fundamental research into application. One indicator for this is the considerably lower number of patents awarded in Europe compared to the USA. Moreover, Europe is still trailing the USA in regards to the amount of capital invested into innovation, with the consequences of wasting the knowledge generated and thus causing financial losses.

Within Europe, there are also differences in the state of the field between different countries. The UK has been a leading actor in Europe, and this can be also observed when looking at the numbers of established biofoundries, the compositions of the EUSynBioS members and iGEM teams. With 'Brexit' now fully achieved, the EU has lost its leading member. Thus, it remains to be seen what will be the EU's strategy to increase its competitiveness in this crucial scientific field, whether the UK will retain its status as a major European hub for synthetic biology and whether any of this will have an impact on the European continent as a whole.⁷⁸

In order for European synthetic biology innovation to reach its full potential, both private and public institutions in Europe will have to provide an important contribution, both within the economical and, for the latter, also legislative frameworks. In the meanwhile, communities like EUSynBioS act as nucleating points for early stage researchers (and beyond) to meet like-minded people, analyse cutting edge research and develop their network. Such spaces are fundamental to discuss new scientific breakthroughs, to foster the dissemination and application of novel ideas. Moreover, considering the inherently applied overlook of synthetic biology, a fundamental element is the creation of bridges between the academic and industrial environments. Connecting the scattered European scientific ecosystem will contribute in maintaining the competitiveness of Europe in the field of synthetic biology.

Author contributions

All authors contributed in writing the manuscript. SD, IB, SG, CW and KM analysed and visualised data.

Declaration of competing interest

All authors declare that they have no conflicting interests.

References

- 1 Leduc S. La Biologie Synthétique. vol. 2. A. Poinat; 1912.
- 2 Szybalski W. In Vivo and in Vitro initiation of transcription. In: Kohn A, Shatkay A, eds. Control of Gene Expression. vols. 23–24. Springer US, 1974.
- Szybalski W, Skalka A. Nobel prizes and restriction enzymes. *Gene*. 1978;4:181–182.
 Benner SA, Yang Z, Chen F. Synthetic biology, tinkering biology, and artificial
- biology. What are we learning? Compt Rendus Chem. 2011:14 372–387.
 5 Nielsen J, Keasling JD. Engineering cellular metabolism. Cell. 2016;164:1185–1197.
- 6 Khalil AS, Collins JJ. Synthetic biology: applications come of age. Nat Rev Genet. 2010;11:367–379.
- 7 Shapira P, Kwon S, Youtie J. Tracking the emergence of synthetic biology. *Scientometrics*. 2017:112 1439–1469.
- 8 Castle SD, Grierson CS, Gorochowski TE. Towards an engineering theory of evolution. Nat Commun. 2021;12:3326.
- 9 Ausländer S, Ausländer D, Fussenegger M. Synthetic biology-the synthesis of biology. Angew Chem, Int Ed Engl. 2017;56:6396–6419.
- 10 Flores Bueso Y, Tangney M. Synthetic biology in the driving seat of the bioeconomy. Trends Biotechnol. 2017;35:373–378.
- 11 Chui M, Evers M, Manyika J, Zheng A, Nisbet T. The Bio Revolution: innovations transforming economies, societies, and our lives. https://www.mckinsey.com/indust ries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economi es-societies-and-our-lives; 2020.
- 12 Engineering Biology Research Consortium. Engineering Biology & Materials Science: A Research Roadmap for Interdisciplinary Innovation. 2021. https://doi.org/10.25498/ E4F592.
- 13 Mao N, et al. Future trends in synthetic biology in Asia. Advanced Genetics. 2021;2.14 Clarke LJ, Kitney RI. Synthetic biology in the UK an outline of plans and progress.
- Synth Syst Biotechnol. 2016;1:243–257.
 15 New techniques in biotechnology. Food Safety https://ec.europa.eu/food/plants/ genetically-modified-organisms/new-techniques-biotechnology it.
- 16 Hillson N, et al. Building a global alliance of biofoundries. *Nat Commun.* 2019;10: 2040.
- 17 Bonfadelli H. Communications about biotechnologies and GMOs across Europe. In: Jamieson KH, Kahan DM, Scheufele DA, eds. *The Oxford Handbook of the Science of Science Communication*. Oxford University Press; 2017.
- 18 Woźniak E, Tyczewska A, Twardowski T. A shift towards biotechnology: social opinion in the EU. Trends Biotechnol. 2021;39:214–218.
- 19 Kennedy B, Thigpen CL. Many publics around world doubt safety of genetically modified foods. *Pew Research Center*; 2020. https://www.pewresearch.org/fact-ta nk/2020/11/11/many-publics-around-world-doubt-safety-of-genetically-modifie d-foods/.
- 20 Kuntz M. Technological risks (gmo, gene editing), what is the problem with Europe? A broader historical perspective. Front Bioeng Biotechnol. 2020;8, 557115.
- 21 Lamelas NC. Introducing the global alliance of regional SynBio associations. *iGEM Blog*; 2021. https://blog.igem.org/blog/2021/4/14/introducing-the-global-allia nce-of-regional-synbio-associations.
- 22 Cameron DE, Bashor CJ, Collins JJ. A brief history of synthetic biology. Nat Rev Microbiol. 2014;12:381–390.

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- 24 Pei L, Gaisser S, Schmidt M. Synthetic biology in the view of European public funding organisations. Publ Understand Sci. 2012;21:149–162.
- 25 CORDIS. https://cordis.europa.eu/.
- 26 European Federation of Biotechnology organizes first congress on applied synthetic biology in Barcelona. https://www.biocat.cat/en/news/european-federation-biotech nology-organizes-first-congress-applied-synthetic-biology-barcelona.
- 27 Senior M. Europe's biotech renaissance. *Nat Biotechnol.* 2020;38:408–415. 28 Le Deu F, da Silva JS. Biotech in Europe: a strong foundation for growth and
- 28 Le bet P, da stiva 35, bloteri in Europe, a storig foundation for grown and innovation. https://www.nckinsey.com/industries/life-sciences/our-insights/biot ech-in-europe-a-strong-foundation-for-growth-and-innovation; 2019.
- 29 Infographic: capital landscape for European biotechs is maturing, but it continues to trail the United States. https://www.mckinsey.com/industries/life-sciences/ourinsights/infographic-capital-landscape-for-european-biotechs-is-maturing-but-it-co ntinues-to-trail-the-united-states; 2021.
- 30 Freedom of establishment and freedom to provide services. https://www.europarl. europa.eu/factsheets/en/sheet/40/freedom-of-establishment-and-freedom-toprovide-services.
- 31 Infographic: biotech hot spots in a fragmented European landscape. https://www. mckinsey.com/industries/life-sciences/our-insights/infographic-biotech-hot-spots-i n-a-fragmented-european-landscape; 2021.
- 32 Can European biotechs achieve greater scale in a fragmented landscape?. https:// www.mckinsey.com/industries/life-sciences/our-insights/can-european-biotechsachieve-greater-scale-in-a-fragmented-landscape; 2021.
- 33 Rusu VD, Roman A. Entrepreneurial activity in the EU: an empirical evaluation of its determinants. Sustain Sci Pract Pol. 2017;9:1679.
- 34 van Doren D, Koenigstein S, Reiss T. The development of synthetic biology: a patent analysis. Syst. Synth. Biol. 2013;7:209–220.
- 35 Shapira P, Kwon S. Synthetic Biology Research and Innovation Profile 2018.
- Publications and Patents; 2018. https://doi.org/10.1101/485805. bioRxiv 485805.
 Benaich. Universities in the UK and Europe Have a Start-Up Problem. Financial Times (North American edition).
- 37 Bomgardner MM. Ginkgo acquires Dutch DNA for fungal strains, Chem Eng News, 20210522 https://cen.acs.org/biological-chemistry/biotechnology/Ginkgo-acquires -Dutch-DNA-fungal/99/i19.
- 38 Canton B. Ginkgo acquires FGen AG, ultra-high-throughput screening platform. Ginkgo Bioworks; 2022. https://www.ginkgobioworks.com/2022/03/14/fgen/.
- 39 Carayannis E, Jones P, Liargovas P, Apostolopoulos N. Entrepreneurship and the European Union policies after 60 years of common European vision: regional and spatial perspectives. Int J Enterpren Small Bus. 2020;32:517–522.
- 40 Press corner. European commission European commission. https://ec.europa.eu/ commission/presscorner/detail/en/fs_20_426.
- 41 Kirk D. A different culture shaping synthetic biology in Europe. Labiotech.eu http s://www.labiotech.eu/in-depth/synthetic-biology-culture-europe-us/; 2020.
- s://www.labiotech.eu/in-depth/synthetic-biology-culture-europe-us/; 2020.
 Patterson & Josling. Regulating Biotechnology: Comparing EU and US Approaches. Environmental Policy in the EU doi:10.4324/9781849771221-24/regulatingbiotechnology-comparing-eu-us-approaches-lee-ann-patterson-tim-josling.
- 43 Pelkmans J, Renda A. Does EU Regulation Hinder or Stimulate Innovation?. 2014.
- 44 Press corner. European commission European commission. https://ec.europa.eu/ commission/presscorner/detail/en/ip_20_628.
- 45 Legal provisions of COM. 103 commission communication an SME strategy for a sustainable and digital Europe - EU monitor. https://www.eumonitor.eu/9353000 /1/j4nvhdfcs8bljza_j9vvik7m1c3gyxp/vl6uqf09i3x7; 2020.
- 46 Home. https://www.bbi.europa.eu/.
- 47 eureKARE. https://eurekare.eu/.
- 48 Bughin, Windhagen, Smit, Mischke & Sjatil. Innovation in Europe. Changing the Game to Regain a Competitive Edge. McKinsey Global Institute.
- 49 Smyth. Finance, Culture, Talent: Why Europe Struggles to Commercialise its Biotech Expertise. Financial times (North American edition).
- 50 EuropaBio. Core ethical values: EuropaBio. J BioLaw Bus. 2002;5:63.

- 51 New association for synthetic biology. Gates Cambridge -. https://www.gatescambridge.org/about/news/new-association-for-synthetic-biology/; 2015.
- 52 Molloy J. In: Registration Opens for EUSynBioS Symposium 2016: Engineering Biology for a Better Future; 2016. https://www.engbio.cam.ac.uk/news/eusynbios-2016.
- 53 EUSynBioS SC. EUSynBioS becomes a registered non-profit organization! —. EUSynBioS https://www.eusynbios.org/blog/2019/8/26/eusynbios-becomes-a-regis tered-non-profit-organization; 2019.
- 54 EUSynBioS Symposium 2017: Engineering Biology for a Better Future. Spanish National Centre for Biotechnology http://www.cnb.csic.es/index.php/en/events/p revious-events-at-the-cnb/1869-eusynbios-symposium-2017-engineering-biology-fo r-a-better-future.
- 55 Le-Gal A. In: EUSynBioS Symposium 2018 in Toulouse. France: Toulouse White Biotechnology; 2018. https://www.toulouse-white-biotechnology.com/en/eusynbio s-symposium-2018-toulouse/.
- 56 Hamadache S. In: International Symposium on Synthetic Biology in Toulouse, France (Part 1) —; 2018. SynBio Canada https://www.synbiocanada.org/news /2018/11/9/international-symposium-on-synthetic-biology-in-toulouse-france-part -1.
- 57 Masaryk University. EUSynBioS Symposium 2019 & Biomania. Faculty of Science MU https://www.sci.muni.cz/en/all-events/u/eusynbios-symposium-2019 -biomania
- 58 5th applied synthetic biology in Europe. FEMS https://fems-microbiology.org/oppor tunities/5th-applied-synthetic-biology-in-europe/; 2020.
- 59 EUSynBioSeminars. EUSynBioS https://www.eusynbios.org/eusynbioseminars.
- 60 EUSynBioS SC. Entrepreneurship in Synthetic Biology for early-career researchers: an introduction —. EUSynBioS https://www.eusynbios.org/blog/2021/2/1/entreprene urship-in-synthetic-biology-for-early-career-researchersnbsp-an-introduction; 2021.
- 61 Giornata nazionale della Bioeconomia 2021. https://assobiotec.federchimica.it/agen da/tutti-gli-eventi/2021/05/27/default-calendar/giornata-nazionale-della-bioecon omia-2021.
- 62 Krink N, Löchner AC, Cooper H, Beisel CL, Di Ventura B. Synthetic biology landscape and community in Germany. *Biotechnology Notes*. 2022;3:8–14.
- 63 GASB. https://gasb.de/.
- 64 GCSB. https://www.gcsb.info/.
- 65 Synthetic biology in action: beyond standard metabolism. https://www.embl.org/ about/info/course-and-conference-office/events/syn22-01/.
- 66 EMBL. EMBO Workshop Creating Is Understanding: Synthetic Biology Masters Complexity - 22 - 25 September 2019. https://www.embl.de/training/events/2019/ SYN19-01/.
- 67 Synthetic cell. Synthetic Cell https://www.syntheticcell.eu; 2017.
- 68 Warmbrod KL, Trotochaud M, Gronvall GK. iGEM and the biotechnology workforce of the future. *Health Secur.* 2020;18:303–309.
- 69 IGEM. http://igem.org.
- 70 Schmitt F-J, Frielingsdorf S, Friedrich T, Budisa N. Courses based on iGEM/BIOMOD competitions are the ideal format for research-based learning of xenobiology. *Chembiochem.* 2021;22:818–825.
- 71 Diep P, et al. Advancing undergraduate synthetic biology education: insights from a Canadian iGEM student perspective. *Can J Microbiol*. 2021;67:749–770.
- 72 Nadra AD, Rodríguez PE, Grunberg R, Olalde LG, Sánchez IE. Developing synthetic biology in Argentina: the Latin American TECNOx community as an alternative way for growth of the field. *Crit Rev Biotechnol.* 2020;40:357–364.
- 73 Startups igem.org. https://old.igem.org/Startups.
- 74 IGEM Grand Jamboree. https://jamboree.igem.org/.
- 75 Team List For All Years. https://old.igem.org/Team_List?year=all.
- 76 Kitney RI, Bell J, Philp J. Build a sustainable vaccines industry with synthetic biology. Trends Biotechnol. 2021;39:866–874.
- 77 Vickers CE, Freemont PS. Pandemic preparedness: synthetic biology and publicly funded biofoundries can rapidly accelerate response time. *Nat Commun.* 2022;13: 453
- 78 Foster B. Brexit and scientific research? Eur J Engl Stud. 2021;25:11-18.