Biotechnology Notes 3 (2022) 124–134

Contents lists available at ScienceDirect

Biotechnology Notes

journal homepage: www.keaipublishing.com/en/journals/biotechnology-notes/

Building the SynBio community in the Czech Republic from the bottom up: You get what you give

Stanislav Juračka [a,b,1], Barbora Hrnčířová [a,b,1], Barbora Burýšková [a,b,c,1], Daniel Georgiev [d,e], Pavel Dvořák [a,b,c,*]

[a] Department of Experimental Biology (Section of Microbiology, Microbial Bioengineering Laboratory), Faculty of Science, Masaryk University, Brno, Czech Republic
[b] Member of iGEM team, Brno, Czech Republic
[c] Former EUSynBioS Steering Committee Member, Czech Republic
[d] Department of Cybernetics, Faculty of Applied Sciences, University of West Bohemia, Pilsen, Czech Republic
[e] Member of iGEM team, Czech Republic

ARTICLE INFO

Keywords
Synthetic biology
Czech Republic
EU13 countries
Community
iGEM
Research landscape
Biotechnology and bioengineering
Public perception

ABSTRACT

Given its highly innovative character and potential socioeconomic impact, Synthetic Biology is often ranked among prominent research areas and national research priorities in developed countries. The global evolution of this field is proceeding by leaps and bounds but its development at the level of individual states varies widely. Despite their current satisfactory economic status, the majority of 13, mostly post-communist, countries that entered the European Union family in and after 2004 (EU13) have long overlooked the blossoming of Synthetic Biology. Their prioritized lines of research have been directed elsewhere or "*Synthetic Biology*" did not become a widely accepted term to encompass their bioengineering and biotechnology domains. The Czech Republic is not an exception. The local SynBio mycelium already exists but is mainly built bottom-up through the activities of several academic labs, iGEM teams, and spin-off companies. In this article, we tell their individual stories and summarize the prerequisites that allowed their emergence in the Czech academic and business environment. In addition, we provide the reader with a brief overview of laboratories, research hubs, and companies that perform biotechnology and bioengineering-oriented research and that may be included in a notional "shadow SynBio community" but have not yet adopted *Synthetic Biology* as a unifying term for their ventures. We also map the current hindrances for a broader expansion of Synthetic Biology in the Czech Republic and suggest possible steps that should lead to the maturity of this fascinating research field in our country.

1. Introduction

Synthetic Biology (SynBio) is known as a multidisciplinary research field that aims to transfer engineering principles such as modularity, abstraction, standardization, and characterization into biology. SynBio emerged in the 2000′s with founding studies on the first synthetic genetic circuits in living cells,[1–3] advanced DNA-assembly and genome-editing techniques,[4,5] or the first chemically synthesized bacterial genome.[6] The fundaments of SynBio were built on decades of previous research in molecular biology, biochemistry, biotechnology, genetic engineering, civil and electrical engineering, or information technology, and on parallel developments in SynBio-related fields of protein engineering, metabolic engineering, and systems biology. The latter bioengineering disciplines partially overlap with SynBio and are included in SynBio by some authors while others find distinct paradigms for each of them and distinguish them strictly.[7–10] In general, it is difficult to find a single comprehensive definition of SynBio that would be widely accepted.[11–13] While a one-to-one correspondence between existing bioengineering disciplines and Synthetic Biology is not possible, it is clear that the emphasis of Synthetic Biology on enabling methods and bottom-up principles is unifying the community and accelerating technological developments.

From its very beginning, SynBio has had an ambition to both (i) surmount the complexity of a living cell and unveil the secret of life and

* Corresponding author. Department of Experimental Biology (Section of Microbiology, Microbial Bioengineering Laboratory) Faculty of Science, Masaryk University, Kamenice 735/5, Brno 62500, Czech Republic.
E-mail address: pdvorak@sci.muni.cz (P. Dvořák).
[1] These authors contributed equally.

https://doi.org/10.1016/j.biotno.2022.11.002
Received 9 October 2022; Received in revised form 23 November 2022; Accepted 23 November 2022
Available online 9 December 2022

(ii) become one of the pillars of modern biotechnologies and participate in solving the global problems faced by humanity in this century.[14,15] Numerous achievements connected with SynBio in the 2010s that included commercial-scale biosynthesis of artemisinic acid, CRISPR/Cas-based genome editing, carbon dioxide fixation in engineered *E. coli*, chemical synthesis of yeast chromosomes and complete *E. coli* genome, or a new generation of antiviral vaccines drew the attention of investors, policymakers, and public and indicated that this ambition may not be overweening.[16–22] Indeed, the more recent public offerings by flagship SynBio companies such as Zymergen, Ginkgo Bioworks, and Twist Biosciences are cementing the position of Synthetic Biology in the modern bioeconomy sector. Effective translation of lab-born accomplishments into real-world technologies remains a challenge. However, it is more and more evident that the 21st century will indeed be a century of bioengineering and SynBio.

Let us have a brief look at some numbers. In 2012, the World Economic Forum (WEF) placed SynBio and metabolic engineering as number 2 on the list of top ten technologies that will have major global impacts.[23] More recently, in 2021, SynBio got on the top of the agenda of the Global Technology Governance Summit hosted by WEF.[24] The number of research papers published per year that encompass the term *Synthetic Biology* increased >10-times between the years 2000 and 2021 (from 518 to 5914, NCBI PubMed database).[25] SynBio is now understood as a research field that can substantially contribute to the societal transformation on the way towards sustainable development, as well as a great business opportunity. Based on the recent Global Synthetic Biology Market Forecast to 2028, the SynBio market is expected to grow from US$ 10,544.16 million in 2021 to US$ 37,850.85 million by 2028 (almost 300 % increase in seven years).[26] The growth is being driven mainly by rising investments and the increasing number of SynBio start-ups that hold genome-editing technologies, DNA reading and writing, or enzyme and pathway engineering in their portfolio. This is a big chance for leading SynBio countries with already established infrastructures and strong communities as well as for "SynBio freshmen".

Continental Europe, traditionally more conservative on genetic modifications, still lags the SynBio leaders such as the US, UK, or China. But the situation in countries across Europe differs substantially.[27] Some states of the European Union (EU) including the Netherlands or Germany have already mature SynBio communities and infrastructure that are built on the activities of local SynBio associations, start-ups, SynBio-dedicated professorships, iGEM (International Genetically Engineered Machine) teams, research centers as well as individual research groups that emerged all around Europe in the last decade.[28,29]

The situation in the EU13 states (Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovakia, and Slovenia) was more complicated due to their lower economic status and therefore worse starting conditions for SynBio expansion.[30] The economic situation has improved significantly in most of these countries, yet, even among them, the state of local SynBio communities varies from juvenile to basically non-existent.[31] For instance, the Slovenian team led by prof. Roman Jerala (Department of Biotechnology at the National Institute of Chemistry, Ljubljana) successfully participated in the iGEM competition already in 2006 and has amassed an impressive collection of prizes since then. Some of their iGEM ideas evolved into projects eventually published in high-impact journals. This success together with previous research achievements also attracted a prestigious ERC grant in Jerala's group and enabled the establishment of the Department of Synthetic Biology and Immunology in Jerala's domestic institute.[32,33] Dedicated SynBio research units or even whole centers of research excellence can also be found in other eastern European countries, e.g., in Hungary (Synthetic and Systems Biology Unit in Szeged Biological Research Centre) or in Estonia with its progressive Estonian Centre for Biosustainability, which unites SynBio oriented research laboratories from the University of Tartu and Tallinn University of Technology.

The Czech Republic is an example of a EU13 country that has necessary prerequisites to become a local SynBio leader. It seems that it has not fully leveraged this potential thus far as SynBio is still a rather marginal discipline nurtured by the interest of a small number of enthusiasts and visionaries. In this commentary article, we explore the possible causes of this state and document the current position of the recently born SynBio community in our country. Our investigation suggests that the seemingly unsatisfactory situation is largely due to the lack of use of the term *Synthetic Biology* in the academic, private, and public domains. The country can otherwise benefit from the relatively strong (bio)technological background and the growing number of companies and academic and research units that use bioengineering and SynBio approaches for fundamental research or to produce competitive biotechnologies. This foundation, together with the popularization activities of the newly established SynBio community, gives hope for the expansion of Synthetic Biology in the Czech Republic in the years to come.

2. Prerequisites of the Czech Republic for the nascency of the SynBio community and its current status

With its population of 10.5 million inhabitants and area of 79,000 km^2 the Czech Republic (CR) ranks among the medium-sized EU countries. Average among 27 EU members is also the country's ranking according to the European Innovation Scoreboard 2022.[34] In 2020, domestic expenditures on R&D reached 2 % of GDP, which was the second highest number among the EU13 members.[35] CR can draw on a rich tradition of academic and research institutions, advanced industries, and scientific visionaries that were founded or were active in the Czech lands in the past. It also has a strong background in traditional biotechnologies, engineering, chemistry, and physics, and currently is at the forefront of development in information technology (IT) and nanotechnology sectors. In the following sections that focus on the Czech academic and research environment, biotech business, governmental activities, or public views, we discuss how the country's capacity is, and whether at all, being used to build a new SynBio and bioengineering domain.

2.1. SynBio in the Czech academic environment

It is not surprising that the primary sites of emergence of SynBio communities worldwide are universities that provide education in life sciences or technology. Universities and research institutions have had a notable impact on life in Czech lands since 1348 when the Holy Roman Emperor Charles IV. established the Charles University in Prague. Since then, other quality public universities and research institutions of the Czech Academy of Sciences (CAS) - a major research body in CR whose roots date back to the 18th century - were founded in regional capitals including Olomouc, Brno, Ostrava, České Budějovice, or Plzeň (Pilsen). These cities became centers of knowledge and gave rise to innovative, sometimes revolutionary, ideas of, e.g., Jan Evangelista Purkyně (contributed to the cell theory), Gregor Mendel (formulated principal laws of heredity), or Antonín Holý (co-developed antiretroviral drugs Tenofovir, Viread, or Hepsera used worldwide for the treatment of AIDS and hepatitis B).

STEM (science, technology, engineering, mathematics) disciplines, including biotechnology, have undergone significant developments in the academic environment of former Czechoslovakia (1918–1993) and today's Czech Republic during the 20th and at the beginning of the 21st century. There are currently more than 50,000 students enrolled in life-science study programs including Cell Biology, Biochemistry, Physiology, Immunology, Bioinformatics, Biomedicine, or Biotechnology (mainly food, animal, plant, environmental, or microbial biotechnology and applied microbiology) offered by major public universities spread around the country (Fig. 1A).[36] Some of these schools also provide study programs in advanced molecular biology, genetics, and genetic engineering (Charles University, Masaryk University, University of

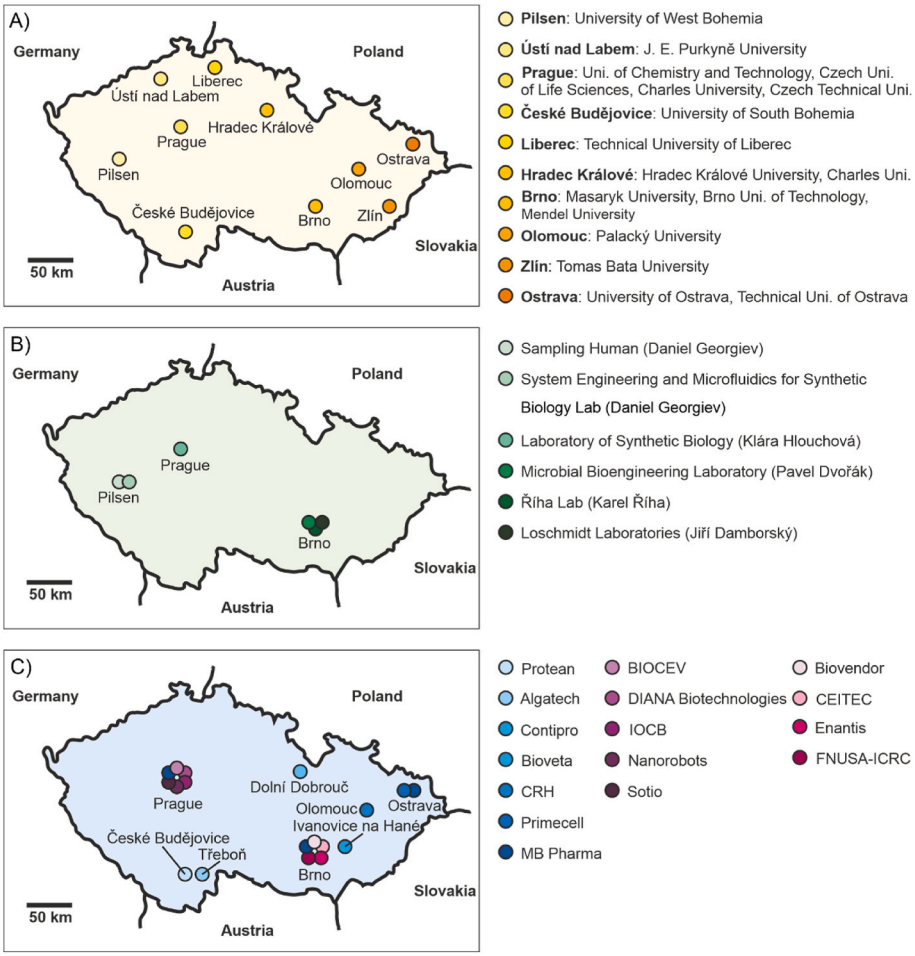

Fig. 1. Geographical distribution of the major Czech public universities with life-science or technology study programs **(A)**, academic and business units forming the "core" Czech SynBio community **(B)**, and wider Czech academic and business bioengineering-oriented "shadow" SynBio community **(C)**. Note that the figure does not capture complete Czech biotechnology and bioengineering sector. Abbreviations: Algatech, Center for Algal Biotechnology; CRH, Centre of the Region Haná for Biotechnological and Agricultural Research; BIOCEV, Biotechnology and Biomedicine Center of the Academy of Sciences and Charles University; IOCB, Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences; Nanorobots, The Nanorobots Research Center; CEITEC, Central European Institute of Technology; FNUSA-ICRC, The International Clinical Research Center of St Anne's University Hospital in Brno.

Chemistry and Technology in Prague, Palacký University, University of South Bohemia). Technical disciplines relevant to SynBio including IT, nanotechnology, chemical engineering, or cybernetics are studied mainly in Prague, Brno, Ostrava, Olomouc, Pilsen, Pardubice, Zlín, and Liberec. On top of that, there are more than 50 institutes of the CAS with > 11,000 skilled research staff spread all around the country. Some of these centers, e.g., the Institute of Organic Chemistry and Biochemistry (IOCB), Institute of Molecular Genetics (IMG), and Institute of Biotechnology (IBT, all three positioned in Prague) are recognized for their cutting-edge research in the fields (e.g., protein science, molecular genetics, biomaterials and tissue engineering, immunology, oncology, biochemistry, or cell biology) that are being revolutionized by SynBio throughout the world.

Czech research infrastructure has blossomed since the country joined the EU in 2004. Regional research competitiveness was massively supported by EU funds, especially after 2007. The relevant examples of newly built centers of research excellence in which SynBio could thrive include the Biotechnology and Biomedicine Centre (BIOCEV) of CAS (includes IMG, IBT) and Charles University in Prague, a new Masaryk University campus in Brno-Bohunice, Central European Institute of Technology (CEITEC) that unites four universities and two CAS institutes in Brno, International Clinical Research Centre (FNUSA-ICRC) in Brno, Center for Algal Biotechnology (ALGATECH) in Třeboň, Centre of the Region Haná for Biotechnological and Agricultural Research (CRH) in Olomouc. Prestigious grants from the European Research Council (ERC) can be considered one of the indicators of excellence in research. 56 ERC grants, the second highest number among the EU13 countries, have been awarded to researchers in CR since 2007 (personal communication with the Technology Centre of Czech Academy of Sciences). The vast majority of these grants were assigned to projects in physical sciences, life sciences, and engineering, with most of the successful applicants coming from universities and CAS institutes in Prague and Brno.

The data provided above suggest that CR can capitalize on two to four knowledge hubs that connect major public R&D organizations whose joint expertise of highly educated working power, state-of-the-art infrastructure, and financial capital could be harnessed to form strong SynBio subcommunities. Such conditions are found especially in Prague and Brno and potentially also in Olomouc or Ostrava. The first embryos of the Czech SynBio community indeed popped up in the academic environment in Prague and the nearby University of West Bohemia in Pilsen and also in Brno. However, in comparison with, e.g., Germany, where the first professorships entirely dedicated to SynBio were officially announced already in 2009 and where the German Association for Synthetic Biology (GASB) has united students with established researchers and SynBio stakeholders since 2015,[28] the Czech academic SynBio community is still scattered, unorganized, and completely dependent on bottom-up activities of several research teams and groups of enthusiastic undergraduates. Here we tell the stories of several laboratories that openly declare their connection to the SynBio field and whose activities contribute to the installation and popularization of SynBio in CR.

Dr. Daniel Georgiev, a systems theorist and synthetic biologist, came back to CR in 2010 after a postdoc in Klavins Lab at the University of Washington to establish his laboratory of Systems Engineering and Microfluidics for Synthetic Biology at the Department of Cybernetics at the University of West Bohemia in Pilsen. In 2014, he started a semestral course "Introduction to cellular system modelling", which introduces engineering students to basic biochemical, conceptual, and

experimental principles of bioengineering. The multidisciplinary team of the Georgiev Lab adopted systems theory and software engineering together with molecular and cell biology to design yeast-based biocomputers and biosensors that could detect diverse medical phenotypes in blood. The idea of using microbes for diagnostics was presented at iGEM 2015 by the very successful Pilsen team – the first Czech team at this competition. Importantly, the project was later capitalized in one of the first Czech SynBio spin-off companies XENO Cell Innovations (currently Sampling Human), which aims to develop a breakthrough platform for clinically relevant access to the spectrum of single-cell data. Another former expat who was inspired by a postdoc experience in the United States is Dr. Klára Hlouchová. Klára's Laboratory of Synthetic Biology is affiliated with the Faculty of Science of Charles University since 2017 and is based at the BIOCEV campus near Prague. The group is interested in various aspects of protein evolution ranging from astrobiology and origins of life to protein engineering and synthetic life.[37,38] Their research topics include the effect of the amino acid alphabet on protein structure, protein reverse evolution, or dark protein space.

In 2009, researchers from Loschmidt Laboratories, the protein engineering group and department led by prof. Jiří Damborský at Masaryk University in Brno, initiated an interdisciplinary project that adopted protein engineering, metabolic engineering, and SynBio approaches including the DBTL (Design-Build-Test-Learn) cycle for the design of biocatalysts for the biodegradation of toxic anthropogenic pollutants. The project introduced several new concepts in the biodegradation & bioremediation field.[8,39] One of the outcomes, reconstruction and engineering of the orthogonal biodegradation pathway in heterologous host *Escherichia coli,* was published in 2014 as the first article by Czech authors in the newly founded SynBio flagship journal ACS Synthetic Biology.[40] Together with Dr. Karel Říha from CEITEC, who is one of the pioneers of Czech plant SynBio, Loschmidt Laboratories (namely the Molecular and Structural Biology team leader Dr. Martin Marek) were also at the birth of the first semester-long *Synthetic Biology* course at Masaryk University in 2020. To the best of our knowledge, a similar semestral course mentioning SynBio directly in its title is offered only by one more Czech university – the University of Chemistry and Technology in Prague (*Synthetic Biology and Genetically Modified Organisms*). A whole *Synthetic Biology* study program is not yet available in CR, but the first such program is being prepared by Loschmidt Laboratories.

The experience from Loschmidt Laboratories and his postdoctoral stay in de Lorenzo's lab in CNB–CSIC in Madrid inspired Dr. Pavel Dvořák to establish the Microbial Bioengineering Laboratory (MBL) at the Faculty of Science of Masaryk University in 2019. The laboratory adopts methods of SynBio and metabolic engineering to boost bacterial cell factories for biodegradation and valorization of residual plant biomass and derived organic substrates.[41,42] Pavel leads the semestral course "Introduction to the Metabolic Engineering and Synthetic Biology of Microorganisms" and delivers occasional lectures on SynBio for the public. MBL also co-organizes the biannual Biomania Student Scientific Meeting in Brno, which introduces ideas of bioengineering for biotechnology and biomedicine to Czech undergraduates and postgraduates and provides a space for the interaction of students with renowned guest speakers from abroad. In 2019, The Biomania Meeting organized as a joint event with EUSynBioS (the European Synthetic Biology Society) gave rise to the first Brno iGEM team.

Besides the aforementioned SynBio promoters, there are many more Czech investigators whose research orients in the SynBio direction. They are based at the top institutes of the CAS (IOCB, IMG), centers of research excellence (BIOCEV, CEITEC, FNUSA-ICRC), as well as at the leading Czech universities. We may mention the group of Dr. Milan Vrábel from IOCB that combines modern organic chemistry with chemical biology tools to create hybrid biological systems with unique features,[43] Jan Konvalinka's group from the same institute, which develops chemo-biological tools that use specific ligands attached to a polymeric carrier or a DNA oligonucleotide for the "high-throughput" identification and isolation of various proteins, their ligands and inhibitors,[44] or the group of prof. Martin Pumera, director of the Center for Advanced Functional Nanorobots at the University of Chemistry and Technology in Prague. Our domestic Synbio community can also take advantage of contacts with expats that shape the face of SynBio on a global scale. For instance, Jiří Zahradník, a postdoc in the group of prof. Gideon Schreiber at the Weizmann Institute of Science, co-developed an enhanced yeast display platform for the rapid evolution of challenging targets, which has recently found its use in mapping potentially infectious mutations in the receptor-binding protein of SARS-CoV-2 spike protein.[45,46] The name of Martin Jínek from the University of Zurich, a former postdoc in Jennifer Doudna's lab and the first author of a revolutionary Science paper that started the era of CRISPR/Cas-mediated genome editing, is probably known to all SynBio fans.[17]

It can be concluded that there exist in fact two parallel Czech academic SynBio communities – a small one, which includes laboratories that openly declare their connection to SynBio (Fig. 1B), and a much bigger "shadow" community (Fig. 1C) of labs that use SynBio tools and approaches but do not apply the term *Synthetic Biology* in their propagation materials. Thus, the SynBio community in the Czech academic environment was already born, is starting to bloom, and addresses a palette of attractive topics, but it lacks a common umbrella organization as well as broader attention of many potential members. One important message here is that proactive academicians with experience from abroad play an essential role in shaping the Czech domestic SynBio landscape. As noted above and developed in the following section, these PIs and their students were also at the beginning of the first Czech iGEM teams.

2.1.1. *The experience and impact of Czech iGEM teams*

The iGEM competition is an initiative that stems from the very heart of the SynBio field and is intrinsically linked to it. In its 19 years of existence, the competition gave rise to 3600 projects by 70,000 participants from 46 countries (https://igem.org/). iGEM introduced an innovative approach to the education of future SynBio scientists, brought the global SynBio community together, and contributed to the propagation of the term *Synthetic Biology* across the world. The competition has thus greatly contributed to the development of the field into its current stage. Moreover, some of the successful student projects have grown into valuable scientific articles or even business ideas.[47] SynBio leading states often have a larger representation in the competition, and success in iGEM has become an indirect indicator of the maturity of SynBio and bioengineering in a given country. Despite the overall low attention dedicated to SynBio in the Czech Republic, two Czech iGEM teams have already participated in the competition with success.

The first Czech iGEM team from Pilsen took part in the competition in 2015. Daniel Georgiev put together a group of cybernetics and biology students to develop a project called The Iod Band. The team invented a diagnostic method to find rare metastatic cancer cells in the blood. Their solution was an Input-to-Output Diploid (IOD) system made of modular input and output haploid yeast cells mating together and forming diploids. While the input haploid had genes capable of receiving signals from the environment, the output haploid acted as an actuator and emitted diverse signals. The fusion of distinct haploid genomes gave rise to a functional synthetic circuit. The diagnostic test was based on mixing the modified yeast cells with a blood sample. The idea impressed the jury and the IOD Band was awarded the First Runner-Up in the undergraduate category. Besides, the project won the Health & Medicine track, The Best Model award, and The Best Software Tool award. Unfortunately, the team did not continue in the following years. On the other hand, the research idea has been developed in the start-up Sampling Human.

The second Czech iGEM team was established in Brno and it participated in iGEM 2020 and 2021. Its path started at The Biomania Student Scientific Meeting & EUSynBioS Symposium 2019 where two undergraduate students of Molecular Biology and Genetics at Masaryk University attended a breakout session led by The European Ambassador

for the iGEM Foundation Nemanja Stijepovic. In the end, the team consisted of 15 students from Masaryk University and Brno University of Technology (molecular biologists, biochemists, and students of IT, law and finance, or business economy). The students then approached several group leaders at Masaryk University some of whom became the team PIs and provided the necessary lab space. They also managed to obtain financial support from the Faculty of Science and other institutions and private companies. The 2020 and 2021 Brno iGEM projects were intended to solve a practical local problem of the Brno Reservoir, which regularly struggles with cyanobacterial blooms. In 2020, the Cyanotrap project focused on creating a device that would flow on the surface of the reservoir, kill the overpopulated cyanobacteria, and clean the water from their toxins (Fig. 2). In 2021, the Phoscage project targeted the cause rather than the effect of the problem when it aimed to capture excess phosphorus from surface water bodies, thus reducing cyanobacterial growth. Both projects were awarded gold medals, and the Cyanotrap received a nomination for the Best Environment track award. The jury also appreciated the fact that the students went one step further and founded a non-profit organization called Generation Mendel (https://www.generationmendel.cz/). This NPO focuses on science popularization and education in the field of biology and particularly SynBio. Its members write online minicourses for the public on various scientific topics, create educational content on social media, and give talks about genetic modifications at schools or libraries.

The Brno iGEM team had to overcome many difficulties. Besides the limited guidance from the side of supervisors, who could only help the team in their free time, the students also struggled, especially after iGEM 2021, with the disinterest from the media and even from the PR department of their own institution. The Brno iGEM team is thus a notable example of a bottom-up activity of talented proactive undergraduates who built their success in the competition from scratch and predominantly on their own. Their story can serve as a model for other teams emerging in non-leading SynBio countries.

Unfortunately, similarly to their Pilsen predecessors, the Brno iGEM team has not continued in the competition after 2021, mainly due to study responsibilities of the key members. Yet, the students plan to support future generations of iGEMers in Brno by establishing a special university course dedicated to the competition. This idea aims to relieve the future contestants from some of the organizational issues the former team had to deal with and help the instructors in allocating more of their time to helping the students. The new course would also serve to transfer some of the essential experience and skills such as team leadership, cooperation, project design, independence in experimental design and execution, accounting, administration, and project promotion, from the previous participants to the next.

Both iGEM teams have undoubtedly contributed significantly to the promotion of SynBio in the Czech Republic. Their success was covered by the national and regional Czech press, radio, and even television. Nonetheless, their rapid rise and equally rapid demise once again confirmed the main weakness of the Czech SynBio community – its fragmentation and the lack of systemic support to ensure its sustainable long-term development.

2.2. SynBio in the Czech business environment

The business sector is inevitably a core part of any deep technological field such as SynBio as it links publicly funded basic and exploratory research projects with market opportunities and societal challenges. CR has a long history of traditional biotechnologies, which started already in the Middle Ages with the production of wine, beer, and dairy

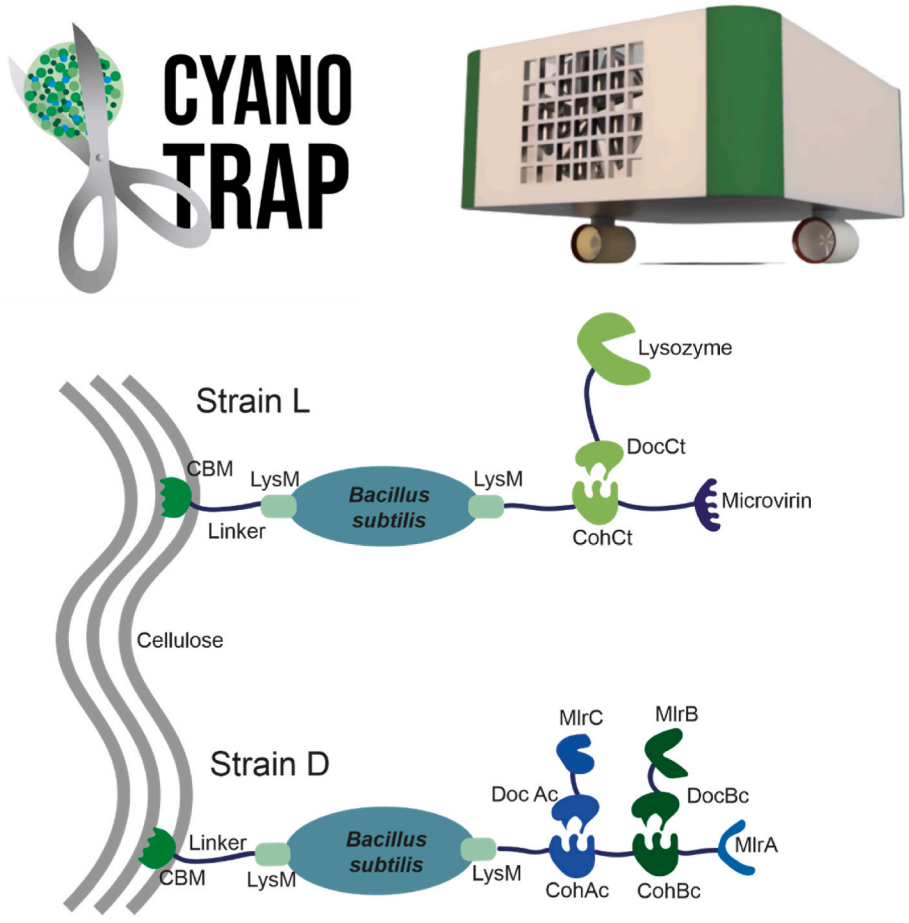

Fig. 2. Graphical representation of the Cyanotrap project of Brno iGEM team 2020. The "trap" mentioned in the project name is a device that would float on water, filter out large particles and feed the water with cyanobacteria into a chamber containing engineered *Bacillus subtilis* anchored on cellulose beads. *B. subtilis* was designed to display various proteins on its surface using the interaction of the LysM module with its cell wall. The CBM (carbohydrate binding module) serves to immobilize the cells on cellulose, microvirin and lysozyme anchored to Strain L catches the cyanobacterial cells and disrupts their envelopes, respectively. The MlrA, MlrB, and MlrC enzymes anchored to Strain D degrade microcystin, a toxin released from the lysed cyanobacteria. All modules are either directly fused to synthetic protein scaffolds or attached to them through a strong, non-covalent interaction of cohesin-dockerin modules.

products. Currently, the sector got substantially bigger as more advanced technologies and products found their place in the region, and most of the major biotechnology types (industrial, agricultural, environmental, medical) are now present in the country. Two biotechnology areas that have expanded the most in the past few years are nanotechnology and human healthcare. For example, Contipro, a biotech company based in a small town Dolní Dobrouč, is an already well-established global producer of hyaluronic acid extracted from the cell walls of the bacterium *Streptococcus zooepidemicus*. Since 2012, the company exploits its own nanofibre machine to produce innovative materials for applications in biomedicine, tissue engineering, targeted drug delivery, or wound healing. Nafigate is another interesting Czech corporation, currently trying to expand on the market with polyhydroxyalkanoates, an environment-friendly biological alternative to synthetic plastics. The company licensed the Hydal biotechnology for the microbial bioproduction of polyhydroxyalkanoates from waste frying oil, developed by researchers at the Brno University of Technology.[48] In addition, there is an increasing number of Czech companies that focus on the development of biomedicine and *in vitro* diagnostic tools (e.g., BioVendor, Generi Biotech, Elizabeth Pharmacon). For an interested reader, the Czech biotech business sector has been thoroughly mapped in the recent reviews of Márová (2020) and Hájek et al. (2021).[36,49] It is also worth mentioning here the well-developed pharmaceutical (e.g., Zentiva), chemical (e.g., Fosfa), IT (e.g., Avast), instrumentation (e.g., Photon Systems Instruments), or 3D printing (Prusa Research) industries, that could profit from the employment of SynBio and bioengineering. In return, SynBio in CR can benefit from the resources and know-how of these established industries. Such collaborations should form an environment with great potential for the emergence of new SynBio companies.

Currently, there are only a handful of Czech companies that use technologies that we would classify as advanced SynBio (adopt bottom-up computational design, advanced genome-editing techniques, genetic circuits, or cell-free systems), and only one of them openly claims to apply the principles of Synthetic Biology and thus can be included in the "core" Czech SynBio community (Fig. 1). Sampling Human, a start-up that emerged from the previously mentioned Czech iGEM project The Iod Band, aims to develop single-cell analysis based on genetically engineered yeast cells (Fig. 3). These should detect a variety of pathologically changed cells in a blood sample using antigen-antibody recognition. Recently, the company reached a milestone and received funding from the Czech Ministry of Industry and Trade and the EU to bring their technology into the stage of clinical research. Several steps further in their technology development is another firm, Sotio, which we can categorize, together with some other companies mentioned below, in the "shadow" SynBio community (Fig. 1). Sotio focuses on developing next-generation cancer immunotherapies based on patients' own T-cells. The company was founded by Czech billionaire entrepreneur Petr Kellner. In their cell therapy pipeline, they add additional ("bolt-on") transgenes to available CAR T (Chimeric Antigen Receptor T cells) technology to improve the resistance of CAR T cells acting in a solid-tumor environment. One of the products is expected to reach the clinical phase in 2022.

Besides, at least three other bioengineering-oriented companies work with cell-free systems. IOCB Tech (a technology transfer office and subsidiary enterprise of the Institute of Organic Chemistry and Biochemistry CAS) runs the iBodies project, which is developing modular synthetic antibodies for detection assays.[44] They bypass the difficulties of eukaryotic expression systems by chemically synthesizing polymeric antibody mimetics that can replace classical antibodies in biomedical applications. iBodies are currently offered for co-development and licensing. Diana Biotechnologies is a spin-off that grew on the invention of an ultra-sensitive detection assay called DIANA (DNA-linked Inhibitor ANtibody Assay). The technology combines classical ELISA and qPCR for boosting detection limits and can be used for diagnostics or high-throughput screening, e.g., in drug discovery.[50] The company's growth is mainly attributed to the revenues from COVID-19 diagnostic services (they covered 20–25% of Czech testing capacity) carried out by classical RT-PCR kits. It is noteworthy that both iBodies and DIANA technologies evolved from student projects in Konvalinka's lab in IOCB. Elphogene is a Prague-based biotech start-up that implements its oncoMonitor liquid biopsy technology into non-invasive monitoring of patients in advanced stages of colorectal cancer.

Employment of bioengineering methods is also found in the company Primecell in Ostrava. Primecell uses adeno-associated viral gene therapy to deliver unique pyroptosis-inducing technology that causes tumor cell or pathogen death via immunity activation. Specificity is ensured by the promoter of the delivered pro-caspase-1 gene and the need for an active inflammasome for caspase activation in target cells. The company runs other projects focused on, e.g., NK/CAR T platform cell-based immunotherapy or 3D bioprinted scaffolds in collaboration with various partners in CR and abroad.

Enantis, a Masaryk University spin-off takes advantage of the protein engineering know-how of Loschmidt Laboratories to produce stabilized proteins for commercial purposes. An interesting product is a highly stabilized fibroblast growth factor 2 that finds its use in stem cells cultivations, can be used also in cosmetics and veterinary medicine, and aims to become a game changer molecule in the cultured meat field

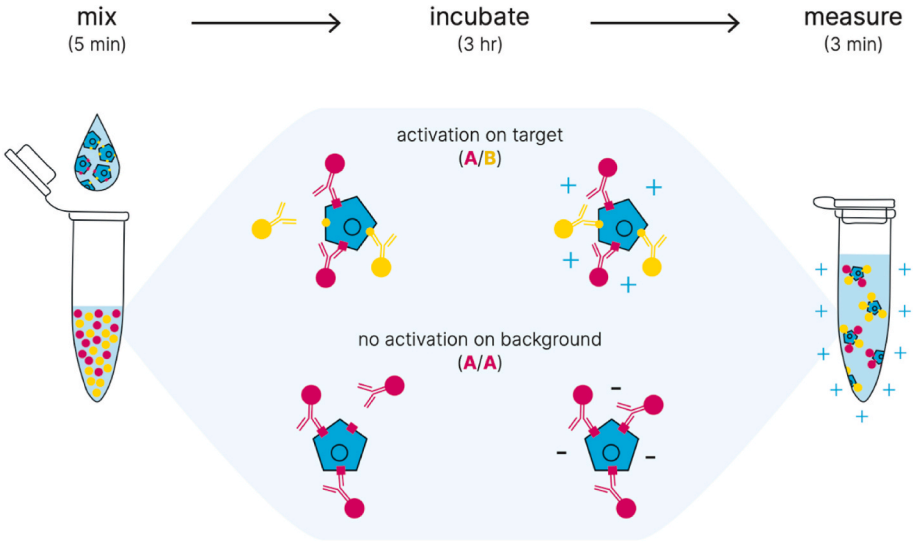

Fig. 3. Sampling Human's Diagnostics On Target working principle. Diagnostics On Target (DOT) assays contain dried yeast genetically engineered to perform tasks normally executed by complex instruments. The engineered cells bind to cells in a sample and evaluate their immuno profiles. If a cell matches the targeted profile, the engineered yeast cells exit their dormant state and enter an activated state wherein they produce easily measurable reporter signals. The method is highly modular. By mixing and matching the types of engineered cells the user can modify the target profile using basic logic gates. For instance, a two-input "AND" gate profile requires two specific antigens to both be present on the bound cell to trigger a positive readout. The adaptability of the DOT platform allows for the analysis of anything from rare epithelial cells in samples of lysed blood to apoptotic T-cells in primary cell cultures.

(FGF2 is a key component of cultured meat media).[51] Speaking of synthetic meat production, it is certainly worth mentioning two more start-ups BeneMeat and Mewery, which are pioneering synthetic meat production in CR.

Apart from the aforementioned "core" or "shadow" SynBio pioneers, most Czech biotech companies that implement bioengineering are limited to the use of standard recombinant DNA technologies and genetically engineered bacteria or yeast for the production of recombinant proteins for commercial purposes or as a customized service. These include, but are not restricted to, Bioveta and Dyntec from the vaccine business, or BioVendor, Protean, and MBPharma offering a range of recombinant proteins.

A lot of companies named here started or are still start-ups or spin-offs. The initial support to translate the idea into a final product is thus extremely important. This is especially true for the SynBio business due to slow returns on investments. And this is where start-up accelerators and incubators play an essential role. An important institution is i&i Prague, a biotech hub under the wings of the CAS and its IOCB, which sources and provides valuable mentorship to such starting businesses. In their portfolio, we can find some of the aforementioned companies such as Sampling Human, Elphogene, Enantis, Diana Biotechnologies, or iBodies. A similar institution is JIC (South Moravian Innovation Centre) based in Brno. In addition to a variety of other services, JIC provides start-up projects with laboratory core facilities and office space in the INBIT incubator in the fast-developing environment of the Masaryk University Campus in Brno Bohunice. In Ostrava, the biomedicine incubator 4MEDi accelerates early-stage red biotech companies such as Primecell.

To sum up, there are several promising firms in CR that employ advanced SynBio techniques and focus predominantly on red biotech (biomedicinal) applications (Fig. 1). Some others perform attractive biotechnological research with bioengineering elements. Our survey among Czech biotech companies showed that most of the bioengineering-related businesses based in CR rely on well-established molecular biology and genetic engineering tools and techniques such as variants of PCR, molecular cloning, gene synthesis, or heterologous protein production that helps them yield their revenue. They do not adopt advanced SynBio strategies. This can be caused by the overall socio-economic position of CR and the fact that most of these companies are small businesses with a maximum of dozens of employees oriented on the local market.[36] Risky investments with slow returns might not be a viable option for small and developing companies if they do not have solid institutional support. Moreover, similarly to the academic environment, we learned that there is some awareness of the term *Synthetic Biology* in the Czech private sector but its understanding is very ambiguous. Hence, the fundamental question is whether the companies are even aware of the possibilities that the SynBio sector offers (e.g., multidisciplinary engineering-based approach that may come up with breakthrough, out-of-the-box solutions, reveal hidden potential of living systems to solve practical problems, toolbox of advanced genome-editing methods, numerous available mathematical models of living systems that help to predict and simulate their behavior etc.).

To point out another problem, only a handful of companies openly present and explain their technologies. This is, of course, partially caused by strict IP protection. However, based on our information, another important reason is that some companies do not see it as an advantage to openly present the complexity and "foreignness" of their bioengineering technologies since it could discourage potential customers from buying their products. This is also the reason why some biotech firms capitulated on the use of GMOs (personal communication with representatives of several biotech companies).

2.3. Public perception of SynBio and related topics in CR

There are several media outlets through which the public in CR can gain information on up-to-date science including biotechnology and SynBio. The most prominent one is a TV discussion series and podcast called Hyde Park Civilizace (Hyde Park Civilization), produced by Czech Television. The program offers interviews with renowned scientists from all around the world. One of the founding fathers of SynBio, Steven Benner, appeared on the show in 2018. Since 1963, Czech Radio has been broadcasting a show called Meteor, which offers science reports, interviews, and documentaries for all. The journal Vesmír (Universe), which publishes science-popularizing articles in all scientific fields, has been around even longer - the first issue was published in 1871. Moreover, there are also many web pages and social media accounts that focus on popularizing science. Noteworthy is the project called Vědátor (The Scientist), which delivers scientific news in an entertaining manner. Biotrin (https://www.biotrin.cz/), which is doing a great job in responsibly informing the Czech public on modern biotechnologies and GMOs, is a non-profit organization run by researchers mainly from the University of Chemistry and Technology in Prague. The available information-spreading channels are thus many, but the mentions of SynBio are rather rare.

To the best of our knowledge, there is no extensive study or public opinion poll data that would describe the viewpoint of the Czech people on Synthetic Biology. It would be beneficial to perform such a study because its results could guide the Czech SynBio community in their science-popularization and education efforts. These activities are pivotal as positive public perception of SynBio will help activate the attention of the political representation and promote additional funding for research and development in this field.

In 2021, the Brno iGEM team asked the non-scientific public about their opinion on the team's project. Some of the questions were more general and therefore can be used to paint the picture of the public's outlook on SynBio, GMO, and similar subjects. However, it needs to be said that due to the nature of the poll distribution (mainly sharing on Facebook), the students did not manage to get a representative set of respondents (the resulting data are biased because three-quarters of respondents were women, the majority of respondents were younger than 30, and circa 75% of respondents either had a university degree or were working towards it). From the results of the poll, the students found that 12.6% of respondents thought that the regulation of GMOs in the EU is too strict, 15.5% thought that it is adequate and 9.7% thought that it is insufficient. However, 62.2% of respondents had no opinion on this issue. This result points to a lack of foreknowledge on this topic, showing a possible direction for educational efforts. Furthermore, 37.4% of respondents believed that modified foods should appear on the shelves, 21.2% were against it, and 41.1% of respondents remained undecided.

An example of a more extensive public opinion poll focused directly on the issue of GMOs is the survey done by The Public Opinion Research Centre (Institute of Sociology, Czech Academy of Sciences).[52] According to this survey, most people have heard of genetic modification of crops (74 %, Fig. 4). However, the interest of the Czech public in genetically modified crops (GMC) is low, as roughly the same percentage of respondents (78 %) say they are not interested in the topic. At the same time, 70 % of people think that there is insufficient availability of information regarding the GMC topic. The public opinion on the health risks of GMC, willingness to take a drug produced by a GMO, or the necessity of GMOs for the survival of humanity in future was also sought (Fig. 4).

The results of the aforementioned studies paint a picture of an indecisive society without sufficient information on and interest in GMOs and related topics. The Czech public is not very critical nor supportive of the products of genetic modifications that are an integral part of SynBio.

2.4. Governmental initiatives and state's support of SynBio

As mentioned in the introductory paragraph of Section 2, CR's annual investments in its R&D increase continuously and are higher

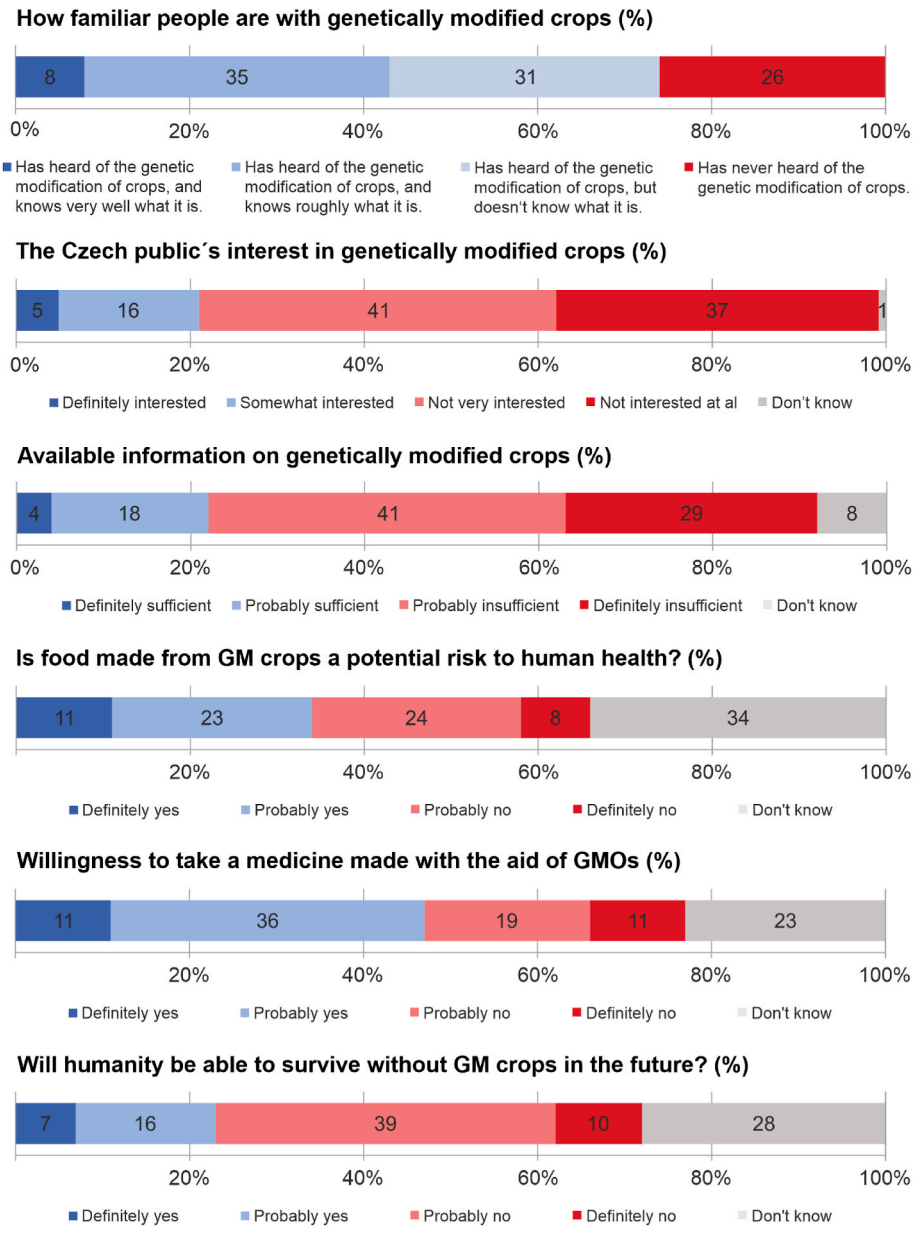

Fig. 4. Selected outcomes of the public opinion poll on the topic of GMOs by The Public Opinion Research Centre (Institute of Sociology, Czech Academy of Sciences,[52] modified).

than in the vast majority of other EU13 countries. Fundamental and applied research in CR is supported by two major domestic public sources: the Czech Science Foundation (GAČR, supports fundamental research projects) and the Technology Agency of the Czech Republic (TAČR, supports collaborative applied projects between academia and the private sector). In addition, researchers and companies can apply for a scale of national ministry grants or enter international, mainly EU, grant schemes. Czech companies that invest in their own R&D can also benefit from tax deductions.[36] Both GAČR and TAČR can and do finance biotechnology-oriented projects. However, only GAČR mentions *Synthetic Biology* specifically as one of the disciplines that can be supported by its life science P302 Microbiology, Parasitology, Immunology, and Biotechnology panel. Nonetheless, granted SynBio-oriented projects are rare based on our investigation. TAČR and The Ministry of Industry also offer funds for commercial enterprises at all levels through programs such as Application (approx. €120 mil. allocated annually) and Trend (approx. €80 mil. allocated annually).

A national strategy is a formal recognition from the government of an innovation field and as such it provides direction to researchers, funding agencies, universities, reviewers, and large corporations. Specifically, a SynBio strategy needs promote investment, encourage platform development, clarify the unique demands on the workforce in biodesign, commit to supporting a productive business environment through appropriate but not excessive regulation, and lastly explain future plans to expand national and international partnerships.[53] Unfortunately, CR does not have any official policy toward SynBio and this term is not used in any governmental or strategic documents. Nevertheless, when we take a closer look at the national strategies for the future development of the country, we can find many references to biotechnology as one of the key investment areas. Both the Innovation Strategy of the Czech Republic 2019–2030 (Country for Future)[54] and the National Research and Innovation Strategy for Smart Specialisation of the Czech Republic 2021–2027 (National RIS3 Strategy)[55] talk about biotechnologies in a broader sense (e.g., industrial biotech, biomedical innovations, agricultural biotechnologies), recognize them as advanced in our country, and consider them a promising sector for further support. The 2017

Czech Academy of Sciences Strategy AV21, which aims to respond to current social challenges through cutting-edge collaborative science, does not involve the *Synthetic Biology* term either.[56] It only mentions the use of state-of-the-art genome editing techniques for greater efficiency in breeding and agricultural production or for future advanced medical therapies in its research programs The Foods for the Future and Towards Precision Medicine and Gene Therapy, respectively.

SynBio is closely related to the topic of GMO. In terms of GMO regulations, CR follows European legislation. It used to be one of the most open countries for GM crop cultivation in Europe. For instance, in 2010, CR was the only EU country where both Bt maize and GM potatoes Amflora were cultivated for production, the maize on almost 5000 ha.[57] However, due to the problematic sales of GM crops on the Czech and European markets, the interest in their sowing was decreasing year by year and today they are no longer grown in CR. In response to this negative trend, numerous Czech researchers and representatives of top research institutes in the country joined the initiative of European scientists who have long been campaigning for the European Union to allow the use of the new CRISPR crop breeding methods that are now subjected to European GMO regulations. Given its importance for the future food security of Europe, this topic has been selected as one of the priorities for the Czech Presidency of the Council of the European Union in the second half of 2022.[58]

3. Summary of current bottlenecks for the expansion and maturation of the Czech SynBio community and possible steps to remove them

In this section, we summarize the major verdicts of each of the four previous chapters arranged here in the fashion of the DBTL cycle for building a SynBio community from the bottom-up (Fig. 5). We identify key issues and propose steps to tackle them.

***ACADEMIA AND iGEM*:** The SynBio stakeholders from the Czech academic environment certainly **DESIGN** and shape the local SynBio landscape. The role of former expats with the experience from SynBio-oriented laboratories abroad, certain local established researchers, and talented active students has proven to be crucial for the birth of the Czech SynBio community. The potential for its further growth is considerable, there are probably dozens of laboratories in the country that adopt state-of-the-art bioengineering techniques in their research. The iGEM competition has served as an accelerator and unifying element for individuals interested in engineering biology. It is also one of the rare opportunities for the Czech Life-Science students to practice creativity, problem-solving, and thinking out of the box in a team fashion.

Major issues: The "core" SynBio community is very narrow and unorganized and lacks a common platform for meetings, discussions, dissemination and communication of its activities. The awareness of *Synthetic Biology* as a term defining a new era of biotechnology is rather shady in Czech academia. Some may perceive only the very core poses of Synthetic Biology (e.g., efforts to create a synthetic cell), some may see SynBio only as "a new label for old laundry". Czech life-science university curricula put very little emphasis on adopting engineering principles in biology and problem-solving. There is lower research support from the industrial partners compared to other EU states with more developed SynBio landscapes.[28,29,36]

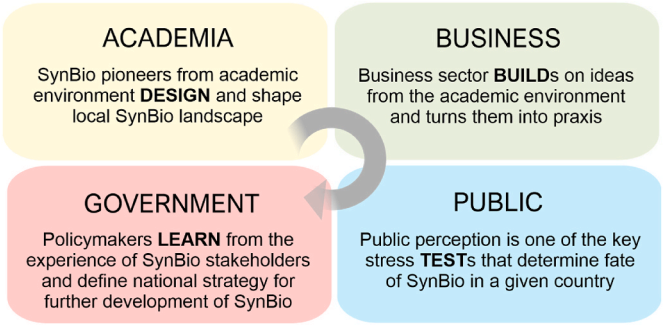

Fig. 5. Design, build, test, and learn when forming a local SynBio community.

Possible solutions: Major local SynBio stakeholders should unify in a standalone SynBio organization or make it a branch of an already existing relevant scientific society such as the Czech Biotechnology Society. They should collaborate with and learn from SynBio communities in neighbor countries. The establishment of a single SynBio organization that would unify small communities from several EU13 states is also an option. Technical universities and universities with a broader life science portfolio should promote SynBio study programs and professorships that would combine the fundamentals of biology and engineering. Major Czech public universities should financially and technically support the sustainability of at least one or two iGEM teams whose composition would break borders between diverse study fields. iGEM may become a part of their life science curricula. Similarly, welcome packages or awards for promising young scientists such as Primus or Masaryk Award in Science and Humanities granted by Charles University in Prague and Masaryk University in Brno, respectively, could be adopted to attract foreign researchers or Czech expats educated in SynBio. These and other steps (see the TEST section) towards the rootage of SynBio in the Czech academia and public domain will result in its popularization and will attract industrial partners to collaborate on SynBio projects with a potential to react on and mitigate local problems (e.g., high meat consumption, intensifying drought, aging population suffering from civilization diseases).

***BUSINESS*:** The business sector often **BUILD**s on ideas from the academic environment and turns them into praxis. A successful business ecosystem must inevitably include: (**i**) an effective mechanism for technology transfer, (**ii**) a growth-oriented investment network, (**iii**) an innovation-friendly market environment, and (**iv**) a strong advisory and mentoring network to provide guidance in practical matters (IP, legal, licensing, financial, logistical challenges). The Czech ecosystem includes traces of these elements but has a long way to go in catching up with the flourishing ecosystems established in some other countries (e.g., the UK, Switzerland, Netherlands, Denmark, France, Germany, or the USA). Organizations such as the IOCB or JIC have accelerated technology transfer. Regional investment funds have taken a stronger interest in the life sciences and biotech sectors. The emergence of companies implementing some of the SynBio methods has created a demand for the SynBio skillset. This work must be intensified to make modern biotechnologies a part of the Czech knowledge-based economy.

Major issues: Biotech companies in CR are predominantly small. The majority depend on standard molecular biology and genetic engineering procedures. While CR taunts a strong history in the life sciences, the region's entrepreneurial history is short-lived. Out-licensing to large corporations continues to be the focus of academic institutions and a national prioritization of spin-off companies is missing. Only a few non-dilutive grant opportunities exist for startups and these programs are plagued by administrative costs that cannot be absorbed by small companies. Early-stage companies in the UK, USA, France, Switzerland etc. often leapfrog large capital expenditures and operational costs by partnering with big corporations that have their headquarters or R&D facilities in biotech hubs. Corporate facilities of large biotech companies such as Lonza and Baxter, located in the CR, often lack decision-making autonomy and hence fail to support local partnerships.

Possible solutions: Selected institutions are painting the way forward. IOCB has massively accelerated its tech transfer efforts through its successful subsidiary i&i Prague. While the IOCB tech transfer office remains focused on out-licensing opportunities, i&i Prague focuses solely on spin-out and startup ventures. The subsidiary structure gives i&i Prague the executive flexibility required to provide financing and support in a timely manner and with minimal administrative overhead. Similar structures are now being adopted by other institutions (e.g., Charles University Innovations Prague). Regarding financial support,

prominent regional investment groups such as BPD Partners have emerged in the biotech and life sciences sector as sources of dilutive funding and debt financing for sufficiently advanced projects (e.g., Sampling Human, DIANA). Access to larger growth-oriented funds, however, is still missing forcing companies to re-position themselves abroad. A well-formulated national policy that will provide resources, remove commercialization barriers, and attract large corporations to the region is needed. In this regard, successful roadmaps established by other nations can serve as a template for deploying a multi-pronged strategy for building a modern bioeconomy sector.

***PUBLIC PERCEPTION*:** Public perception is one of the key stress **TEST**s that can determine or at least considerably influence the fate of a given field in a country. SynBio in CR can build on the relatively neutral attitude of Czech citizens towards the closely related topic of GMOs and former experience with GM crops growing. It can also take advantage of solid channels in the Czech public space for the communication of its achievements.

Major issues: Public awareness of SynBio is difficult to assess because a public opinion survey on the subject has never been commissioned. Available data from surveys on the related topic of GMOs indicate low public interest in bioengineering technology and poor awareness of its potential benefits and related realistic threads. Biological engineering does not have a strong tradition in the country. The concept of *Synthetic Biology* is essentially absent in the Czech public space.

Possible solutions: A responsible well-coordinated information campaign on SynBio, its benefits, and potential threats is urgently needed in the Czech public space. The topic must be clearly explained by PR experts from academia and business, ideally united on the common platform of the newly established SynBio society. Academicians, researchers, and interested students should dedicate part of their time to SynBio popularization and communication. Public perception of SynBio can be built on success stories from praxis. Recent SynBio achievements in the world can be used as examples of making public good through bioengineering.[16,20,22] Accordingly, the business sector should communicate the use of GMOs and bioengineering in its R&D and production pipelines more openly and explain the benefits of these technologies. A better-informed public can be later interviewed in the survey organized by the SynBio community in collaboration with, e.g., the Czech Academy of Sciences. The obtained data would be used for further co-ordinating steps in the information campaign and would serve as one of the entry materials for discussions with policymakers.

***GOVERNMENTAL SUPPORT*:** Czech authorities and policymakers can appreciate the opportunity to **LEARN** from the information and experience gathered by the local and foreign SynBio and biotech stakeholders. They can also take a lesson from the previous mistakes such as an unfortunate unclear and inconsistent approach to explaining and tackling the Covid-19 pandemic and the vaccination campaign. The country has reasonably developed funding schemes for life sciences and applied research, and biotechnology is considered one of the key strategic fields for further development.

Major issues: The weakest points are the absence of national funding program(s) focused specifically on the support of SynBio and bioengineering projects in academia and industry and the lack of a clear national position on Synthetic Biology. National strategic documents usually use vague formulations when it comes to defining the country's priorities in biotech research. Existing grant schemes are often backpedaled by heavy administration and bound by many regulations that limit the freedom to use grant funds according to the actual needs of a researcher or a company.

Possible solutions: As can be seen in examples of some large countries (e.g., UK or USA) as well as medium-size European countries such as the Netherlands (a country comparable with CR by population and land area) their national SynBio strategies or targeted funding from national entities are key factors that boost innovative research and the emergence and success of high-tech spin-offs and startups.[29,53] It is, therefore, fundamental to start a debate on the SynBio topic on the ground of the Czech Parliament and the Czech Government. Such a debate could be promoted by the Czech SynBio stakeholders through The Council for Research, Development and Innovation (RDI) - an expert and advisory body of the Czech Government under the leadership of the Minister for Science, Research and Innovation. The Council can establish a panel of local and foreign experts from academia and industry and formulate a clear national position on Synthetic Biology, which will be approved by the government. If SynBio is considered a perspective field for further country development, its particular areas should be included in the national strategic documents and the government should name a single body that will clearly communicate its position to the public. The positive attitude should be then translated into concrete actions such as broader financial support of the field through, e.g., whole SynBio-oriented panels in GAČR and TAČR or targeted ministry grants for collaborative projects between academia and industry. Prioritized topics such as SynBio in Human Health, Sustainable Agriculture, or Environmental and Industrial Biotechnology could be also united in a new research center. All these actions will further foster the development of SynBio in the Czech academia, business, and public space and the DBTL cycle can repeat until the full maturation of the field is reached in the country (Fig. 5).

4. Conclusions

We provided an overview of the current state of the Synthetic Biology field in the Czech Republic. The newly born SynBio community in CR has some fair cards in hand but lacks leadership, dedicated institutional and governmental support, and the attention of the public and many of its potential members. The work on this paper gave us the opportunity to map the "core" and "shadow" Czech SynBio community, which is the first necessary step for its integration. However, given the low awareness of Synthetic Biology in the public space, its intensive propagation by individual stakeholders in academia and business is needed for achieving a better position of this scientific discipline in our country. A newly planned SynBio study program, inter-university iGEM team, popularization activities, as well as ongoing scientific and business enterprises demonstrating the ability of SynBio to solve practical problems, will contribute to this process. The near-future development of the Czech SynBio community will thus most probably continue to unfold from the bottom-up in line with the proverb: "You get what you give".

CRediT authorship contribution statement

Stanislav Juračka: Conceptualization, Investigation, Visualization, Writing - original draft. **Barbora Hrnčířová:** Conceptualization, Investigation, Visualization, Writing - original draft. **Barbora Burýšková:** Conceptualization, Investigation, Writing - original draft, review & editing. **Daniel Georgiev:** Conceptualization, Visualization, Writing - review & editing. **Pavel Dvořák:** Conceptualization, Funding acquisition, Investigation, Resources, Supervision, Visualization, Writing - original draft, review & editing.

Declaration of competing interest

Dr. Daniel Georgiev is a founder of Sampling Human.

Acknowledgements

This work was funded by Czech Science Foundation grant (22-10845S) and the Grant Agency of Masaryk University GAMU MASH Junior award (project NEWGEN) granted to PD. BB is a Brno Ph.D. Talent Scholarschip Holder – Funded by the Brno City Municipality.

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