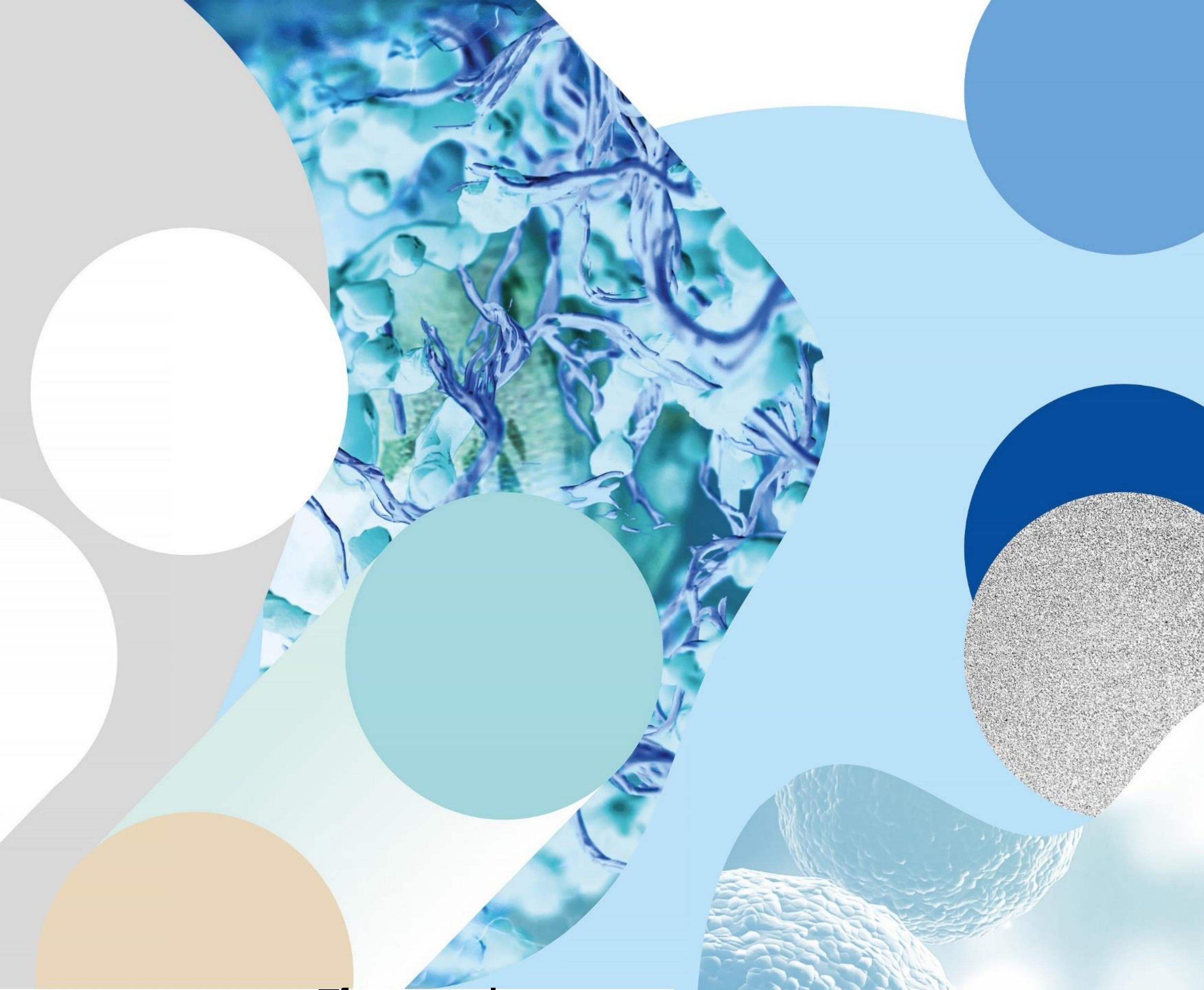
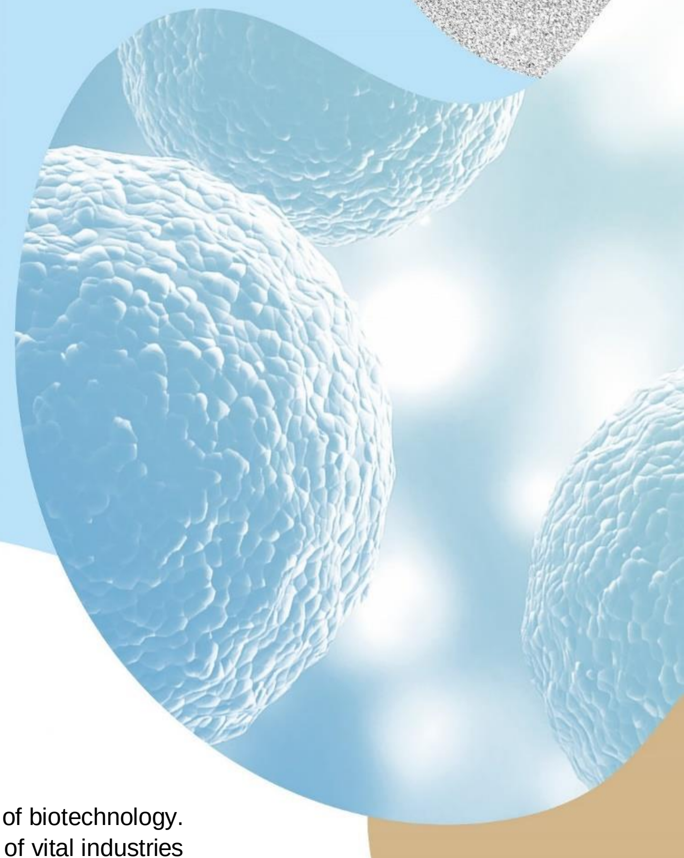


The series "Sources of new industries"

ISSUE 2



SYNTHETIC BIOLOGY

Synthetic biology is a new page in the history of biotechnology. Science that will secure the future for a range of vital industries and will solve the global issues of humanity.

ST. PETERSBURG

2022

SOURCES OF NEW INDUSTRIES. ISSUE 2. SYNTHETIC BIOLOGY.

Expert report

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This report was prepared jointly by the Center for Strategic Research "North-West" and Innovations and Youth Initiatives Support Fund of St. Petersburg with the support of the Government of St. Petersburg.

The basis was the Foresight project "Frontiers in New Sciences". The aim of the project was to identify long-term trends and prospects for the development of new industrial and technological markets; to identify on this basis the most promising areas of research and development in the so-called "frontier" areas of R&D — advanced chemistry, synthetic biology, artificial intelligence and environmentally friendly industrial technologies.

The methodological basis of the report is based on the analysis of the results of a foresight session with the participation of leading and young scientists, the processing of scientific data, a series of interviews with leading researchers from SPbU, ITMO University, DSTU, KFU, Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry, National Medical Research Radiological Centre, the evaluation of strategies of large industrial concerns, the analysis of venture capital markets.

The report consists of seven sections that consider the application of an engineering approach in biology, which causes the emergence of synthetic biology, its role, breakthrough importance, development prospects and frontier areas that open up completely new technological markets of the future, and the importance of this scientific and technological field for Russia, particularly given the current geopolitical situation.

The results of the project formed the basis of the experimental BlueSkyResearch competition "Artificial Intelligence in Science", held in 2022 jointly by the Foundation "Center for Strategic Research "Northwest" and Innovations and Youth Initiatives Support Fund of St. Petersburg.

The report is addressed to the government officials and specialists in the field of the development of science and technology, representatives of the scientific community, participants in the biotechnology sector, residents of innovation centers, representatives of private entrepreneurship and start-ups in the field of biotechnology, as well as for a wide range of people interested in the development of biotechnology and bioeconomy.

The series "Sources of new industries"

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Contents

Glossary

BioCAD	system for automated design of biological objects, construction of models for biotechnological, pharmaceutical and medical purposes.
CRISPR	genome editing technology for higher organisms that uses the immune system of bacteria to alter genetic sequences.
FACS	technology for measuring the chemical and physical properties of cells by using laser light.
In Silico	computer modelling (simulation) of a biological experiment.
In Vitro	technique of performing biological experiments when they are carried out "in vitro" - under artificial conditions, outside the body or natural environment.
In Vivo	technique for conducting biological experiments on (or within) living tissue in a living organism.
Machine Learning In biology	genomic data analysis, medical image marking, drug generation, medical diagnostics.
Research and Development (R&D)	research and development, a body of work aimed at obtaining new knowledge and practical application in the creation of a new product or technology.
Bacteriophages (or phages)	viruses and micro-organisms that can target only pathogenic bacteria.
Bioengineering	branch of science and technology that develops the application of engineering principles in biology and medicine.
Bioinformatics	interdisciplinary scientific field combining general biology, molecular biology, cybernetics, genetics, chemistry, computer science, mathematics and statistics.
Biocatalyst	substance that causes the acceleration (positive catalysis) or inhibition (negative catalysis) of biochemical processes.

Bioreactor	equipment for stirring the culture medium in the microbiological synthesis process.
Bioremediation	a range of methods for treating water, soil and the atmosphere using the metabolic potential of biological objects
Biosensors	analytical devices that use biological materials to "recognise" certain molecules and provide information on their presence and quantity as an electrical signal.
Biofoundry	organisation that provides an advanced infrastructure allowing the rapid design, creation and testing of genetically reprogrammed organisms for biotechnological research.
Genom	complete DNA set of an organism, including all of its genes, as well as its hierarchical three-dimensional structural configuration.
Genomics	interdisciplinary field of biology that focuses on the structure, function, evolution, mapping and editing of genomes.
Deoxyribonucleic acid (DNA)	macromolecule that provides storage, transfer from generation to generation and implementation of the genetic programme concerning the development and functioning of living organisms.
Cell biology	science that studies living cells, their organelles, structure and functioning, and the processes of cellular reproduction, ageing and death.
Cell factory	container for the cultivation and culturing of cells used in the production of medicines and other biologically active components, as well as viruses, cell populations and vaccines.
Unicorn companies	private companies with a market capitalisation of $1 billion or more.
Small molecules	low molecular weight substances that have some kind of biological activity (ability to regulate or influence biological processes).
Microbiology	science that deals with microscopic creatures called micro-organisms, their biological characteristics and interactions with other organisms.

Microbial fuel cell	biotechnological device that converts the chemical bonding energy of organic substances into electricity via micro-organisms.
Molecular biology	science that studies the functioning of living organisms through the chemical structure of their constituent molecules and atoms.
M-RNA	RNA containing information on the primary structure (amino acid sequence) of proteins.
Nutrients	chemical elements necessary for living organisms in order to function normally.
Organoids (or organelles)	permanent components of a cell, vital to its existence.
Plasmids	small DNA molecules physically separated from the chromosome and capable of autonomous replication.
Polymerase chain reaction	experimental method of molecular biology, a way of significantly increasing small concentrations of certain nucleic acid (DNA) fragments in a biological material (sample).
Proteomics	science that studies the protein composition of biological objects, as well as the modifications and structural and functional properties of protein molecules.
PCR test	polymerase chain reaction method for the diagnosis of infectious diseases.
Reporter molecules (genes)	genes that are attached to the regulatory sequences of other genes to study gene expression in cell cultures.
Ribonucleic acid (RNA)	one of the three main macromolecules (the other two are DNA and proteins) found in the cells of all living organisms consisting of a long chain of nucleotides.
Ribosome	the most important non-membrane organelle of all living cells, serving for protein biosynthesis from amino acids based on a given matrix and genetic information provided by matrix RNA.

RRNA	several RNA molecules that form the basis of the ribosome. The main purpose of rRNA is to perform 'translation' - reading information from mRNA by adapting tRNA molecules and to catalyse the formation of peptide bonds between amino acids attached to tRNA.
Site-directed mutagenesis	molecular biology technique that is used to create specific and deliberate changes in the DNA sequence, gene and gene products.
Sequencing	general name given to methods that allow the sequencing of nucleotides in a DNA molecule.
Synthetic biology	scientific discipline in biology concerned with the design and creation of biological systems with predetermined properties and functions, including those that have no analogues in nature.
Translational studies	concept of using basic research directly in practice (from the laboratory bench to the patient's bedside), using a particular combination of research phases
Transposition mutagenesis	biological process that allows genes to be transferred into the chromosome of a host organism, disrupting or modifying the function of an existing gene in the chromosome and causing a mutation.
T-RNA	RNA that enables the interaction of an amino acid, ribosome and matrix RNA (mRNA) during gene translation.
Fag library	pool (list) of bacteriophages that match the required biological and chemical properties.
Fazmids	molecular vectors, artificial hybrids of phages and plasmids.
Strain	pure culture of bacteria, fungi, rickettsiae or other micro-organisms isolated from a specific source and identified by modern classification tests.

List of figures, tables and cases

Introduction

In January 2022, American bioengineers from the Craig Venter Institute and the University of Illinois at Urbana-Champaign, together with German colleagues, developed a three-dimensional, complete kinetic model of a living minimal cell, which fully simulates the processes taking place in a real cell. In the early 2000s, researchers from the Craig Venter Institute had already attempted a similar feat: deleting as many genes as possible from Mycoplasma mycoides to produce a simplified synthetic life form capable of feeding and reproduction. Despite the fact that modelling protozoan organisms (mycoplasmas and Escherichia coli) still require a major investment in science and technology and the process of putting together the complete gene and nutrient community is still a work in progress, even for relatively simple bacteria[1], this event demonstrates that humanity continues to make rapid progress towards a major biotechnological revolution.

To meet the challenges of designing and assembling biological systems, synthetic biology has been a distinct scientific and technological field since 2000[2]. Synthetic biology working at the fundamental level of living systems has a direct application effect on various sectors of the economy, radically changing their end product manufacturing processes (value-added generation). The influence of synthetic biology extends to the fields of health care (molecules for targeted drug delivery), food industry (synthetic food), pharmacology (vaccines and diagnostics), agriculture (biopesticides), energy (biofuels)[3]. These are just a few examples.

Worldwide, synthetic biology has developed into quite a large sector, not just as a field of scientific knowledge (current publication volume is estimated at over 26,000 publications, and the average annual publication growth rate since 2000 is 30%), but also as an independent market with a large number of start-ups, worth at least $7 billion. Entire synthetic biology research centres and consortia have been formed in the US, EU and China to tackle synthetic cell and proteome synthesis challenges.

In Russia, the synthetic biology sector has also started to develop. It is currently a field of science without major industrial investment. But it is already of great importance to the country's economy, particularly in light of the events of 2022 and the problems raised by the COVID-19 pandemic in recent years. Synthetic biology technologies are now crucial to the future development of pharmaceuticals, food security, broken production chains in agriculture and to many other fields.

Given the aftermath of the events of February 2022, it is important to understand that development of synthetic biology as an industry will be hindered by trade and economic restrictions imposed on Russia and the breakdown of international research links and collaborations. Nevertheless, the key points of the report remain relevant and some of them, such as the transformation of production chains using synthetic biology solutions, are taking on a new meaning.

This report examines the history of synthetic biology, its technological tools, challenges and frontier research directions, as well as market trends (in selected sectors, investment volumes, corporate market structure) and the prospects for regulatory systems.

1 Scientists have built a complete model of a living cell for the first time // Gazeta.ru. URL: gazeta.ru/science/news/2022/01/24/17182579.Shtml.

2 Lionel Clarke, Richard Kitney; Developing synthetic biology for industrial biotechnology applications. Biochem Soc Trans 28 February 2020; 48 (1). doi.org/10.1042/BST20190349.

3 Bruynseels K. (2020). Responsible innovation in synthetic biology in response to COVID-19: the role of data positionality. Ethics and information technology, 23(Suppl 1).doi.org/10.1007/s10676-020-09565-9.

1 HOW SYNTHETIC BIOLOGY WORKS AND WHAT IS ITS BREAKTHROUGH VALUE

Synthetic biology as a scientific field emerged at the beginning of the 21st century on the basis of the accumulated scientific and technological background and discoveries in the fields of systems biology, biotechnology, molecular biology, bioengineering and genetic engineering. The formation of synthetic biology as a distinctive field date back to 2000-2010, when the first discoveries were made on the standardisation of DNA parts, combinatorial synthesis of the genetic network, synthetic circuits to aid bacterial invasion of tumour cells etc., when the first research centres and teams (Craig Venter Institute and Centre for Synthetic Biology and Innovation at Imperial College London) were formed and the first international conference on synthetic biology was held. Since 2010 there has been intensive development in this area, as well as an increase the number of developments with applications (creation of the first synthetic cell, synthesis of artemisinin, the first computer-generated genome, etc.). One of the main factors in the development of synthetic biology was the expansion of data analysis and modelling capabilities, active digitalisation of research and development of interdisciplinary areas, such as bioinformatics. Today, the fields of application of synthetic biology (medicine, pharmaceuticals, food industry, agriculture, cosmetics, textile industry, energy, etc.) are actively expanding, which leads to the strengthening of its role in economic growth. Synthetic biology today is an interdisciplinary scientific field that emerges from the intersection of different fields of biology, mathematics, information technology, chemistry and engineering (see Figure 1). The development of synthetic biology is linked to one of humanity's most ambitious goals: to learn how to reproduce life: synthesizing the cell and its components and creating biological systems with given properties.

Engineering approaches and principles are fundamental to the development of synthetic biology, because full-cycle engineering (including design, assembly, testing, data analysis) of large numbers in biological sequences is required to produce products with properties that address the new challenges in different industries [4].

The fields of application of synthetic biology are not limited to life science, but include a range of sectors: food industry (synthesised foods, various bioreactor-grown food components), bioenergy (biofuels), pharmaceuticals and medicine (new drug delivery methods, new antimicrobials, new generation gene-based vaccines), industry (new types of materials)[5]. Synthetic biology contributes to transforming production chains, significantly reducing the cost and production time of products compared to their existing counterparts. In general, synthetic biology is a purely applied science: any synthesised biological object is not created by itself, but for a specific industry task, which is one of the main intentions of synthetic biology.

4 Romanowski S., Eustáquio A.S. Synthetic biology for natural product drug production and engineering. Curr Opin Chem Biol. 2020. doi:10.1016/j.cbpa.2020.09.006.

5 Global Synthetic Biology Industry Outlook — Futuretech TechVisionOpportunity Engine, TechVision Group of Frost & Sullivan, TechVision Opportunity Engines /D835/30.

FORMATIVE DISCIPLINES

OBJECTS OF SYNTHETIC BIOLOGY

BIOLOGY (AND RELATED*) — biological systems, organisms and methods of modelling them, mechanisms of storage and transmission of genetic information, genome evolutionary pathways

MATHEMATICS — methods for calculation, analysis, prediction, description of quantitative relations and spatial forms of phenomena

IT — biological systems, organisms and methods of modelling them, mechanisms of storage and transmission of genetic information, genome evolutionary pathways

ENGINEERING — invention, development, creation, implementation, improvement of techniques, materials or processes

ORGANIC CHEMISTRY — structure, properties and synthesis methods of hydrocarbons and their derivatives

BIOLOGICAL CONSTRUCTS, "BIOMODULES" (NUCLEOTIDES, MOLECULES)

LIVING SYSTEMS (CELL, BACTERIA, TISSUES, ORGANS, PLANTS)

↓

PRODUCTS (VACCINES, FOOD INGREDIENTS, BIOFUELS, ETC.)

↓

FIELDS OF APPLICATION

MEDICINE
- Biosensors
- Biotherapeutics (CAR-T)
- Biocatalysts
- Creation of optomers
- Protein modification for medical purposes

BIOPHARMACEUTICALS
- Recombinant vaccines
- Synthetic immuno-modulators
- New drug delivery systems

FOOD INDUSTRY
- Product stewardship
- Food substitutes
- Personalised nutrition

AGROSECTOR
- Agricultural biosensors
- Biological agricultural processing

BIOENERGY
- Microbial fuel cells
- New biofuels and biodegradable polymers

ECOLOGY
- Bioremediation
- Ecological biosensors
- Genetic pest control

BIOTECH PRODUCTION
- Functional biomaterials
- Raw material chemicals
- Biologically manufactured materials

Figure 1.

A principal diagram of the structure of synthetic biology as a field of scientific knowledge

Source: Frost & Sullivan

* Evolutionarily and specifically bioengineering is the closest field to genetic engineering

Shityakov S.V., Leading Research in Chemoinformatics, ITMO University; Research Professor of Theoretical (in silico) Synthetic Biology, University of Würzburg (Germany)	Source: Interview in preparation of the report with S.V. Shityako from 15.10.2021

“Today, synthetic biology is a somewhat amorphous discipline and has not yet been formed to end. This is the process of the next five years. Synthetic biology in a broad sense is the editing, design and creation of bioconstructs. In a narrower sense, it is working with biomolecules, with proteins. In other words, synthetic biology is aimed at creating biological systems, their development, design (for example, the design of proteins that do not exist in nature). Manipulation and work with proteins is impossible without changing genes. Manipulation aimed at genes in order to obtain new proteins is one of the basic directions of synthetic biology. By its structure, synthetic biology is a direction in which breakthrough technologies and methods are used, for example, bioinformatics and the use of computers to solve biological problems. Synthetic biology includes many sub-sectors, so it is difficult to distinguish between them.

In Europe, the development of synthetic biology is slowing down due to the high level of development of ethics committees, issues of data security, including patient data. European countries are characterized by strict regulation of clinical trials and experimental studies, which greatly hinders the development of synthetic biology.

There is no such system in China. Today China and Southeast Asia are the main hubs for the development of synthetic biology in the world. In China and Southeast Asia, there is a very rapid development of synthetic biology, including due to the absence of such barriers. Research is carried out quickly without the need for detailed research. On the one hand, it's bad, but greatly accelerates the development of synthetic biology.

Ensuring cyberbiosecurity is one of the important issues in the development of synthetic biology. Securing biological data can be a barrier, but it shouldn't. Today, new algorithms based on blockchain technologies are emerging to ensure data security. These algorithms can be used to shape the security of synthetic biology data.

One of the problems in the development of synthetic biology in Russia is the concentration of science in several centers, while in the rest of the regions there are not only special scientific centers, but even an understanding of breakthrough technologies. Another side of the problem of the development of synthetic biology is related to the logistics of biological materials and chemical reagents for research”.

Korzhikov-Vlakh V. A., Deputy Head of the Interdepartmental Laboratory of Biomedical Chemistry, St. Petersburg State University; Secretary of the Laboratory of Biohybrid Technologies, St. Petersburg State University	Source: Interview as part of the report preparation with Korzhikov-Vlakh V.A. dated 25.10.2021

"The field of synthetic biology is based on chemical entities with a biomedical applications. Synthetic biology involves the application of chemical principles at the level of biology, at the level of constructing and working with living organisms. This makes it possible to create synthetic organisms - controlled biological systems that are used to solve specific problems. This is reflected in the fields of pharmacology and biomaterial science. The tools of synthetic biology, on the other hand, include molecular biology, CRISPR-Cas, working with living cells - singling out cells and creating new cells from them or the transformation of isolated cells.

The breakthrough significance of synthetic biology is that human beings are becoming the most important factor in the creation of new organisms. Before the advent of synthetic biology, new biological structures came about through evolution, through the formation of mutations. Now, humans can create new organisms through new skills associated with the creation of new species. It's a fundamental scientific breakthrough».

To illustrate, Table 1 provides some examples of the challenges faced by individual industries and the technological solutions that synthetic biology approaches offer as a response to these challenges.

№	Industry	Challenges	Technological solutions
1	Medicine [6]	Fighting cancer, infections, neurodegenerative diseases, allergies	Proteins for programming cellular behaviour Edited proteins for cancer therapy
		Disease diagnostics (PCR testing, antibody detection)	Diagnostic tools based on biosensors
		New ways of treating and preventing disease	Programmable organoids Cellular therapies and prophylaxis
2	Biopharmaceuticals[7]	Prompt response to new diseases	Cell-free protein synthesis systems Living virus vaccines Phenotypic screening Synthetic cell models
		New ways to deliver drugs precisely	Artificial biopharmaceuticals
		Combating antibiotic resistance	Antimicrobial medicines
3	Food industry	Population growth of about 2 billion people by 2050. Increased food consumption (especially meat). Global food production needs to increase by 70% by 2050 to meet demand[8]	Food substitutes Foods and crops with specific properties and nutritional values Cultivated foods (e.g. meat)
		Well-being (individual diet)	Food biosensors
4	Agrisector	Pesticides and agrochemicals cause 200,000 deaths from poisoning each year[9]	Agricultural biofertilisers, biopesticides, biosensors
		Farming practices cannot keep up with the rate of growth in food consumption and are not environmentally sustainable	Nitrogen retaining microbes Photoautotrophic organisms Artificial, modified crops

№	Industry	Challenges	Technological solutions
5	Energy [10]	Climate change and the post-carbon agenda, implementation of ESG standards	Materials with improved selectivity Microorganisms at the biotic / abiotic interface
		Limited fossil resources, energy sources (coal, oil, gas)[11]	Microbial fuel cells Biological fuels Enzymes for biocatalysis
6	Ecology [12]	Pollution of land, water, air	Artificial enzymes and organisms for bioremediation
		Reduction of biodiversity, disruption of ecosystems	Genetic pest control products Bioalgae
7	Biomaterials	Transition to biological technologies production and implementation of ESG standards	Biologically manufactured materials Subtle chemical compounds Raw chemicals

Table 1. Applications of synthetic biology and examples of synthetic biology solutions, products, technologies

Source: Science Direct, Frost & Sullivan, VTARC, Innovations in Pest Management, Renewable Gas and Fuel Production and Plastic Recycling, CSIRO

6 Advancements in Gene Therapy, Synthetic Biology, Diagnostic Assays,Imaging Tracers, and Biopharma--Life Sciences, Health & WellnessTechVision Opportunity Engine, TechVision Group of Frost & Sullivan, TechVision OpportunityEngines /D759 /04.

7 Advancements in Gene Therapy, Synthetic Biology, Diagnostic Assays,Imaging Tracers, and Biopharma--Life Sciences, Health & WellnessTechVision Opportunity Engine, TechVision Group of Frost & Sullivan, TechVision OpportunityEngines /D759 /04. Brooks S. M., Alper H. S. Applications, challenges, and needs for employing synthetic biology beyond the lab. Nat Commun 12, 1390 (2021). doi.org/10.1038/s41467-021-21740-0.

8 Marc-Sven Roell, Matias D. Zurbriggen, The impact of synthetic biology for future agriculture and nutrition, Current Opinion in Biotechnology, Volume 61, 2020, ISSN 0958-1669, doi.org/10.1016/j.copbio.2019.10.004.

9 FoodNet: Trends and barriers to development, COS Consulting, October 2021.

10 Future Directions of Synthetic Biology for Energy & Power. Virginia Tech Applied Research Corporation. 2018. URL: basicresearch.defense.gov/Portals/61/Documents/future-directions/Synthetic%20Biology%20for%20Energy%20and%20Power%20-%20Final%20Report.pdf?ver=2018-10-29-133833-863.

11 Predictive Models to Accelerate Gas Fermentation for Biomanufacturing. URL: agilebiofoundry.org/industrial-microbes-gas-fermentation (accessed: 16.01.2022).

12 A National Synthetic Biology Roadmap, CSIRO, August 2021. URL: csiro.au/-/media/Services/Futures/Synthetic-Biology-Roadmap.pdf (accessed: 16.01.2022).

Case 1. Cultivated cellular meat production

One prime example of the application of synthetic biology in the food industry is the production of cultured cell meat. The cycle of cultured cell meat production consists of four phases - collection and preparation of cellular material (usually stem cells, muscle cells, hormones and nutrients are extracted from animal tissue), preparation of culture medium for tissue culture, tissue production by placing cells in culture medium in a bioreactor and subsequent mass production of meat. From 1 gram of muscle tissue, it can be produced up to 10,000 kilo-grams of cell mass. The whole process takes up to four weeks in total. Whereas the traditional farming method takes up to two years to produce a ready-to-cook meat product. Another argument in favor of farmed meat is the rapid reduction in the cost of production (4 times in 6 years - from $ 400 / kg beef in 2013 to $ 110 / kg in 2019 and potentially up to 10 $ / kg in 2024). The main challenge for this type of production in the future will be the use of fully synthesised cells, rather than editing animal cells as is currently the case.

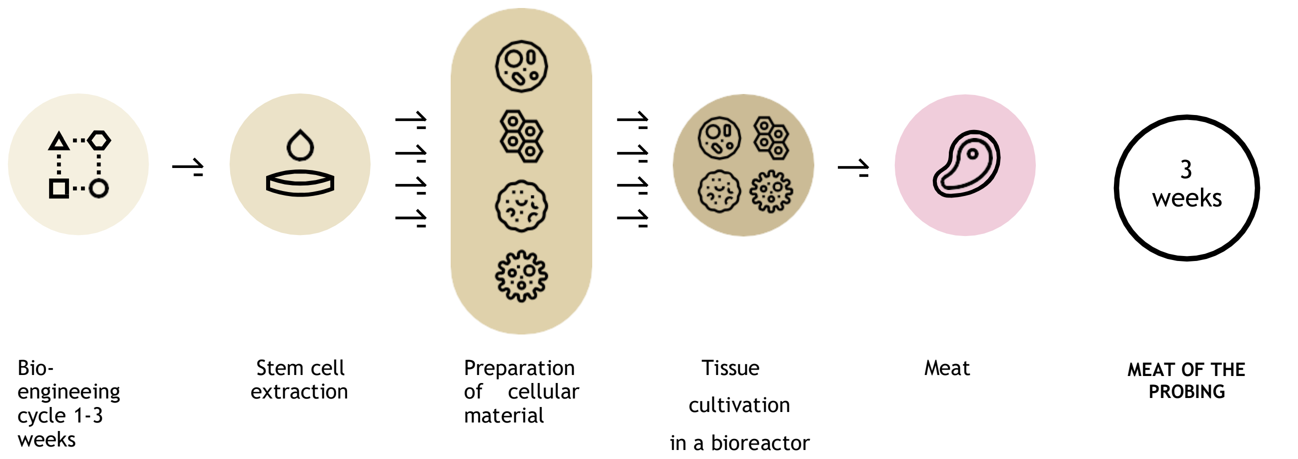
Source: World Economic Forum, Aleph Farms, Kazuko Sato, Cultured Meat Production Technology: Challenges and Future Development, Mitsui & Co Global Strategic Studies Institute Monthly Report November 2020. URL: mitsui.com/mgssi/en/report/detail/__icsFiles/afieldfile/2021/01/18/2011t_sato_e. pdf (accessed:16.01.2022).
Chriki Sghaier, Hocquette Jean-François, The Myth of Cultured Meat: A Review, Frontiers in Nutrition, 7, 2020, DOI:10.3389/fnut.2020.00007, URL: frontiersin.org/article/10.3389/fnut.2020.00007
Scientists from DSTU and VolgGMU will grow rabbit meat cutlets in laboratory conditions. URL: donstu.ru/news/nauka/uchenye-dgtu-i-volggmuvyrastyat- v-laboratornykhusloviyakh-kotletu-iz-kletokmyasa-krolika (accessed:16.01.2022).

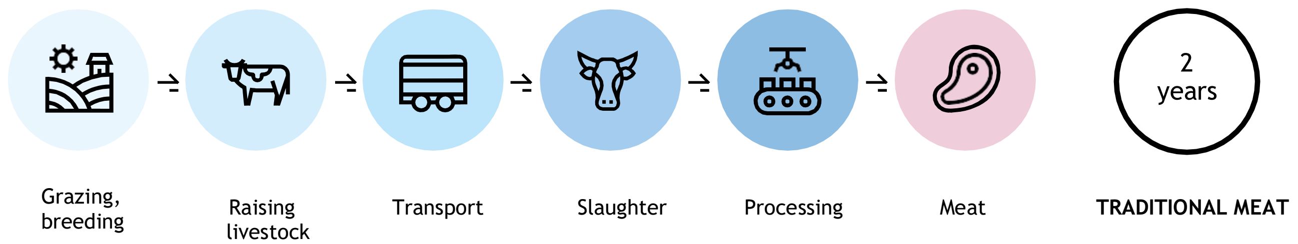
3-4 weeks

	Preparation of cellular material	Preparation of the nutrient medium	Production of tissues for farmed meat	Mass production of cultivated meat
OBJECTIVES	Collection and preparation of cellular material (stem cells, muscle cells, hormones and nutrients)	Preparation of special nutrient media (amino acids, vitamins, glucose, inorganic salt, hormones and nutrients)	Placing cells in a nutrient medium in a bioreactor for growing artificial tissue	Scaling up farmed meat production
BARRIERS	Availability of efficient methods to obtain live cells Small volume of harvested cells from animals Difficult and expensive methods for purification of harvested cells	Availability of methods for mass production of cell nutrient media High cost of hormones Cost of animal hormones and nutrients Inability to scale production of animal hormones and nutrients	Cell death due to heterogeneous nutrient media, high or low temperature, lack of oxygen in the bioreactors Inconsistency of the structure and texture of the cultured meat with the natural	Low productivity of the two-dimensional cell culture method The problem of scalability of cultured meat production
SOLUTIONS (FRONTIERS)	Extraction of living cells using enzymes Cell engineering and synthesis of artificial cells Methods for synthesis of proteins and RNA molecules by gene expression Site-directed mutagenesis	Artificial biological systems (organs) that produce hormones and nutrients Nutrients (hormones and nutrients) of non-animal origin Nutrient production without hormones or nutrients Cell Factories	Methods for harvesting cultured cells, tissues from bioreactors Control systems for internal environment (temperature, oxygen, acid-alkaline balance) in bioreactors Texture and structure simulation of muscle tissue	Three-dimensional cell culture system in a bioreactor Computer simulation of cell cultivation technology Simulation of industrial bioprocess parameters: number of cells, duration of Processes, volumes of a ready-for-extraction batch
EXAMPLES OF	«Merck» - applying cell culture technology from pharma to the food industry **Today - two strategies for preparing the material:** **- stem cells** **- muscle cells** **The future - fully synthesized cells**	«Mosa Meat», a start-up for industrial synthesis of nutrient media «Future Fields» start-ups, "Multus Media» - alternatives to hormones and nutrients	«Matrix Meats» start-ups, "Atlast Food" - muscle tissue texture based on fungal fibres	«Ospin Modular Bioprocessing» - scaling bioprocesses «Impossible Food», «Beyond Meat» - artificial and cultured meat production

Comparison of the effects of conventional and cellular meat production

Type of meat	Cycle features	Timeline	Cost	ESG-options
In vitro meat	Stem cell extraction, cell material preparation, tissue cultivation, scaling	3-4 weeks	110$/kg (2019 г.) 400$/kg (2013 г.)	45 % less energy consumption, 99 % less land use 96% less gas emission
Traditional meat	Grazing, raising livestock, transporting, slaughtering, processing, packaging finished product	2 years	5$/kg	Produce up to 15% of all human-caused gas emissions. Occupies 80% of agricultural land





2 THE ENGINEERING PRINCIPLE AT THE BASIS OF SYNTHETIC BIOLOGY

The use of systems-biological and genetic engineering approaches to the design of living systems makes it possible to distinguish synthetic biology from other areas of natural science. The fundamental principle of the engineering approach to the creation of bioconstructs is modularity, which involves the breakdown of complex systems into manageable biological units, their reorganization or revision, subsequent assembly and connection to endogenous functions (see Figure 2). At the biochemical and cellular levels, such "biomoduli" include nucleotides, molecules, cells, cellular and tissue biological systems. Recombinant DNA technologies and bioinformatics tools are used as the main tools for creating new living objects[13].

13 Synthetic Minimal Cells. URL: bio.academany.org/2018/synthetic_minimal_cells.html. A New Era of Protein Interaction Engineering. URL: labmanager.com/insights/a-new-era-of-protein-interaction-engineering-26741 (accessed:16.01.2022). Center for Strategic Research "North-West" based on interviews with S. V. Shityakov (10/15/2021), I. D. Klabukov (11/02/2021), O. A. Gusev (10/25/2021).

Klabukov I. D., Head of the Department of Regenerative Technologies and Biofabrication, National Medical Research Center for Radiology, Ministry of Health of Russian Federation

Source: Interview in preparation of report with I. D. Klabukoŭ dated 02.11.2021

"The hypothesis of the synthetic biology model in the form in which it was conceived in the 2010s turned out to be not entirely correct. Today, synthetic biology is developing as part of engineering intervention in individual elements of the cell. Instead of thinking about how to design a cell, scientists and researchers are focusing on questions such as how to learn how to synthesize plasmids encoding an already bound receptor in order to obtain a highly sensitive sensor from the cell. At the same time, the tasks of synthetic biology no longer sound so global, they have become applied, the tools have changed.

The original hypothesis of synthetic biology is that by mastering synthesis and understanding how to compare mobile elements with each other, we can get away from traditional genetic engineering, no longer works. The initial idea of synthetic biology was as follows: when mastering the synthesis and understanding of all the small coding sequences, it becomes possible to model and design the desired sequences on a computer, which will significantly speed up the production process. However, it turned out that such sequences do not always work, they can work worse or be eliminated by the cell in the first generations.

Leading Russian research centers in the field of synthetic biology include: Faculty of Bioengineering and Bioinformatics, Moscow State University; UNN named after Lobachevsky is working on applied problems of using synthetic biology; Institute of Fundamental Medicine, Novosibirsk State University; in the field of bioinformatics, these are ITMO, Kharkevich Institute, IBCh RAS.

One of the main areas of application of synthetic biology is medicine and the development of new medical products. For example, it will be critically important for us to create a modified (synthetic) human microbiota — a microflora that can populate the human intestines or mucous membranes to provide therapeutic effects. This is the topic of the project of the student team of the National Research Center for Radiology of the Ministry of Health of Russia at the IGEM competition in 2021 - microbiota for patients undergoing radiotherapy. It is assumed that it should populate the intestinal mucosa. Then the survival of patients will be higher, the degree of radiation complications will be lower, the effectiveness of treatment will be higher due to the possibility of a higher dose of radiation».

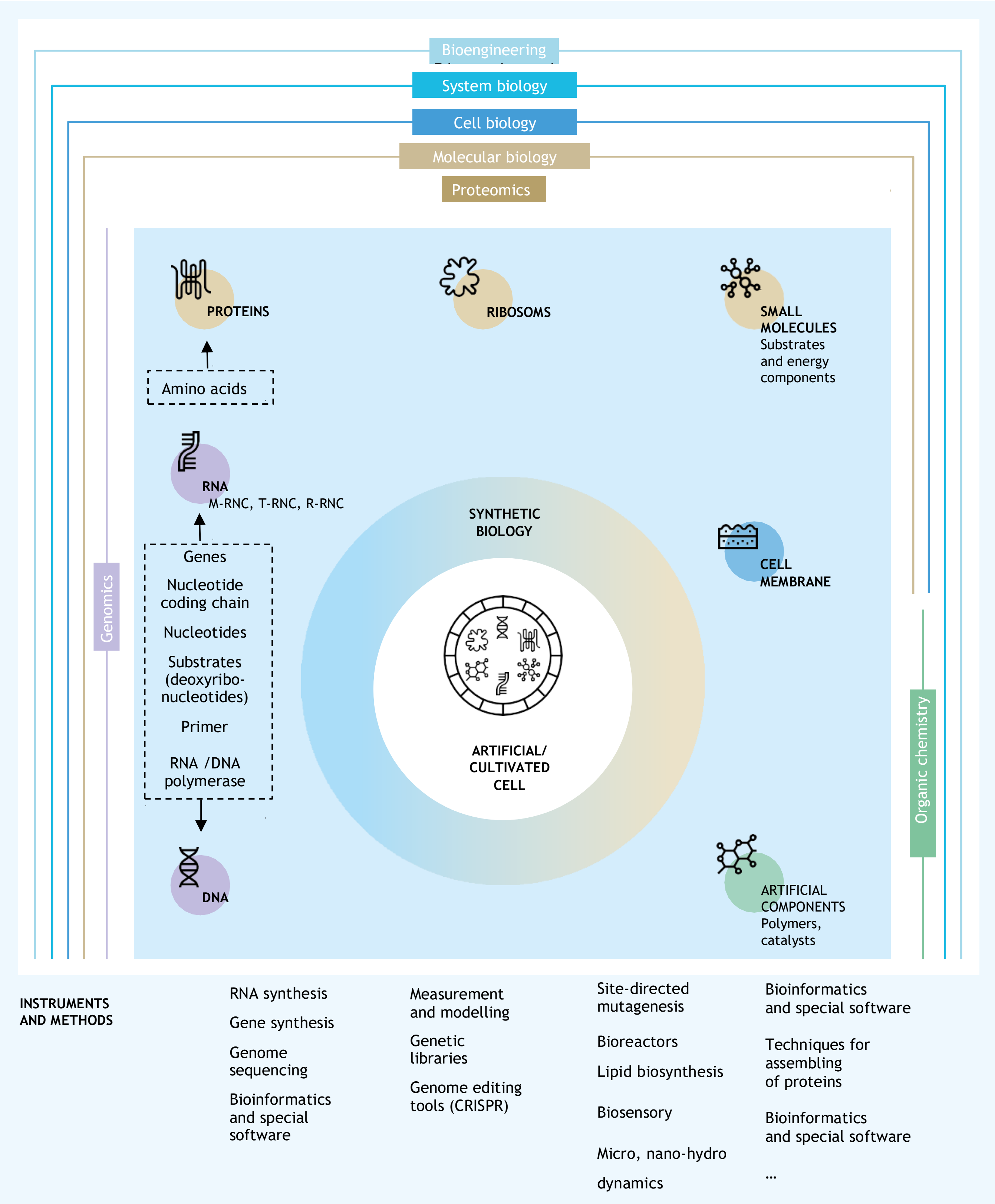


Figure 2.
An engineering principle in synthetic biology - the modular assembly of bioconstruction's (the cell and its Substituents parts)

Source: CSR North West based on Synthetic Minimal Cells URL: bio.academany.org/2018/synthetic_minimal_cells.html and Scopus

Scientific methods, tools

Scientific direction (or subject)

Components, 'modules' of the cell

The typical biological engineering cycle consists of four stages: in silico design, in vitro assembly of synthetic constructs and their testing, in vivo implementation of synthetic constructs and their testing, and data analysis (see Figure 3). The design stage involves the design of new nucleotide sequences, including the selection of design approaches and the selection of the necessary software tools. The subsequent assembly stage involves combining DNA sequences and collecting and storing new strains. This is followed by the testing phase of the resulting strains and the collection of data as a result of the tests performed. The final stage of the bioengineering cycle involves analysing the data obtained from the tests and using the results of the analysis to form new research hypotheses and start a new bioengineering cycle.

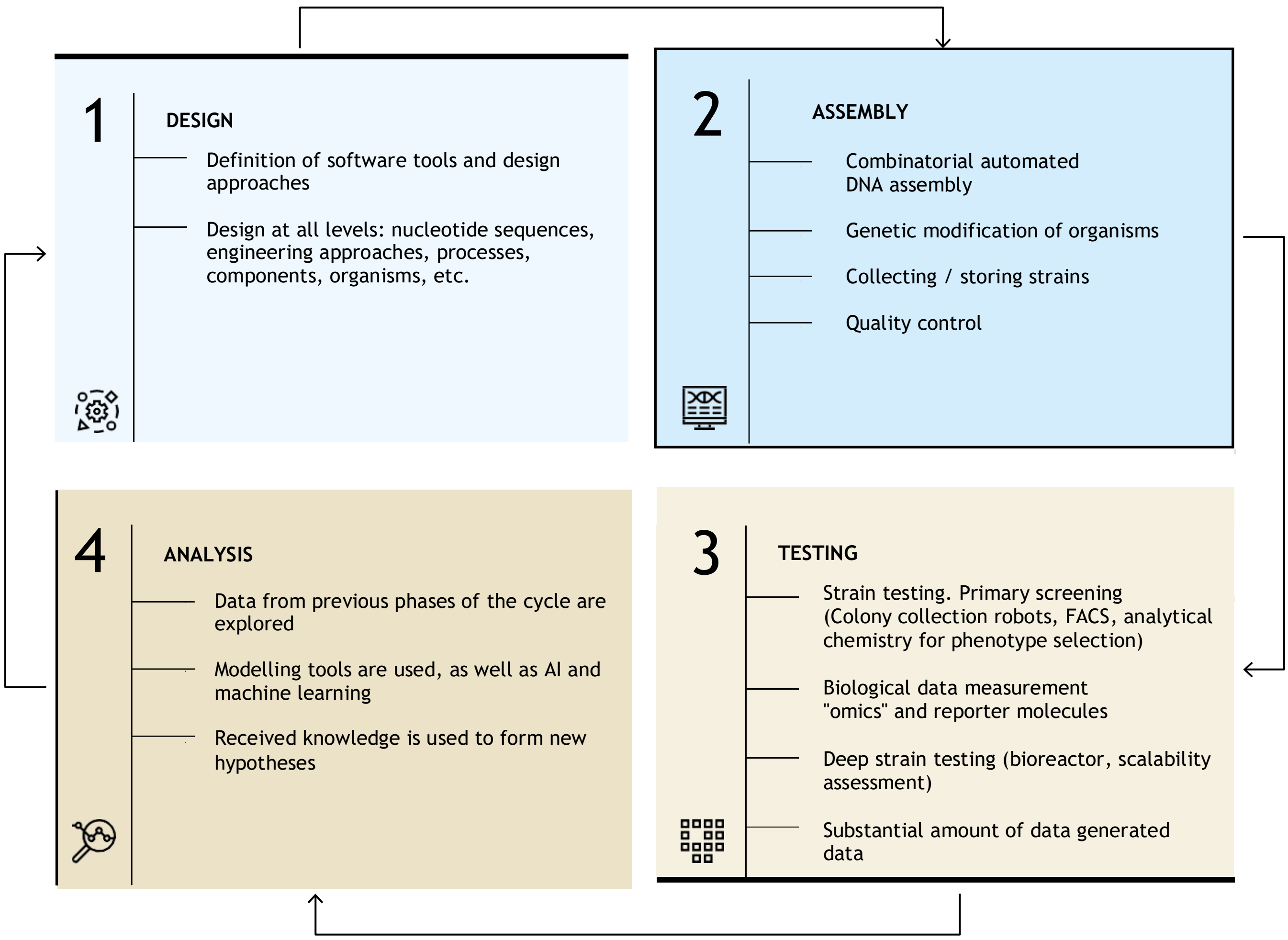


Figure 3.

The biodesign cycle

Source: CSR North West based on Paul S. Freemont; Synthetic biology industry: data-driven design is creating new opportunities in biotechnology. Emerg Top Life Sci 11 November 2019; 3 (5): 651-657. doi.org/10.1042/ETLS20190040

The implementation of the bioengineering cycle in synthetic biology involves the creation of a unified tool platform that provides the ability to detect and analyse thousands of nucleotide fragments, synthesise or revise DNA and RNA sequences as well as genomic and proteomic constructs, analyse and predict the biological properties and functions of newly synthesised biological objects.[14]

14 Xu C., Hu S., Chen X. Artificialcells: from basic science to applications. Mater Today (Kidlington). 2016 Nov;19(9):516-532. doi: 10.1016/j.mattod.2016.02.020. PMID: 28077925; PMCID: PMC5222523. Paul S. Freemont; Synthetic biology industry: data-driven design is creating new opportunities in biotechnology. Emerg Top Life Sci 11 November 2019; 3 (5): 651-657. doi: doi.org/10.1042/ETLS20190040.

3 THE DEVELOPMENT OF SYNTHETIC BIOLOGY AS A SCIENTIFIC FIELD

The prerequisites for the emergence of synthetic biology as a separate scientific field include breakthroughs in molecular biology, cell technology, genetic and protein engineering, organic chemistry, etc. [15] (see Table 2). A breakthrough already took place in the 1950s, when, using knowledge of the molecular basis of biological activity and engineering approaches, scientists began to create biological objects for the first time - this research formed the direction of bioengineering. In the 1970s, genetic engineering began to develop scientific methods and tools aimed at editing the genetic code. The emergence of systems biology in the late 1990s and synthetic biology in the early 2000s has Completely changed the rules for designing micro-organisms and more complex living systems. The main difference between synthetic biology and previous trends is that it considers living systems as programmable at the genetic level and allows the possibility of creating biological objects with predetermined properties.

15 Clarke LJ, Kitney RI. Synthetic biology in the UK — An outline of plans and progress. Synth Syst Biotechnol. 2016;1 (4):243-257. Published 2016 Oct 17. doi: 10.1016/j.synbio.2016.09.003.

	Task at hand	When it came up	Why did it happen	Volume of publications (as for 2021 г.), units.	Growth of publications CAGR (2000-2021), %
1. Organic Chemistry	Studying the properties and reactions of organic compounds, that contain carbon	1830-e	Revisiting the concept of living systems (rejection of life force theory)	749 906	15
2. Molecular Biology	Studying the molecular basis of biological activity within and between cells	1930-e	Research gene structure and the mechanisms of transmission of genetic inheritance	652 724	8,3
3. Bioengineering	Using the principles of biology and engineering to create biological objects	1950-e	Overcoming restrictions in medical and biological sciences	451 072	26
4. Biotechnology	The use of living organisms to solve technological problems	1970-e	Increasing efficiency of technological processes, creation of new products (food industry, agrotech, pharma)	485 355	15

	Task at hand/aim	When it came up	Why did it happen	Volume of publications (as for 2021 г.), units.	Growth of publications CAGR (2000-2021), %
5. Genetic engineering	Recombinant RNA and DNA production, isolating genes from organisms and manipulation at the genomic level	1970- 1980-s	Genetic modification of organisms	189 151	25
6. Systems biology	The study of complex interactions in living systems and modelling thereof	1990-s	The need to understand structure, dynamics and functions of both the organism, individual cell and intracellular compartments	857 437	10
7. Synthetic biology	Designing and construction of biological modules, biological systems and biological machines or redesigning existing biological systems for useful purposes	2000-s	Creating and Designing new biological parts and systems, including those that have no analogues in nature (vaccines, bacteria, materials, etc.)	169 070	12

Table 2.
Evolution of scientific trends in biology, chemistry and engineering

Sources: Science Direct, Scopus, Biotechnology Innovation Organization, National Human Genome Research Institute

Interest in synthetic biology as a research area continues to grow. In the period 2016-2020, the volume of publications on the query "Synthetic biology" amounted to: 12,061 (Scopus), 31,531 (Web of Science), 55,935 (Science Direct). The leading countries in terms of scientific publications in synthetic biology are the USA (more than 6.5 thousand publications in 2016-2020), China (4.6 thousand publications in the same period), and the European Union countries (3.7 thousand publications) with France and Germany among the headliners [16].

16 CSR North West, according to Scopus, Science Direct, Web of Science.

Tennikova T. B., Head of the Interdepartmental Laboratory of Biomedical Chemistry, SPbSU, Deputy Head of the SPbSU Laboratory of Biohybrid Technologies

Source: Interview in preparation of report with Tennikova T.B. dated 01.11.2021

«Synthetic biology is, on the one hand, a new trend, on the other not: the beginnings of synthetic biology were as early as the early 2000s, but increased interest emerged more recently, especially in the last 2-3 years. Synthetic biology aims to create new biological systems that exhibit vital functions (artificial viruses, microbes, cells). This involves constructing new genomes, modifying them or creating blocks of entirely new DNA. Genome manipulation activities are primarily concerned with genetic engineering, and synthetic biology has become a natural extension or offshoot of genetic engineering.

The main barriers to the development of synthetic biology are bioethical issues. It is critical to convince the population that synthetic biology and its technologies are safe and ethical and do not contradict accepted norms. This is difficult, especially given the diversity of the world's population.

There are 2 main barriers to the development of synthetic biology in Russia - financial and human resources. Synthetic biology experiments require huge amounts of money. This is one of the problem points of Russian science and the system of funding and allocation of funds in science. Despite improvements in the quality of education and the establishment of specialised units and laboratories within universities, Russia lacks the education to meet the challenges of synthetic biology. This leads to a shortage of personnel. This is complicated by the fact that the old workforce does not have the new competencies and the new specialists have not yet been formed.

Evgenia Kirichenko, Acting Head of Bioengineering Department, Don State Technical University

Source: Interview as part of the report preparation with Kirichenko E.Yu. dated 05.10.2021

"Synthetic biology is working with an artificial genome, but not with a living one. Biotechnology is a technological field aimed at the production of raw materials. It is important to bear in mind that synthetic biology and bioengineering are different fields. Biotechnology operates with both bioengineering and synthetic biology. It is a different approach to the same tasks. In general terms, biotechnology is a broader concept.

The development of biotechnology, synthetic biology and bioengineering goes hand in hand with bioethical issues. Today, there is an explosion regulation of change. Mankind has managed to get to the source code, and tries to change it without assessing the possible consequences.

Bioethical issues are extremely relevant. Without bioethics, developments in biotechnology and synthetic biology may be aimed at very different ends. It is important to understand the seriousness of these issues. This is also relevant for Russia, especially within the framework of education. Today, disciplines related to bioethics are completely detached from practice.

The widespread development of synthetic biology is related to the growth of the IT sector. IT specialists are able to abstract, look at genomes and design them. This gives a big boost to development. One of the new professions of the future is the bioinformatician, who has the skills of a computer scientist and a biologist. Today, the volume of biodata has grown considerably due to the increase in DNA sequencing, but there is not always a full understanding of what to do with them. It is also important that programmers can analyse the quality of the reed, including It is also important for programmers to be able to analyse the quality of the reed, including that in the public domain.

There are now extensive networks of synthetic biology specialists and R&D institutes around the world. Examples of such R&D institutes with well-established scientific schools include: Harvard Medical School, Craig Venter Institute, Howard Hughes Medical Institute, CNRS Centre National de la Recherche Scientifique, National Institutes of Health NIH. What these research centres have in common is their interdisciplinarity and openness to partnership, as well as their willingness to carry out large-scale full-cycle R&D projects. In the last decade, an increasing number of experimental laboratories have been dedicated to developing and promoting engineering approaches in new segments of biological sciences (e.g. Systems Biology and Synthetic Biology Laboratory (Center for Genome Sciences UNAM Campus Morelos), Laboratory for Synthetic Biology (RIKEN Quantitative Biology Center - QBiC), Synthetic Biological Systems Laboratory (The Danino Lab) or laboratories at faculties of biology and chemistry at leading universities - MIT (Synthetic Biology Center), University of California (Department of Bioengineering), Technische Universität München (Munich Institute of Biomedical Engineering), University of Tokyo (Synthetic Cell Engineering Lab), Tsinghua University (Center for synthetic and systematic biology) [17].

Since 2017, Biofoundries, infra-structural centres for biodesign, based on the BioFoundries concept (BioFAB), have been formed in various countries. Today, there are 29 of them, forming a consortium called the Global Alliance Biofoundries. The goals of Biofoundries are to rapidly design, create and test genetically engineered organisms, accelerate and improve the quality of research in bioengineering and synthetic biology, ensure economic viability by scaling up the testing of genetic constructs, reduce the cost of shared infrastructure, and develop rules and standards for biodesign. The format opens up opportunities for networked, distributed research and larger projects, depending on where the infrastructure and expertise, data, and biospecimens are available. This format opens up opportunities for networked, distributed research and larger projects, depending on infrastructure and expertise, data, biosamples [18].

Recently, consortia have been formed to tackle the technological challenges of engineering new biomolecules and cells. For example, The European Synthetic Cell Initiative, Protein Industries Canada (PIC), The Protein Cluster (TPC) in the Netherlands, Synthetic Biology Innovation Cluster (London), UK Future Biomanufacturing Research Hub (UK Future Biomanufacturing Research Hub)[19], the Commonwealth Scientific and Industrial Research Organisation (CSIRO) and others. The development of a network of such clusters nowadays determines the formation of synthetic biology as a new industry, which is acquiring the features of not only a scientific sector, but also of a full-scale production industry. Russia, solving urgent economic and social tasks related to the necessity of synthetic biology technologies implementation, can create its own alliances of developers and industrial companies in a wide range of areas, from agriculture to medicine and pharmaceutics. Genetic research centres in Novosibirsk, Moscow, St Petersburg and other cities could form the core of such alliances.

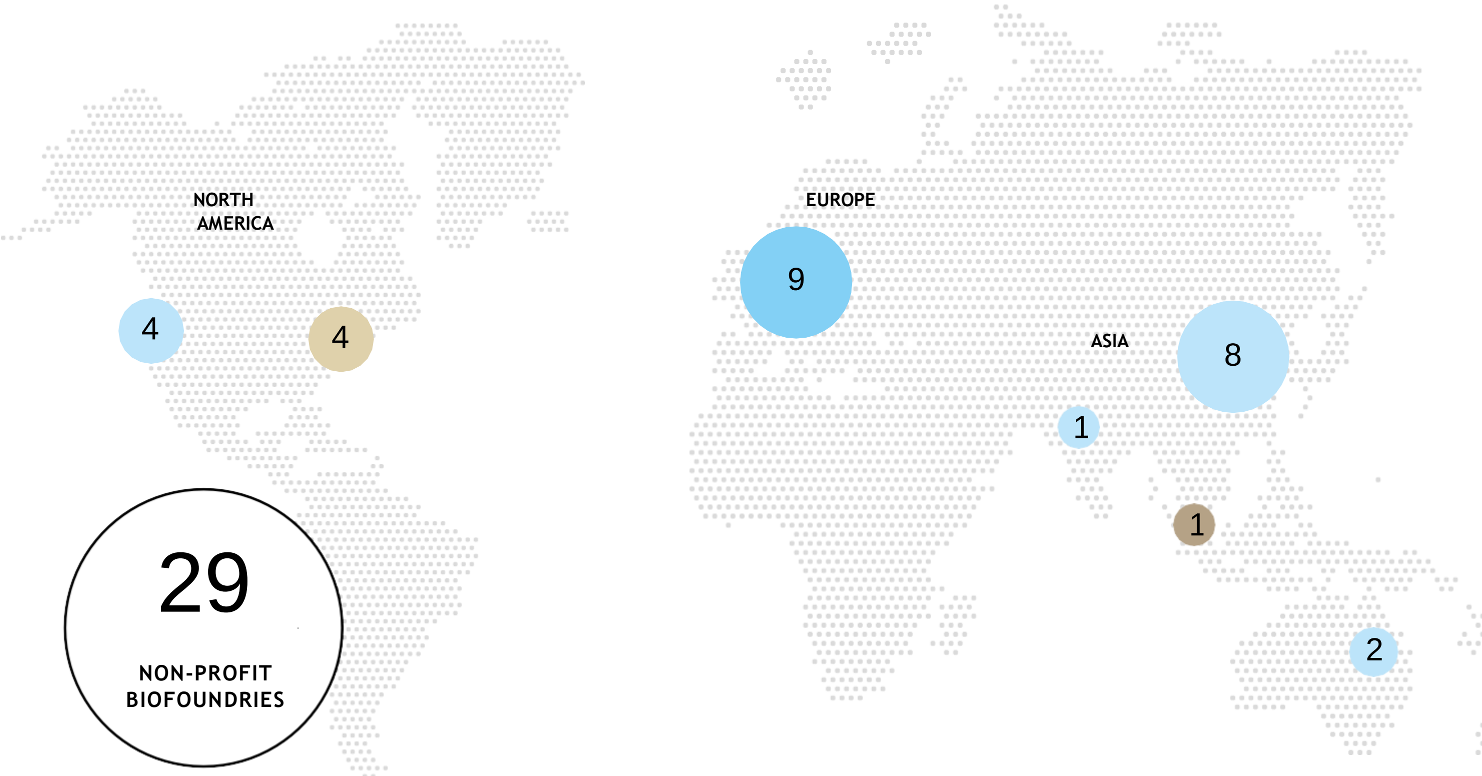
17 Based on interview materials with Shityakov S.V. (15.10.2021), Gusev O. A. (25.10.2021), K. Sarkisian (28.10.2021), Foresight-session "Fronts in the New Sciences" 9-10 November 2021 and Scopus data on organizations with the highest number of publications on the topic of synthetic biology.

18 Based on GlobalBiofoundries Alliance.

19 Synthetic Biology UK A Decade of Rapid Progress 2009-2019. URL: ktn-uk.org/wp-COntent/uploads/2020/08/COLC-COmbined-final.pdf (accessed: 16.01.2022).

Case 2: Global Biofoundries Alliance

Source: Global Biofoundries Alliance, URL: biofoundries.org



iBioFAB, University of Illinois

Produce up to 1,000 genome cell operations per day using TALEN METHODS. The cost of each operation is less than $3 USD (0.3% of the cost of a similar process outside Biofoundry).

Perform multiplex genome engineering of yeast cultures in automatic mode - this speed up the process by more than 10 times with the involvement of a single expert

Edinburgh GenomeFoundry

Perform over 2,000 DNA assembly reactions per week, 20 times faster than assembly without automation or robotics

Singapore SynCTI Foundry

Provide affordable solutions and development for small companies.

Provide access to costly infrastructure and expertise to enable companies to prototype and bring new products to market

Biofoundry tasks

- Rapid design, creation and testing of genetically reprogrammed organisms
- Accelerating and improving the quality of bioengineering and synthetic biology research
- Ensuring economic viability by scaling up genetic design testing processes, reducing infrastructure sharing costs
- Development of biodesign rules and standards

Case 3. Consortia in synthetic biology

Sources: Protein IndustriesCanada Annual Report 2021. URL: proteinindustriescanada.ca/uploads/2021-Annual-Report.pdf (accessed: 16.01.2022), The European Synthetic Cell Initiative. URL: syntheticcell.eu (accessed: 16.01.2022), The Protein Cluster — TPC. URL: theproteincluster.com (accessed: 16.01.2022).

The European Synthetic Cell Initiative

Consortium of scientists and researchers covering the Atomic and Alternative Energy Commissariat, Delft University of Technology, Max Planck Institute for Biochemistry and Oxford University, which along with The Kavli Foundation are the main sponsors of the initiative.

The European Synthetic Cell Initiative does not receive funding from companies or governments, but is funded by research institutes and foundations.

Mission

- Coordinate and strengthen scientists' efforts to create a functioning synthetic cell from its basic components
- Promoting knowledge of the synthetic cell in technological applications

Tasks

- Promoting cooperation between scientists in the field of synthetic cell research
- Encouraging cooperation between scientists and industry to develop new technologies
- Promoting ethical debate and discussion on responsible research and innovation

Since its inception in 2017, the European Synthetic Cell initiative has conducted the following activities: 2017 — Future Symposium on Building a Synthetic Cell (Ringberg Castle, Germany), 2018 — 1st International Symposium on Building a Synthetic Cell (Delft University of Technology, The Netherlands), SynCell, 2019 — Defining the Challenges (Spanish National Research Council, Madrid, Spain).

Protein Industries Canada — PIC

An industry non-profit organization established to position Canada as a global source of high-quality plant-based protein and by-products, and aims to create an innovative ecosystem of plant-based foods, feeds and ingredients. It is one of Canada's five superclusters. Includes 280 member organizations, 13 international participants. 87 small and medium-sized enterprises, 107 scientific and research institutes are involved in implementation of 22 projects. The value of the implemented projects is $357 million.

The aim of PIC

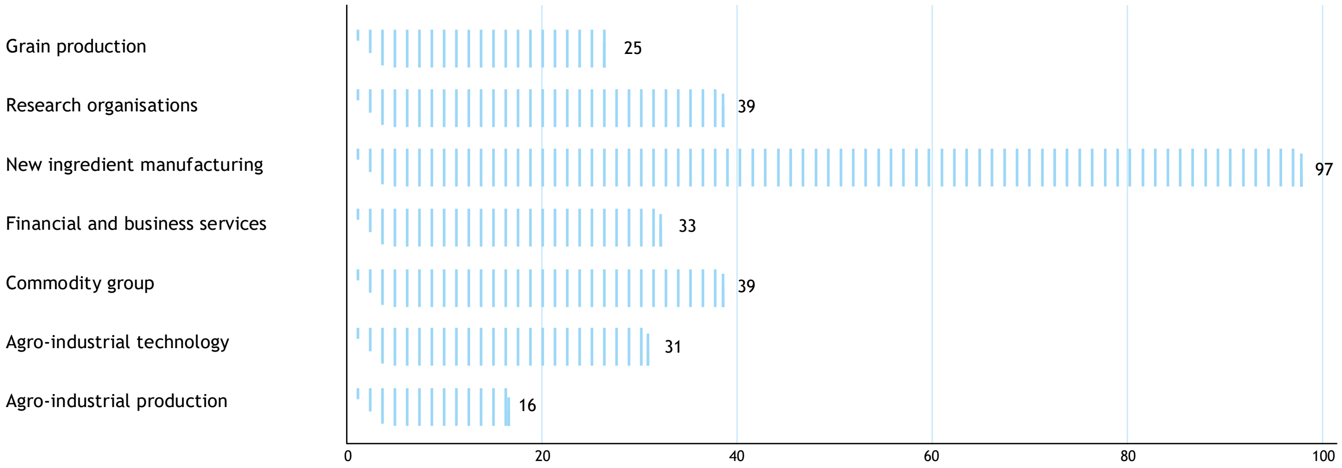
Motivate collaboration between enterprises, institutions of higher education and research institutions to implement projects that can transform the food processing sector in Canada.

In 2020-2021, 13 technology projects with a total value of $210 million have been approved, with investments of $76 million in the protein industry and $134 million in industry.

Project themes

- Development of new plant-based protein ingredients and products for foreign and Canadian markets
- Developing new technologies for protein engineering, editing product properties and improving ingredient functionality
- Developing new pest control technologies
- Developing AI technologies to optimise plant breeding processes

Structure of participants by type of activity



The Protein Cluster - TPC (Netherlands)

A global platform for ingredient suppliers, food manufacturers, retailers, caterers and other stakeholders looking for ready-to-use plant-based, vegan or vegetarian solutions.

TPC helps suppliers of plant-based protein ingredients, semi-finished products, consumer products and technologies to develop and commercialise their innovative products.

TPC is an initiative of Foodvalley NL, Oost NL and the Dutch provinces of Gelderland and Overijssel. TPC offers ready-to-use ingredients, products, technologies and services to accelerate the transition to sustainable plant-based proteins.

Examples of TCP technologies and products

- Microbial fermentation with microalgae
- Natural Microbial Egg Protein Substitutes (FUMI)
- Flavour-enhancing proteins from onion residue streams
- Test facility: green protein accelerator (pilot production line for foodstuffs, enabling clean protein companies to speed up market entry)

4 Key challenges and frontiers of synthetic biology up to 2040

Below are the 5 main areas of synthetic biology development challenges facing the international and Russian scientific community.

1 «Bottom-up»- assembly of the cage

This involves replicating the complete cell life cycle, describing the functions of each gene and reducing their number, ensuring autonomous growth, DNA replication and segregation and cell division (see Figure 4). For comparison, the first cell was obtained using the "top-down" method: in 2010, a minimal functional genome (530 kb) was obtained from Mycoplasma mycoides (a bacterium) by transposon mutagenesis. Subsequent processes (DNA synthesis, assembly of a complete circular chromosome) led to the creation of the JCVI-syn3.0 synthetic genome. Later, several genes were added for normal cell division - JCVI-syn3.0 genome +126, 481 genes (human cell - 30,000 genes, protozoan bacterium - 4,500 genes)[20].

20 Xu C., Hu S., Chen X. Artificial cells: from basic science to applications. Mater Today (Kidlington). 2016 Nov;19(9). doi: 10.1016/j.mattod.2016.02.020. PMID: 28077925; PMCID: PMC5222523; Sleator RD. JCVI-syn3.0 — A synthetic genome stripped bare! Bioengineered. 2016;7(2).doi:10.1080/21655979. 2016.1175847; Boyd M. A., Kamat N. P. Designing Artificial Cells towards a New Generation of Biosensors. Trends Biotechnol. 2021;39(9). doi:10.1016/j.tibtech.2020.12.002; Scientists Create Simple Synthetic Cell That Grows and Divides Normally. URL: nist.gov/news-events/news/2021/03/scientists-create-simple-synthetic-cell-grows-and-divides-normally (accessed: 16.01.2022).

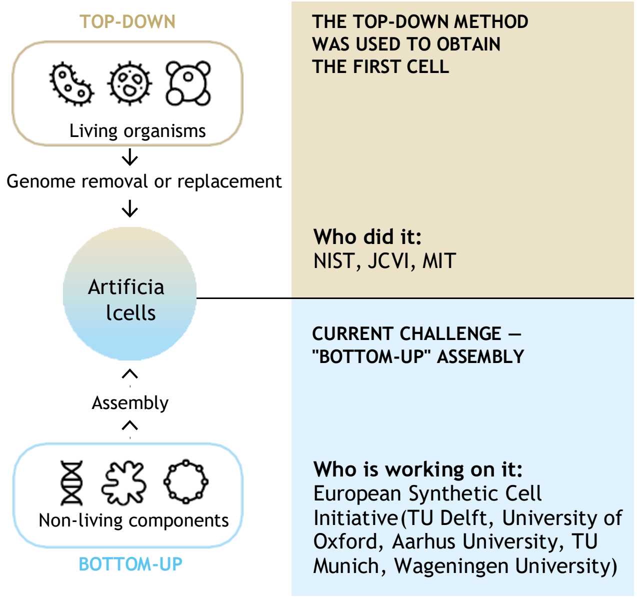


Figure 4.
Key approaches to the assembly of a synthetic cell

Source: Xu C., Hu S., Chen X. Artificial cells: from basic science to applications. Mater Today (Kidlington). 2016 Nov;19(9). doi: 10.1016/j.mattod.2016.02.020. PMID: 28077925; PMCID: PMC5222523; CSR North-West, based on open-source data.

Obtaining a cultured cell depends on solving problems of synthesis of artificial genome and protein molecules, allowing the assembly of cellular structures. At the same time the assembly of an artificial cell, as it was mentioned above, is made for solving a particular industry problem. Acceleration, automation and digitalisation of work processes with genome, data libraries and standardisation of methods and tools for working with biological materials are some of the key research areas for answering this challenge.

2 Protein synthesis

The second important challenge is that proteins and the processes they facilitate are the basis for the reproduction of synthetic cells. They are involved in creating the environment for cell division/growth, cell signalling, metabolism etc. Protein molecules have a complex structure; protein engineering is a multistep, cyclical process of selecting nucleotide sequences, synthesising proteins and assessing the feasibility of the resulting molecular variants (Figure 5 shows the complete cycle of protein engineering). The engineering of protein molecules for a particular application is one of the most complex and urgent tasks of modern proteomics, the success of which will directly determine the speed of development of synthetic biology and its practical relevance [21].

21 Chen T. Liang, Olivia M. A. Roscow, Wei Zhang, Recent developments in engineering protein-protein interactions using phage display, Protein Engineering, Design and Selection, Volume 34, 2021, gzab014, doi.org/10.1093/protein/gzab014.

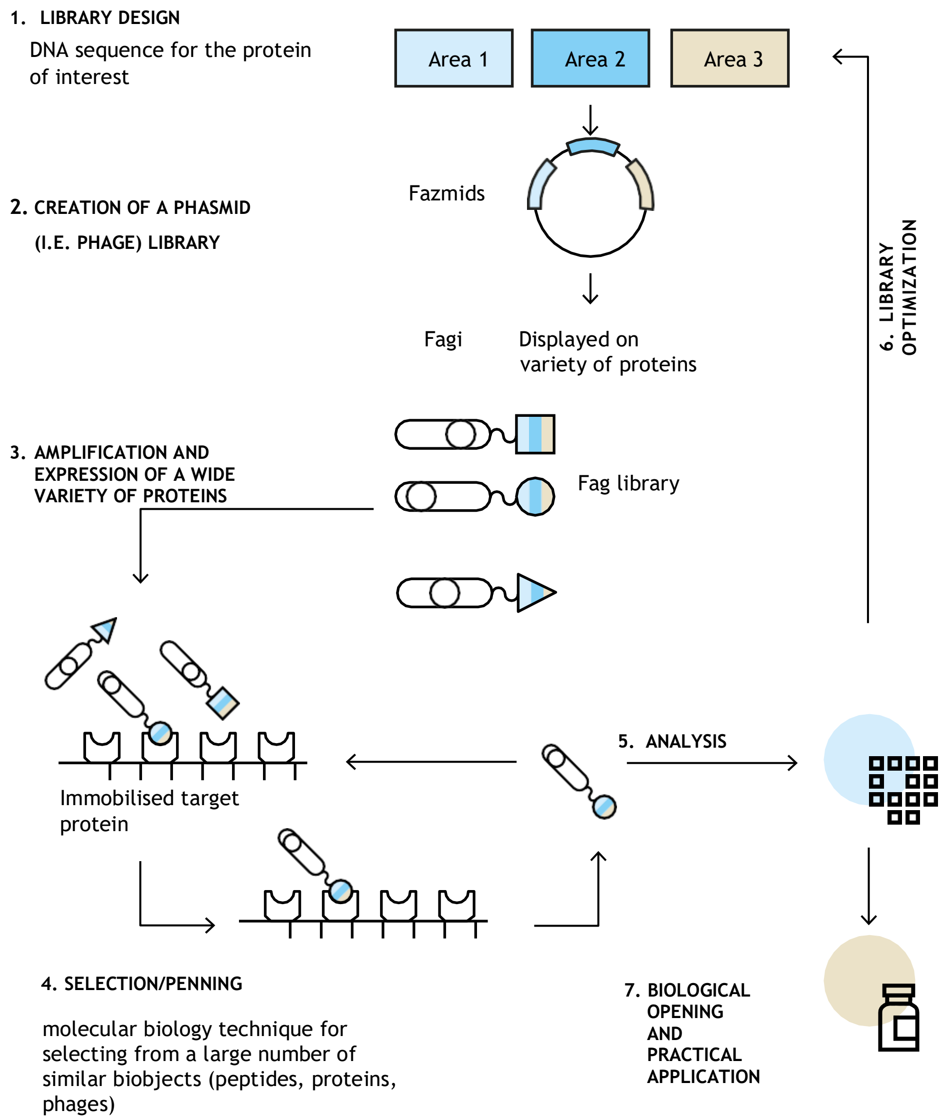


Figure 5.
The proteome design cycle

Source: Chen T Liang, Olivia M A Roscow, Wei Zhang, Recent developments in engineering protein- protein interactions using phage display, Protein Engineering, Design and Selection, Volume 34, 2021, gzab014, doi.org/10.1093/protein/

The importance of the artificial protein assembly challenge is also confirmed by the growing volume of patents - from 3,800 patent applications worldwide on this topic in 2000 to 19,400 in 2021[22]. However, the most active research results in the field of protein synthesis are patented in China. The majority of the world's in vitro protein patents in 2017-2019 are in China's jurisdiction (63.3%). The USA (11.5%), EU (10.1%) and Japan (6%) come in second, third and fourth respectively. The rest of the world accounted for 9% of patents in the period.

22 According to the patent database lens.org

Gusev O.A., Director, Regulatory Genomics Research Centre, Institute of Fundamental Medicine and Biology, KFU; Professor of Medicine, Yuntendo University (Japan)

Source: Interview in preparation of the report with Gusev O. A. dated 25.10.2021

"Synthetic biology stands in the way of practical solutions and optimisation of cell technologies. One of the important directions in the development of synthetic biology is biomimetics. For instance, using the thermoregulatory mechanisms studied in living organisms, the research team has developed a technology for optimising cell culture storage, allowing cell culture to be stored at -30 degrees instead of -80 degrees. This dramatically simplifies the handling with cell cultures.

Biotechnology and recombinant technologies are based on empirically derived objects. Synthetic biology, on the other hand, relies largely on computational biology and modelling. Its key difference is its use of models as influence. Synthetic biology, using a variety of knowledge of omics, structural biology and so on, tries to create a complete system based on this knowledge - not a small empirical impact, but the conceptual implementation of a of a whole workable system.

The main challenge in the field of synthetic biology is to learn how to isolate as correctly as possible modules and components and to understand the implications of their implementation. Today, a huge body of data and knowledge is being generated - sequencing, metabolic profiling, etc. This yields enormous databases. In this context, another challenge arises - the volume of data far exceeds the ability to process it. The availability of data and its accessibility becomes of great importance, i.e., the correct allocation and processing of data and metadata".

3 Forming a technology platform for biodesign or BioCAD

The high rate of development of synthetic biology to date has been driven by the growth of computational capabilities, the development of data science and the acceleration and digitalisation of data processing and the design of new objects. The next step is to create a single platform that will enable the bioengineering cycle to be carried out as quickly as possible and to create living systems with specified properties in the shortest possible time. A major part of research in synthetic biology should focus on developing platforms and assistive technologies that would allow biological design based on algorithms where sequences or parts of individual cell elements can be assembled into larger genetic constructs or even genomes or chromosomes [23]. The technology platforms should enable a faster and more optimised biodesign cycle (see section 2) and significantly increase the number of experiments and the chances of obtaining practical results.

However, the formation and development of such platforms depends directly on the availability and accessibility of biodata. The volume of biodata is approximately doubling every year [24] (Figure 6 shows the evolution of data accumulation by the European Bioinformatics Institute for the main data sources). However, such exponential growth poses serious challenges for data storage, systematisation and cyber security. Figure 7 also shows the growing number of users worldwide with access to biodata. The high growth rate of synthetic biology could lead to increased biosecurity, cybersecurity issues, the need for standards and a revision of the international legal framework in biotechnology[25].

For the Russia, a feature of this group of challenges also includes the need to develop re-engineering of foreign software products, especially in critical design areas. In their absence, Russian research institutes will be constantly at risk of service interruption by foreign vendors, as well as risks of knowledge preservation processes deficits, as it is accumulated in the code and models of the engineering software used, among other things.

23 Emerging Opportunities in Synthetic Biology Platforms, Synthetic Biology as a Profound Transformative Technology, TechVision Group of Frost & Sullivan, TechVision Analysis /D89D / 00; CSR North-West, based on interviews with Kirichenko, E. Y. (05.10.2021), I. D. Klabukov (02.11.2021).

24 According to the European Institute of Bioinformatics (EMBL-EBI).

25 Charles E. cook, Oana Stroe, Guy Cochrane, Ewan Birney, Rolf Apweiler, The European Bioinformatics Institute in 2020: building a global infrastructure of interconnected data resources for the life sciences, Nucleic Acids Research, Volume 48, Issue D1, 08 January 2020, doi.org/10.1093/nar/gkz1033 Trump B. D., Galaitsi S. E., Appleton E., Bleijs D. A., Florin M. V., Gollihar J. D., Hamilton R. A., Kuiken T., Lentzos F., Mampuys R., Merad M., Novossiolova T., Oye K., Perkins E., Garcia-Reyero N., Rhodes C., & Linkov I. (2020). Building biosecurity for synthetic biology. Molecular Systems Biology, 16 (7) [e9723]. doi.org/10.15252/msb.20209723.

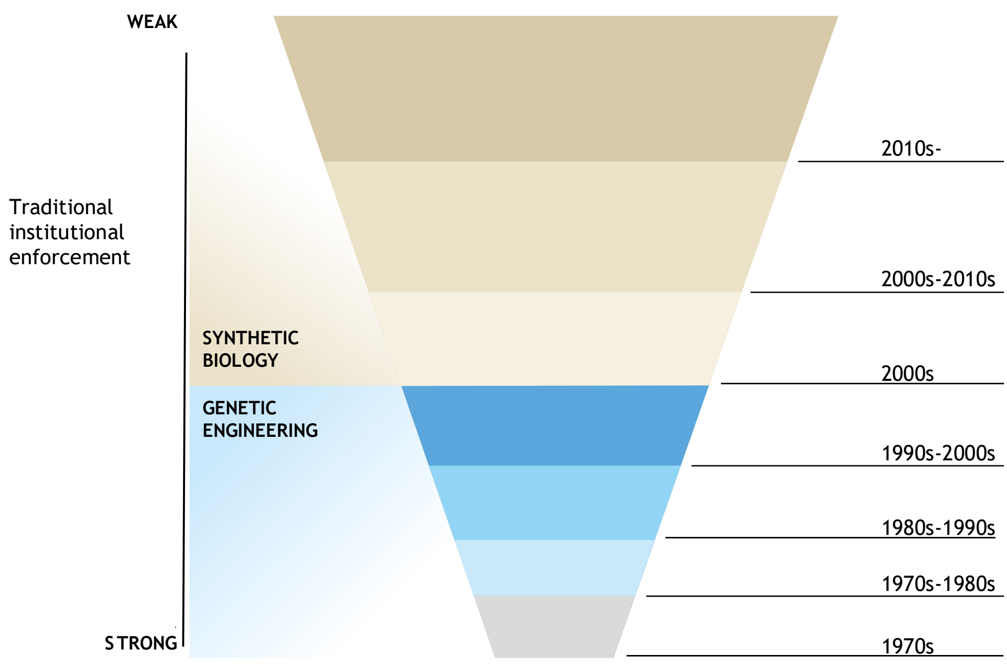


Figure 6.
Dynamics of biodata generation in the world (according to the European Bioinformatics Institute EMBL-EBI)

Source: Charles E Cook, Oana Stroe, Guy Cochrane, Ewan Birney,Rolf Apweiler, The European Bioinformatics Institute in 2020: building a global infrastructure of interconnected data resources for the life sciences, Nucleic Acids Research, Volume 48, Issue D1, 08 January 2020, doi.org/10.1093/nar/gkz1033

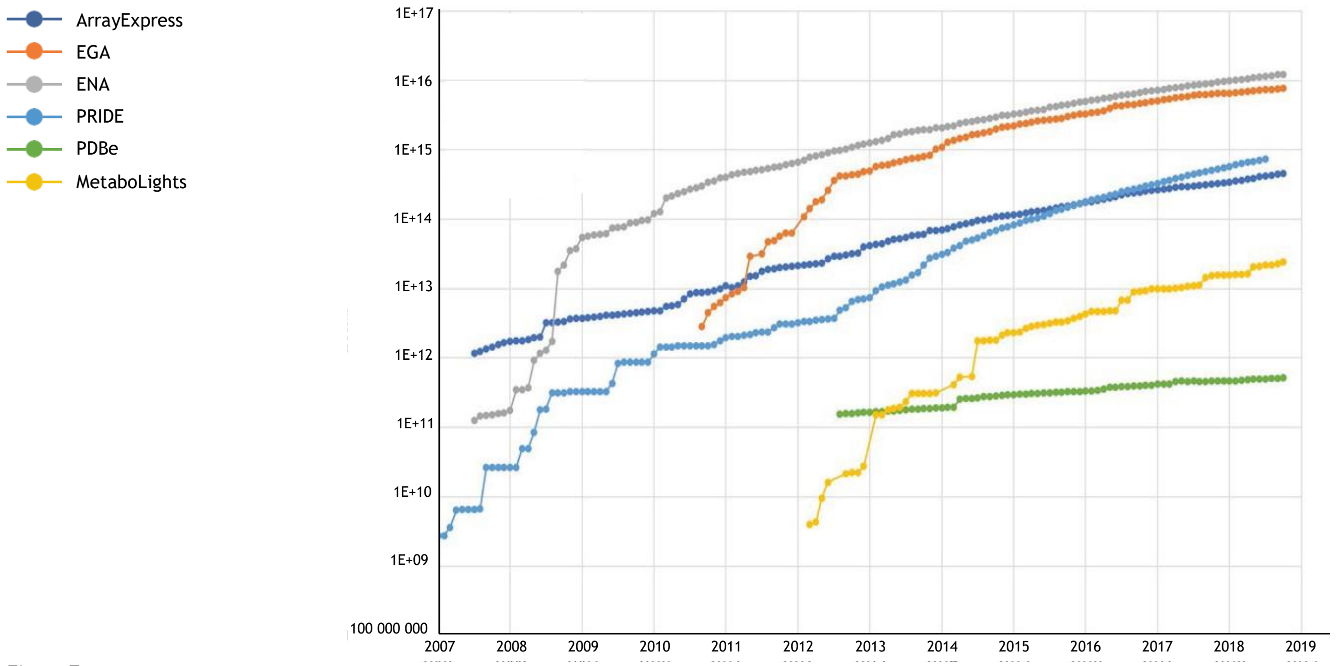


Figure 7.
Evolution of number of users worldwide with access to biological data, genetic engineering (blue) and synthetic biology (orange)

Source: Trump B. D., Galaitsi S. E., Appleton E., Bleijs D. A., Florin M. V., Gollihar J. D., Hamilton R. A., Kuiken T., Lentzos F., Mampuys R.,Merad M., Novossiolova,T., Oye K., Perkins E., Garcia-Reyero N., Rhodes C., & Linkov I. (2020). Building biosecurity for synthetic biology. Molecular Systems Biology, 16 (7), [e9723]. doi.org/10.15252/msb.20209723

ArrayExpress — data from functional genomics

EGA — The European Genome-Phenome Archive

ENA — European Nucleotide Archive

PRIDE — PRoteomics IDEntifications database

PDBe — Protein Data Bank in Europe

MetaboLights — Metabolomics experiment database

4 Challenges and frontier scientific tasks associated with synthetic biology also arise at the junction with different areas of its application, depending on the specifics of the tasks that a particular industry works with

For example, in medicine and pharma - research in the field of regeneration, synthesis of living tissue, drug design and delivery platforms, biocompatibility, antibiotic resistance and infectious diseases (PCR-tests, antibody production), targeted therapies for deadly diseases, etc. In the agricultural sector - restoration of soil fertility, production of new plant varieties; in the food industry - production of alterative protein (non-animal origin), foodstuffs with adjusted properties and variable nutritional value, food biosensors; in energy - production of biofuels, microbial fuel cells, enzymes for biocatalysis; in materials production - production of biodegradable and environmentally neutral materials; in ecology - production of bacteria and microbial consortiums, contributing to pollution elimination and bioremediation (also see Table 1 in section 1).[26]

26 Center for Strategic Research "North-West" based on interviews with Kirichenko E.Yu. (05.10.2021), Golovin S.N. (05.10.2021), Shityakov S.V. (October 25, 2021), Gusev O. A. (25.10.2021), Sargsyan K.S. (28.10.2021), Tennikova T.B. (01.11.2021).

5 Overall, assembling a cell/bio-construction for a specific industry task and then going into production and scaling it up is a major scientific challenge

In this sense, on the one hand, translational research is important to enable the rapid transfer of the fundamental results of scientific experiments and discoveries into applications.[27]

In addition, it should be noted that the discussions of the scientific community (as the results of the foresight session "Frontiers in New Sciences" showed) today are mainly concentrated around the first and second challenges. According to scientists, the current and prospective development of synthetic biology is associated with two main fundamental areas of research — genomics and proteomics. The possibility of cell synthesis depends on the availability of effective tools for working with the genome and the availability of protein assembly mechanisms. At the same time, genomics is a relatively more mature scientific area, which has accumulated a significant number of scientific publications and whose growth is slowing down (the average annual growth (CAGR) of the volume of Scopus publications was 11.6% in 2000-2020, an increase of 9.4 times - from 12,678 publications in 2000 to 119,586 in 2020). Proteomics is developing more actively than genomics (the average annual growth (CAGR) of the volume of Scopus publications was 26.2% in 2000-2020, an increase of more than 100 times - from 559 publications in 2000 to 59,340 in 2020) (see Figure 8). According to research scientists working in the fields of biology and chemistry, “Protein engineering is the challenge of the next millennium”[28].

27 CSR North-West based on interviews with Shityakov S.V. (15.10.2021), Klabukov I.D. (02.11.2021).

28 Based on the foresight session 'Fronts in the New Sciences' 9-10 November 2021.

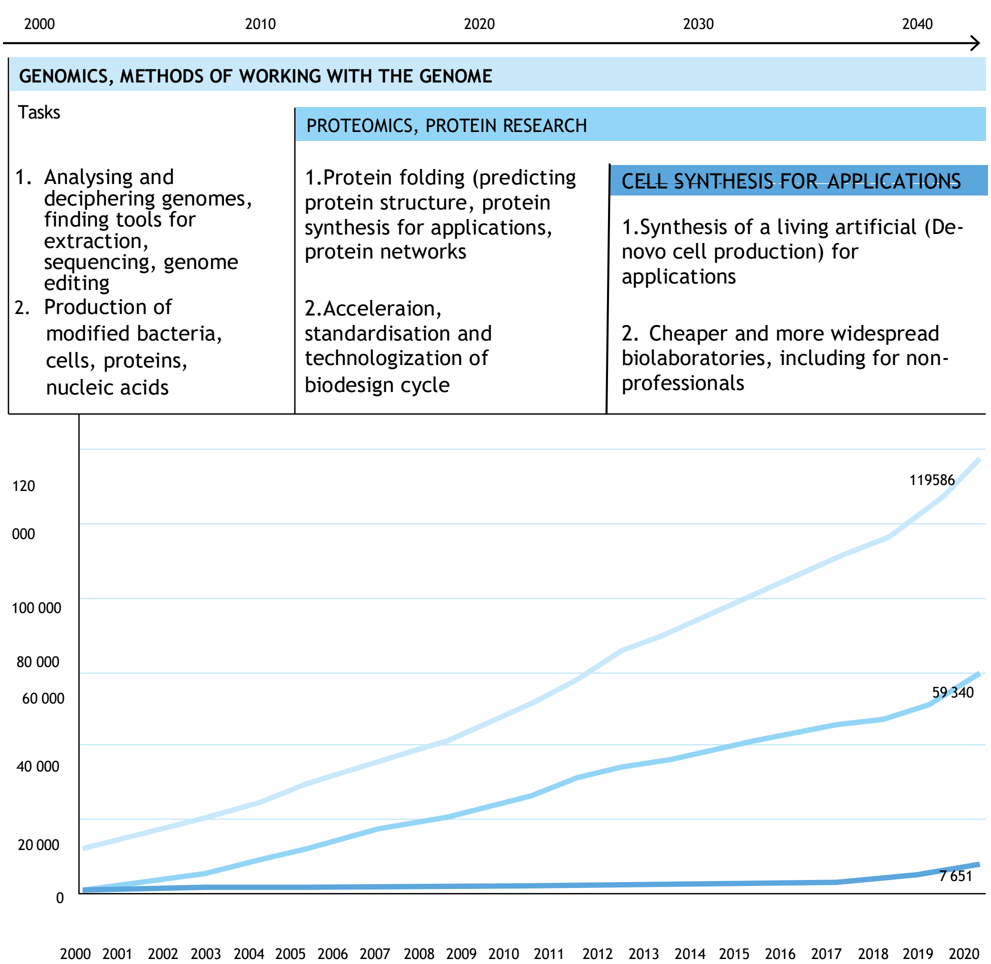


Figure 8
Timeline and priorities for the development of genomics, proteomics and synthetic biology

Source: CSR North-West based on the results of the foresight session "Frontiers in the new sciences" 9-10 November, 2021 and according to Scopus

Table 3* presents the main scientific and technological fronts (scientific topics) that address the tasks and challenges of synthetic biology outlined above. The list of S&T fronts was formed on the basis of the results of the foresight session "Fronts in Emerging Sciences" held on November 9-10, 2021, a series of interviews and scientometric analysis of publications in the Scopus database.

Synthetic biology fronts mainly include scientific topics related to genetic research and genome editing tools (genome sequencing, CRISPR-Cas9, microfluidics, metagenomics, etc.), technologies of working with big biological data (machine learning, biobanks, artificial intelligence platforms, etc.) and tools for proteome synthesis (protein-protein interaction, engineering of protein networks, protein folding, etc.). While research on proteome synthesis tools and approaches (protein-protein interaction, protein network engineering, protein folding, etc.) is gaining momentum, the proteomics frontier is only gathering pace. Appendix 1 provides a detailed list of research centres leading in terms of the volume of publications worldwide and in Russia on the identified frontier topics. Some players have already been mentioned in section 3 of the report: Harvard Medical School, Craig Venter institute, Howard Hughes Medical Institute, CNRS Centre National de la Recherche Scientifique, National Institutes of Health NIH, Chinese Academy of Sciences, Massachusetts Institute of Technology.

* Table 3 shows the key challenges for each science and technology frontier with which it is aligned, the scope of solutions (as per Figure 1), volume of publications, average annual growth rate and citations for the period 2000-2020. The list of research topics is sorted by volume of publications for the period 2000-2020 from areas that are relatively more mature, to directions, in which scientific and publication activity is gaining momentum. The fastest growing frontiers with an average growth rate above 20% are highlighted in colour in Table 3. Abbreviations in the table: SB - synthetic biology, Pharma - pharmacology, APC - agro-industrial complex as a combination of agriculture and food industry.

№	Scientific and technological frontiers	Challenge	Industry	Sciometric indicators, 2000-2020		
				Publ. volume worldwide, thds.	Compound annual growth rate (CAGR), %	Citation rate, average per article
1	Bioinformatics	3, 4, 5	All industries SB	2 745,1	14,0	112,5
2	Gene expression	1, 2, 5	All industries SB	2 539,5	6,6	147,2
3	Biomarkers: cancer markers, markers of ageing	2, 4, 5	Medicine	1 474,7	15,7	130,7
4	Polymerase chain reaction	1, 2	All industries SB	1 127,5	5,7	66,3
5	Obtaining the target metabolites	4, 5	Medicine, pharma	1 085,7	7,7	137,8
6	Cell and tissue culture technologies	4, 5	Medicine, pharma, AIC	969,2	4,7	21,9
7	Machine Learning in biology	3	All industries SB	613,6	23,8	112,6
8	Protein synthesis and mutation	2, 4, 5	All industries SB	307,4	2,4	10,6
9	Protein-protein interactions	2	All industries SB	299,7	6,3	88,6

№	Scientific and technological frontiers	Challenge	Industry	Sciometric indicators, 2000-2020		
				Publ. volume worldwide, thds.	Compound annual growth rate (CAGR), %	Citation rate, average per article
10	Bioreactors	4, 5	Medicine, pharma, AIC, energy	205,3	10,7	88,9
11	Mathematical modelling in bioengineering	3	All industries SB	188,3	14,8	38,4
12	Protein folding (predicting protein structure)	2, 4, 5	All industries SB	163,7	3,0	86,9
13	Microfluidics	4, 5	Energy, environment, biomaterials	129,9	24,0	69,0
14	Genome sequencing	1, 2, 5	All industries SB	126,3	21,0	77,2
15	Protein network engineering	2	All industries SB	127,5	2,9	16,2
16	Obtaining secondary plant metabolites	4, 5	AIC	119,9	13,9	118,2
17	Site-directed mutagenesis	1, 2	All industries SB	109,5	-0,5	17,4
18	Cheaper personalised medicine	4, 5	Medicine	106,5	40,0	16,1
19	Omics technology	4, 5	Medicine, pharma	90,9	54,9	69,1
20	Extraction of genetic material	1, 2, 5	All industries SB	88,6	15,7	15,3
21	Targeted deliveries of biologics, medicines	4, 5	Pharma	78	23,0	70,8
22	CRISPR-Cas9 (since 2013)	1, 2, 5	All industries SB	49,6	119,8	75,6
23	Metagenomics	1, 2, 5	Medicine, AIC	46,2	44,9	51,6
24	Cybersecurity	3	All industries SB	32,7	56,0	23,7
25	Biobank of biodiversity and genetic resources	3, 5	All industries SB	31,8	42,3	67,5

№	Scientific and technological frontiers	Challenge	Industry	Sciometric indicators, 2000-2020		
				Publ. volume worldwide, thds.	Compound annual growth rate (CAGR), %	Citation rate, average per article
26	Analysis of the biotechnological potential of rare extremophilic micro-organisms, plants, fungi	4, 5	AIC	31,6	14,3	16,7
27	Cell factory	1, 4, 5	All industries SB	29,6	32,3	32,6
28	Descriptive analysis of microbial genomes	1, 4	Medicine, AIC, Ecology	25,3	15,6	23,1
29	Neurogenesis and therapy of neurodegenerative diseases	4	Medicine	25,3	19,5	53,4
30	Genetic editing, creating plants with 'pre-programmed' properties	4, 5	AIC	100	12,9	29,6
31	The search for new 'targeting' in medicine	2, 4, 5	Medicine	70,5	13,1	35,0
32	Production of biopreparations	4, 5	Pharma	63,1	11,9	54,5
33	Viral delivery vectors	4, 5	Medicine, pharma	47,7	7,0	18,5
34	RNA synthesis	1, 2, 5	All industries SB	40,9	2,2	44,8
35	Fag libraries	2, 5	All industries SB	37,6	3,7	27,4
36	Molecular machines	1, 2, 4	All industries SB	34,3	8,5	36,4
37	Cellular interactions	1, 4, 5	All industries SB	29,3	2,7	22,3
38	Scaffold protein	2	All industries SB	27,2	9,5	27,2
39	Molecular tools	1, 2, 5	All industries SB	23,6	11,5	26,5
40	The regulation of synthetic biology	4, 5	All industries	23	55,0	23,8
41	Marker-mediated selection	4, 5	AIC	21,7	10,5	8,5

№	Scientific and technological frontiers	Challenge	Industry	Sciometric indicators, 2000-2020		
				Publ. volume worldwide, thds.	Compound annual growth (CAGR), %	Citation rate, average per article
42	The "one health" concept	4	Medicine	18,2	20,9	29,5
43	Production of chimeric proteins (containing the activity of two or more target proteins)	2, 4, 5	All industries SB	16,8	-0,5%	18,3
44	Synthesis of nutrient media for cell cultivation	4, 5	Medicine, pharma, AIC, energy	15,9	10,3	20,6
45	Organisms with modified DNA/RNA	1, 4, 5	All industries SB	14,6	7,9	16,0
46	Biosurfactants	4, 5	AIC, Ecology	14	14,3	22,9
47	Cultivated skin	1, 4, 5	Medicine	13,4	10,7	31,9
48	Human cell editing (blood cells, stem cells and others)	1, 2, 4	Medicine	12,3	47,5	36,2
49	Genome libraries of plants and micro-organisms	3, 5	All industries SB	12	-4,0	16,3
50	A study of glioblastoma, the mechanism of transmission blockage	2, 4	Medicine, pharma	11,3	16,7	22,4
51	Creating recombinant proteins	2, 4, 5	All industries SB	10,1	12,1	59,9
52	Bioprinting of organs	4	Medicine	8,5	119,7	40,5
53	Biodata	3	All industries SB	6,9	15,2	15,0
54	Networked biolaboratories	3, 4	All industries SB	6	6,7	8,9
55	Cell cultivation	1, 5	Medicine, pharma, AIC, biomaterials	5,3	7,9	23,1
56	De novo obtaining cells through genomic editing	1, 4, 5	All industries SB	4,7	39,3	17,1
57	Treatment methods for orphan diseases	2, 4, 5	Medicine, pharma	4,7	14,9	20,1

№	Scientific and technological frontiers	Challenge	Industry	Sciometric indicators, 2000-2020		
				Publ. volume worldwide, thds.	Compound annual growth (CAGR), %	Citation rate, average per article
58	Production of alternative proteins	2, 5	All industries SB	4,5	12,2	16,1
59	Analysis of thermophilic micro-organisms	4, 5	AIC, Ecology	3	6,8	16,5
60	Editing micro-organisms for bioremediation	4, 5	AIC, Ecology	2,2	71,9	27,4
61	Bacterial cell transformation	1, 4, 5	All industries SB	2	6,4	23,0
62	Identifying the ecological roles of symbiotic of micro-organisms	4, 5	Ecology	1,1	17,1	18,7
63	Genetic libraries	1, 2, 5	All industries SB	1	11,8	24,1
64	Digital modelling in biodesign	3, 5	All industries SB	0,8	15,1	11,7
65	Digitisation of consciousness and Wetware for transferring consciousness	3, 4, 5	Medicine	0,57	21,6	8,1
66	Chimera animals	4, 5	Medicine, AIC	0,52	4,0	16,5
67	Storing information with the help of microorganisms (since 2010)	1, 5	All industries SB	0,37	18,5	31,9
68	AI platforms in bioengineering	3, 5	All industries SB	0,35	53,9	12,4
69	Creating artificial nucleic acids	1, 2, 5	All industries SB	0,3	8,6	10,2
70	Creating new drug platforms	4, 5	Medicine, pharma	0,24	61,8	24,8
71	Chimeric micro-organisms	1, 4, 5	Pharma, AIC, Energy, Ecology	0,2	0,6	21,6
72	Personalised veterinary diagnostics (since 2010)	4, 5	AIC	0,17	15,3	6,3

№	Scientific and technological frontiers	Challenge	Industry	Sciometric indicators, 2000-2020		
				Publ. volume worldwide, thds.	Compound annual growth (CAGR), %	Citation rate, average per article
73	Research on dark RNA for use as biomarkers in personalised medicine (since 2016)	1, 2, 4	Medicine, pharma	0,15	8,4	43,0
74	Microbiome, metagenomics, metabolomics (since 2017)	1, 2, 5	Medicine	0,1	165,3	22,7
75	Synthesis of new vaccine platforms	4, 5	Medicine, pharma	0,1	40,0	22,8

Table 3.
Science and technology frontiers of synthetic biology

Source: CSR North-West according to Scopus

Additionally, to table 3, a matrix of S&T fronts is presented as another form of visualisation (the set of science topics in the matrix fully duplicates the list in the table), which visually divides all topics into four segments (see Figure 9). The upper left and right segments deserve special attention, with the fastest growing frontiers that have an average annual publication growth rate of over 12% between 2000 and 2020 (CRISPR-Cas9, omics, protein-protein interaction, metagenomics, cybersecurity, human cell editing, etc.).

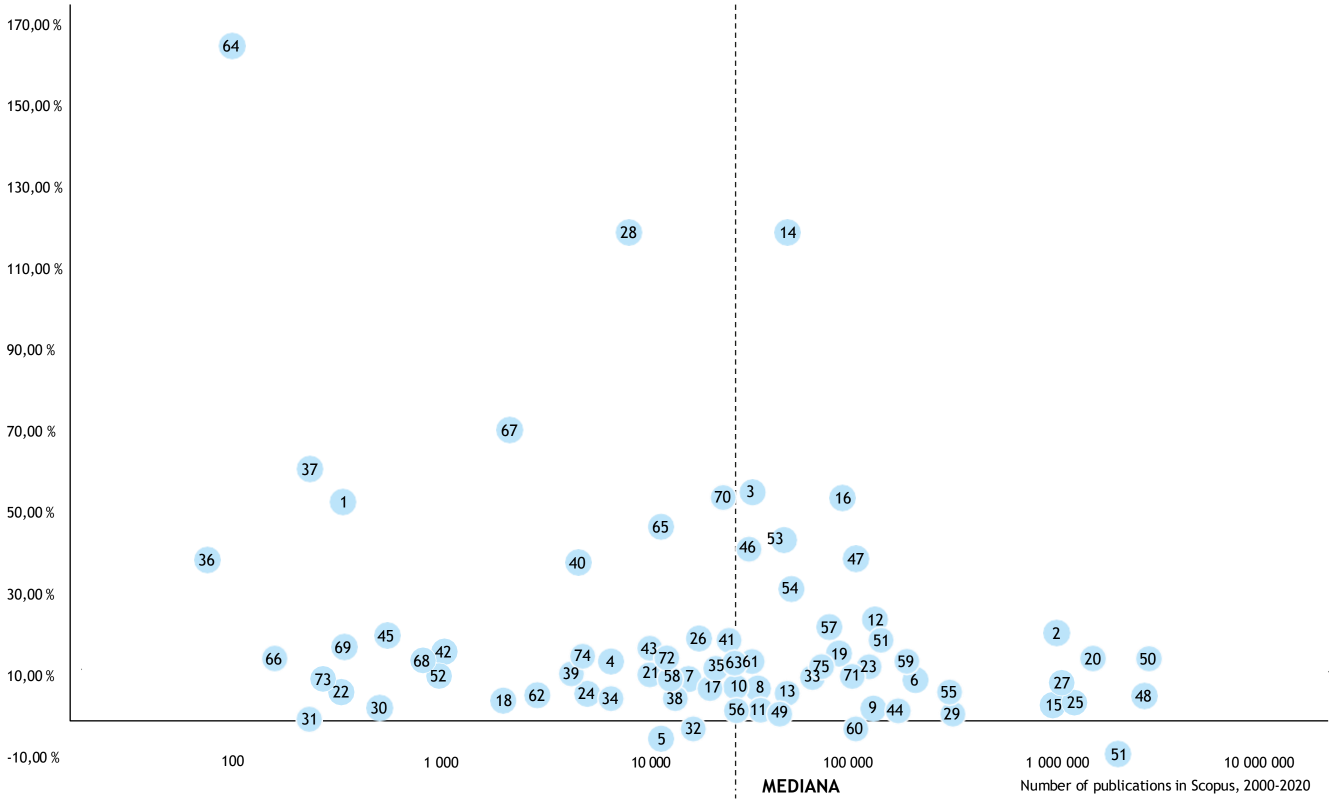


Figure 9.
Matrix of scientific and technological fronts for synthetic biology

Source: CSR North-West based on Scopus data, 2000-2020. Note: The matrix reflects fronts with the volume of
of publications more than 1,000 articles over the analyzed period

1. AI platforms
2. Machine Learning
3. Cybersecurity
4. Biodata
5. Genome libraries
6. Bioreactors
7. Synthesis of nutrient media for cell mass cultivation
8. Molecular machines
9. Protein network engineering
10. Scaffold proteins
11. Phage libraries
12. Microfluidics
13. Viral delivery vectors
14. CRISPR-Cas9
15. Cell and tissue culture technologies
16. Omics technology
17. Marker-mediated selection
18. Bacterial cell transformation
19. Extraction of genetic material
20. Biomarkers: cancer markers, markers of ageing
21. Creating recombinant proteins
22. Creating artificial nucleic acids
23. Obtaining secondary plant metabolites
24. Cell cultivation
25. Polymerase chain reaction
26. The concept of "one health"
27. Obtaining target metabolites
28. 3D bioprinting (organs, tissues)
29. Protein synthesis and mutation
30. Chimera animals
31. Chimeric micro-organisms
32. Chimeric protein production
33. Production of biopreparations
34. Network laboratories
35. Molecular tools
36. Synthesis of new vaccine platforms
37. Creating new medicinal platforms
38. Organisms with modified DNA/RNA
39. Production of alternative proteins
40. De novo cell production through genomic editing
41. Neurogenesis and therapy of neurodegenerative diseases
42. Identifying the ecological roles of symbiotic microorganisms
43. Biosurfactants
44. Protein folding (protein structure prediction)
45. Digitisation of consciousness and Wetware for transferring consciousness
46. Biobank of biodiversity and genetic resources
47. Personalised medicine
48. Gene expression
49. RNA synthesis
50. Bioinformatics
51. Genome sequencing
52. Genetic libraries
53. Metagenomics
54. Cell factory
55. Protein-protein interactions
56. Targeted delivery of biopreparations, drugs
57. Cultivated skin
58. Mathematical modelling in bioengineering
59. Site-directed mutagenesis
60. Analysis of the biotechnological potential of rare extremophilic micro-organisms, plants, fungi
61. Analysis of thermophilic micro-organisms
62. Descriptive analysis of microbial genomes
63. Microbiome, metagenomics, metabolomics
64. Human cell editing
65. Personalised veterinary diagnostics
66. Editing micro-organisms for bioremediation
67. Digital modelling in biodesign
68. Storing information with the help of microorganisms
69. The regulation of synthetic biology
70. Creating plants with 'pre-programmed' properties
71. A study of glioblastoma
72. Vector medicines
73. Treatment methods for orphan diseases
74. The search for new 'targeting' in medicine

5 How the synthetic biology industry is structured and where the breakthrough innovation zone lies

In the area of breakthrough innovations in synthetic biology fall technology solutions aimed at transforming traditional industry technology chains. Biodesign technologies and other technological tools allowing the reproduction of cellular processes used in synthetic biology provide increased productivity, reduced resource costs through the ability to program micro-organisms for the specific industry task at hand. The impact of synthetic biology on process chains will vary and will depend on the specific industry application. In some industries, synthetic biology will change only the raw materials used by the companies without affecting the processes, in others it will fundamentally transform the process chain and the production process. In Case Study 1, Section 1 provides an example of the production of cultured cellular meat, which illustrates this situation well. Other examples are given below.

Case 4. Industry applications of synthetic biology.

Mining

Synthetic biology technologies help to improve the productivity of existing products or processes. The mining industry, for example, uses heap leaching at mining sites for metals such as copper, uranium and gold. Traditionally, alkaline cyanide is used to treat the crushed ore, which produces toxins and generates large quantities of waste. Some companies, such as Rio Tinto (Spain), BHP Cerro Colorado (Chile) and Cananea (Mexico), experiment with bioleaching and bio-oxidation. By using synthetic biology tools, they extract various rare metals using water and microorganisms instead of alkaline cyanide.

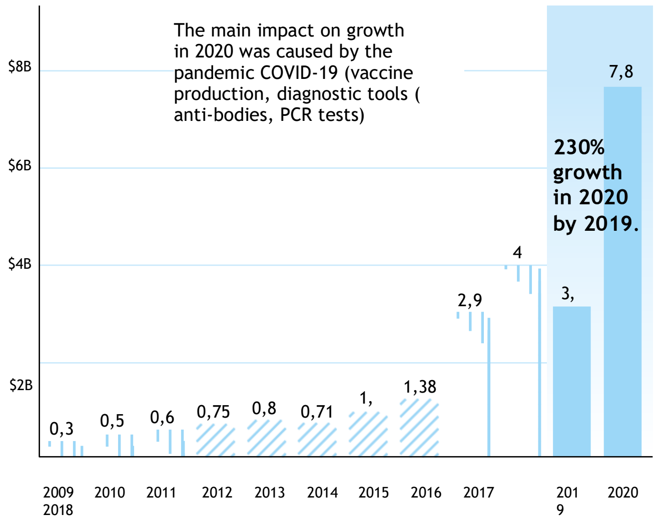
Food industries

Synthetic biology makes it possible to reduce the cost of scarce raw materials by obtaining products through fermentation of plant raw materials. The development of new methods of vanillin production without the use of vanilla bean is an example of a change in the industry's processing chains. Swiss biotech company Evolva has been working with world leader International Flavors and Fragrances (IFF) since 2011 on the laboratory development of vanillin. Evolva has invested in ingredient development, optimising their use and reducing the time needed to scale up production, while IFF is helping to scale up production and speed up the commercialisation process.

Source: Synthetic Biology Is About to Disrupt Your Industry. URL: bcg.com/publications/2022/synthetic-biology-is-about-to-disrupt-your-industry (accessed: 16.01.2022).

Synthetic biology is a fast-growing and investment-attractive market sector. Since 2009, investment in synthetic biology has been on the rise. In the first half of 2020, synthetic biology start-ups attracted US$3 billion[29], and by the end of 2020 investment exceeded US$7.5 billion (see Figure 10). The market for synthetic biology in 2021 was worth $6.88 billion (see Figure 11). By 2028, it is projected to grow to $11 billion, with a compound annual growth rate of 7%.

29 Synthetic Biology Startups Raised $3 Billion In The First HalfOf 2020. URL:forbes.com/sites/johncumbers/2020/09/09/synthetic-biology-startups-raised-30-billion-in-the-first- half-of 2020/?sh=2f131a021265 (accessed: 16.01.2022).



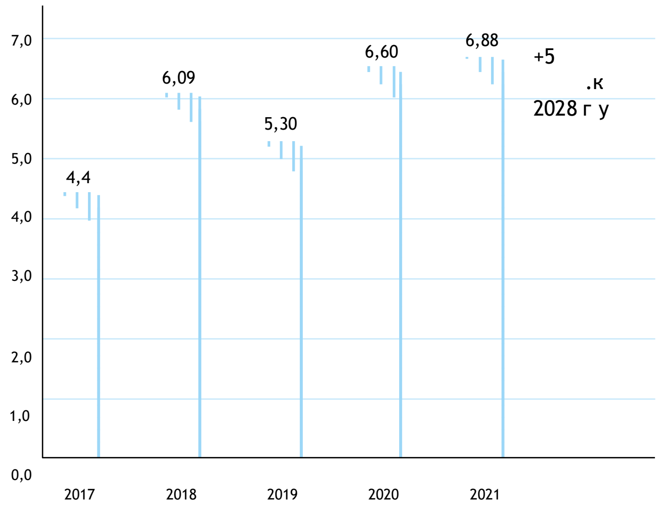


Figure 10
Investment in synthetic biology 2009-2020, billion USD

Source: Synbiobeta marketresearch

Figure 11
Synthetic Biologics Market Size, 2017-2021, billion USD

Source: Synbiobeta market research

Structurally, the synthetic biology market consists of four segments: 1) companies developing various software (software products) for biodesign; 2) companies producing equipment and hard systems; 3) companies producing reagents and chemicals needed for R&D and biomanufacturing; 4) industry start-ups forming new markets (e.g. vaccine markets of a certain type, synthesised spices/meats, biofuels, etc.) (see Figure 12) [30].

30 Synbiobeta: SynBio Stack. URL:synbiobeta.com/the-synbio- stack-part-1/ (accessed: 16.01.2022).

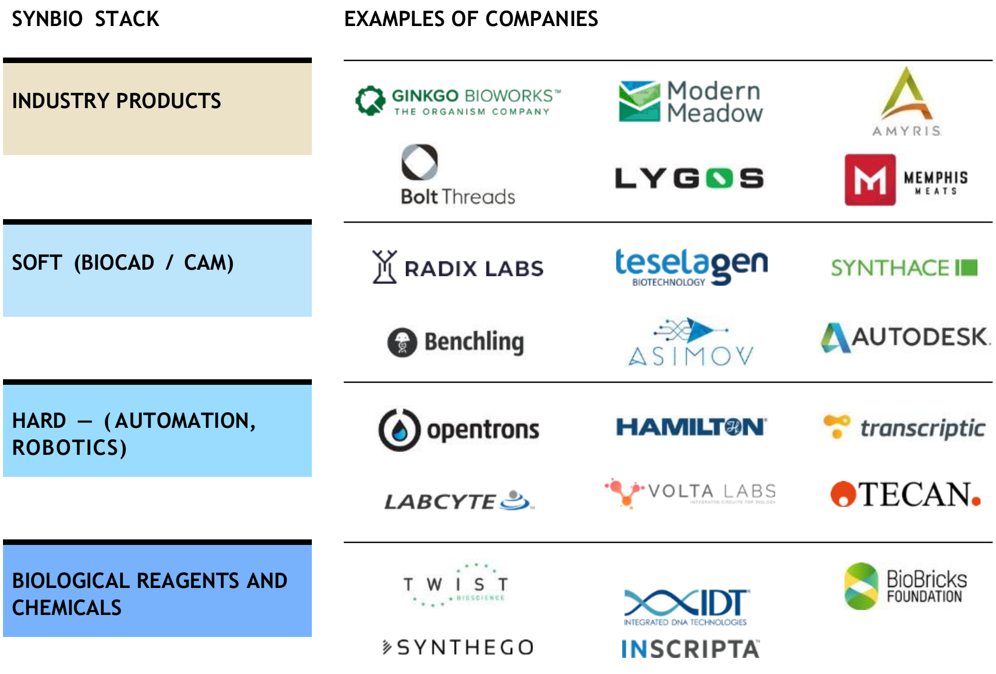


Figure 12:
SynBio Stack - Synthetic Biology Market Structure

Source: Sinbiobeta.
URL: synbiobeta. com/the-synbio-stack-part-1

According to StartUs insights, these segments are home to more than 480 start-ups worldwide in 2020. They also include unicorn companies (start-ups with a capitalisation of more than USD 1 billion) that sell products derived from synthetic biology tools and techniques. These products include, for example, protein compounds for medicine (Aprogen), drug biologics (Biosplice Therapeutics), AI systems for molecular design (XtalPi), alterative food protein (Impossible Foods), biotextiles (Spiber) and others.[31]

In terms of technological specialisation, Frost & Sullivan estimates the fastest-growing markets include low-cost DNA synthesis technology, sequencing, measurement and modelling techniques, and biodata handling techniques and tools. Segments and estimated compound annual growth rates to 2023 are as follows - gene synthesis (CAGR 24.4%), genome editing (CAGR 20%), site-directed mutagenesis (CAGR 20%), micro-, nanohydrodynamics (CAGR 19.9%), next generation sequencing methods (CAGR 17%), cloning and sequencing (CAGR 16%), measurement and modelling (CAGR 16%), bioinformatics (CAGR 16%) (see Figure 13) [32].

31 According to Crunch- base.

32 Frost & Sullivan, Global Synthetic Biology Industry Outlook — Futuretech TechVisionOpportunity Engine. TechVision Group of Frost & Sullivan. TechVision Opportunity Engines / D835 / 3./

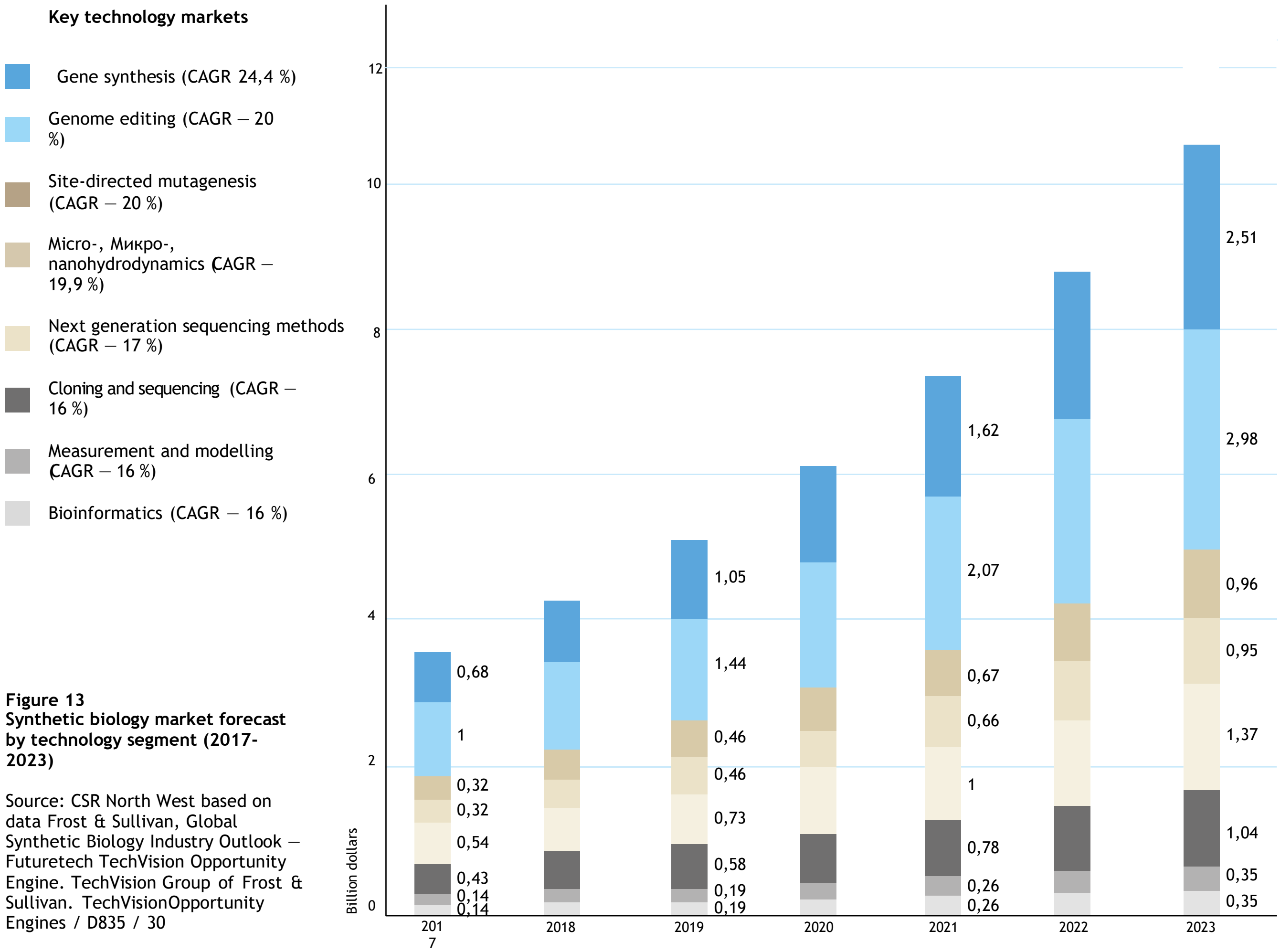


Figure 13
Synthetic biology market forecast by technology segment (2017-2023)

Source: CSR North West based on data Frost & Sullivan, Global Synthetic Biology Industry Outlook — Futuretech TechVision Opportunity Engine. TechVision Group of Frost & Sullivan. TechVisionOpportunity Engines / D835 / 30

The first half of 2021 represented a record for the industry, with investments of $4.7 billion in Q1 and $4.2 billion in Q2. There was also a more than twofold jump in 2020 compared to 2019, largely driven by the need for coVID-19 related solutions in pharma, medicine. The health and food sector are the largest area of investment (more than $5.5 billion in the first half of 2021, or 63% of total investment) (see Figure 14) [33].

33 Synbiobeta. Built with biology Q2 2021 Report.

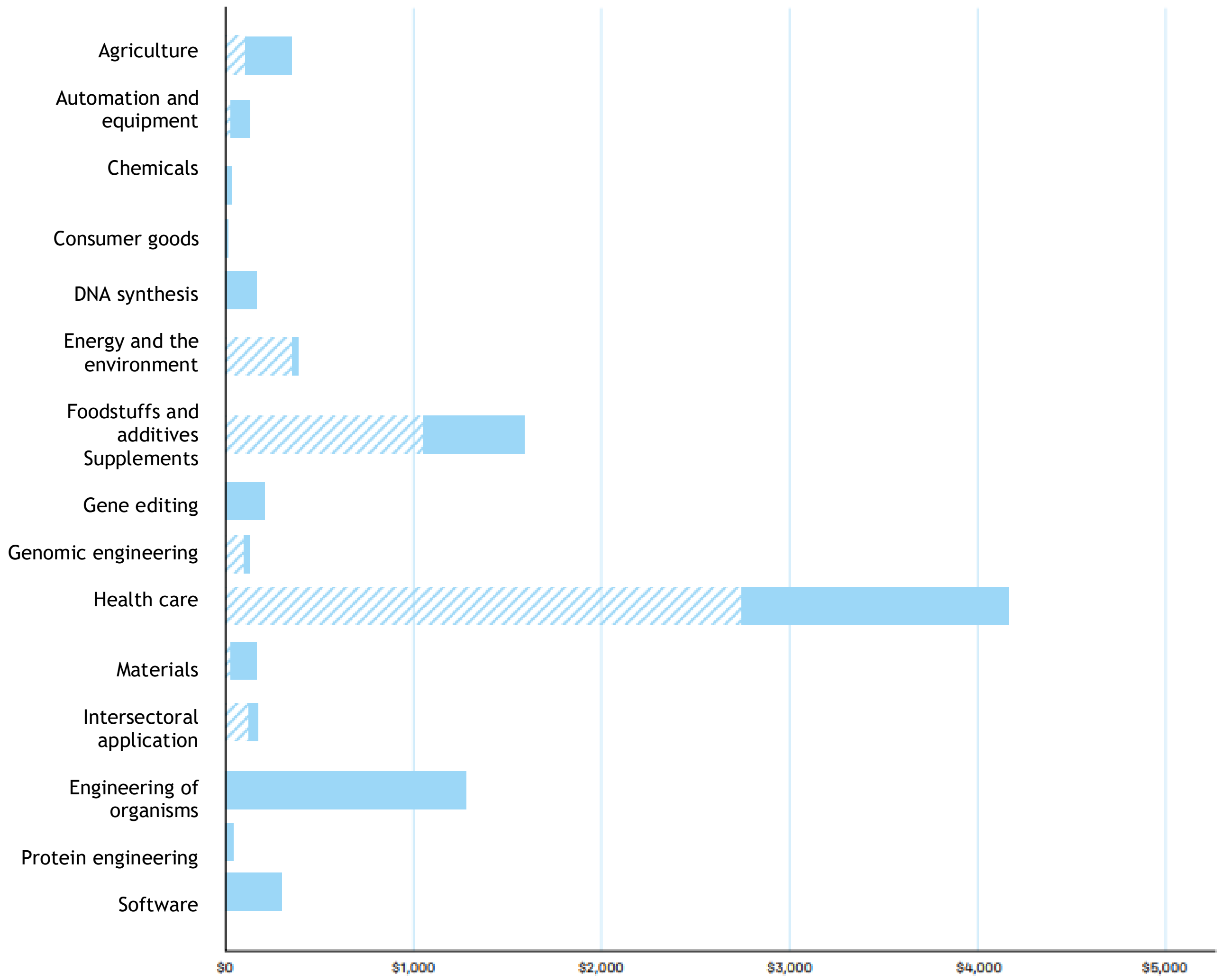


Figure 14
Volume of investments in synthetic biology companies by industry, Q1 and Q2 2021, million USD

Source: Synbiobeta. Built withbiology Q2 2021 Report

The current investor categories include: 1) mature players in the pharmaceutical, food industry and other markets who have budgets for experiments (e.g. Johnson & Johnson, Nestle SE); 2) IT companies that invest in projects at the intersection of digital and biotechnology (Microsoft, Alphabet, Netscape communications); 3) venture companies investing in high-risk projects in synthetic biology (LSP BioVentures (USA), Global Secure Invest (Czech Republic), Casdin Capital (USA), Temasek Holdings (Singapore), Horizons Ventures (China); 4) state funds supporting R&D institutions and experimental laboratories in early stages of research (Blue Sky Research) (EU framework programmes on NTD: priority "Biotechnology, MaxSynBio, Fraunhofer Society) (Table 4).

Types of investors	Feature	Examples
IT companies	Understand how the IT sector works Seeking new growth market segments Investing in companies at the intersection of IT and biotech	Microsoft, Google, PayPal, Sun Microsystems, Netscape, Yahoo!, Venmo
Venture capital funds and investment companies *	Predominantly working with biomedical, biotech, foodtech start-ups	LSP BioVentures (U.S.), Global Secure Invest (Czech Republic), Cascade Investment (U.S.), Casdin Capital (U.S.), Tiger Global Management (U.S.), Viking Global Investors (U.S.), Temasek Holdings (Singapore), Horizons Ventures (China)
Mature players **	Companies that are looking for new growth opportunities and have the budget to experiment	Johnson & Johnson — therapeutics, personal care, diagnostic and drug platforms, vaccines (R&D: $12.1 billion) Saudi Aramco — biocatalyst technologies in oil refining, hydrogen and bioenergy (R&D: $0.7 billion) Nestle SE — protein development platforms, reducing CO2 emissions in supply chains (R&D: $1.7bn) China Everbright Environment Group — green biomass technology, water bioremediation (R&D: $20 million)
Government programmes	Operators of the programmes are - Ministries/Academies of Science UK and USA have special programmes in synthetic biology In most countries synthetic biology is a separate priority of SRT programmes	USA - Department of Defence: «Living Production Systems» Programme China - Programme 973: «Synthesis and Advanced Studies» EU Framework Programmes for SRT: priority «Biotechnology» UK - «Synthetic Biology for Growth» Germany - «Biotechnology 2020+» France - «Investing in the future»

Table 4.
Types of investors in the synthetic biology segment

Source: SynBioBeta, Crunchbase, Ministry of Scienceand Technology of China;
Asia - Pacific Biotech, CORDIS, Biotechnology and Biological Sciences Research Council, DAPRA

* Biggest investors in start-ups that have attracted the highest amount of investment in 2020-2021, as ranked by SynBioBeta and according to Crunchbase (Impossible foods, Ginkgo Bioworks, Intellia Therapeutics, Zymergen, Jellatech, MeliBio).

** The largest companies by market capitalisation in the health, medicine, food and environment (environment, remediation, waste management) sectors.

The ecosystem of players in synthetic biology as a scientific field and global manufacturing industry has now reached a huge scale and encompasses all the key economic centres of the world, including the USA, Canada, Western European countries and China (see map of key players in Figure 15). The ecosystem is made up of universities and research centres (over 60 worldwide), 29 Biofaundries, at least five global specialised consortia (more about R&D market players in Chapter 3) and a number of businesses with strong growth ambitions in various synthetic biology - more than 250 start-ups and 15 unicorn companies.

Types of players

1

R&D centres (universities and research centres carrying out R&D)

2

companies (application customers, start-ups including unicorn-companies)

3

Investors (mature market players, technology companies, venture capital funds, government funds)

4

State (support for science, infrastructure and conditions for innovation, legal regulation)

5

Consortia (groups of players to solve complex problems)

CANADA

- 2 R&D-centres (University of Toronto, Université McGill)
- 13 start-ups (Deep Genomics, Concentric, Ardra Bio)
- 2 BioFoundries

USA

- 32 R&D-centres
- 184 start-ups (Ginkgo Bioworks, iGEM)
- 6 BioFoundries
- 11 companies (Intarcia Therapeutics, Biosplice Therapeutics)
- The Synthetic Biology consortium; The Engineering Biology Research consortium (EBRC)

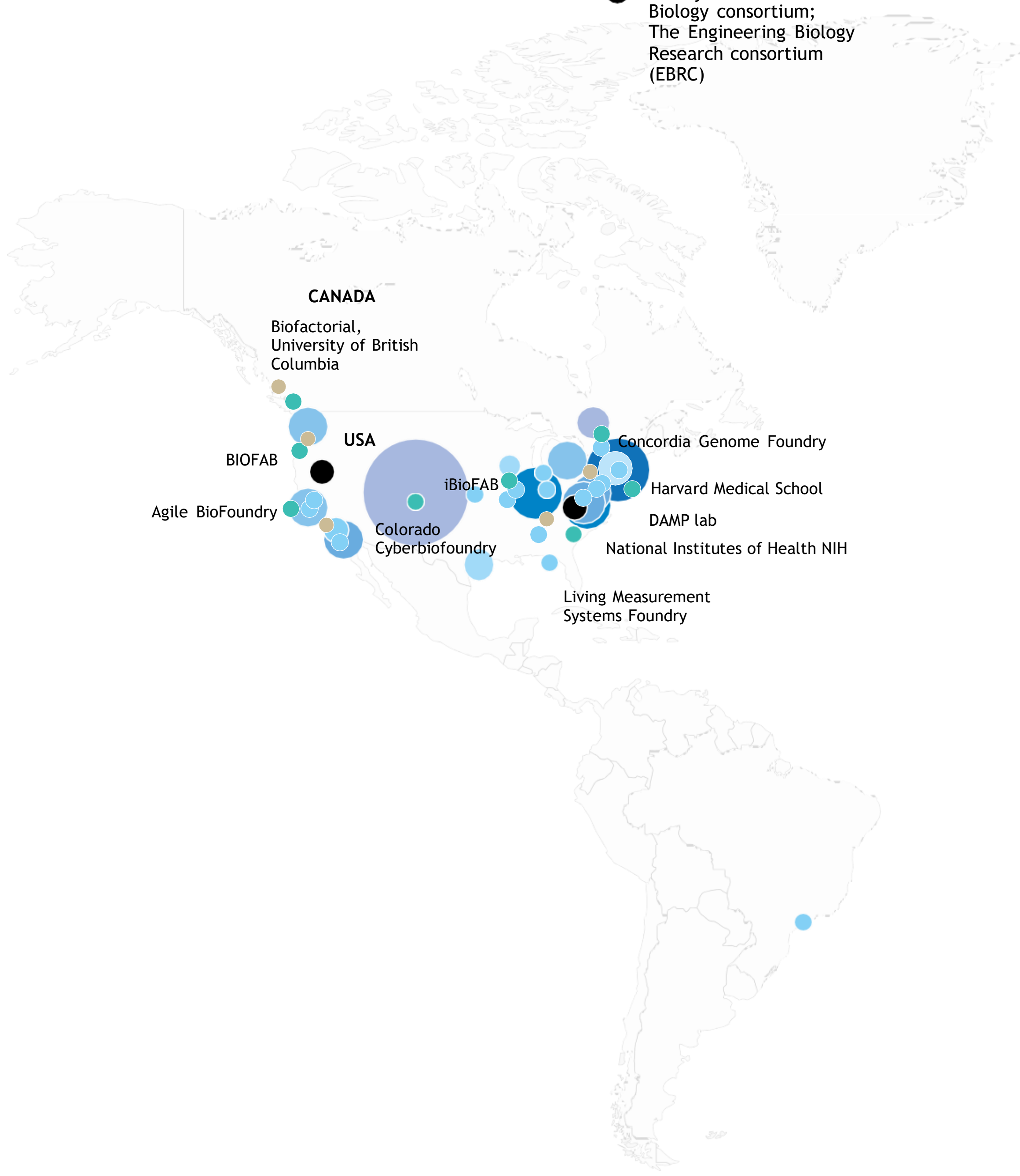


Figure 15
Geographical concentration and typology of synthetic biology players in the world in 2021

Source: CSR North West based on data from Scopus, Golden.com, Global Biofoundries Alliance, CB Insight

- R&D centres - established research schools in gene research, proteomics, etc., and experimental laboratories (by Scopus publication volume)*
- Start-ups (punctuation size - number of start-ups) **
- Biofoundry — worldwide functioning 29 (dedicated infrastructure for biodesign)***
- Unicorns in synthetic biology****
- Consortia

Scopus publication volume

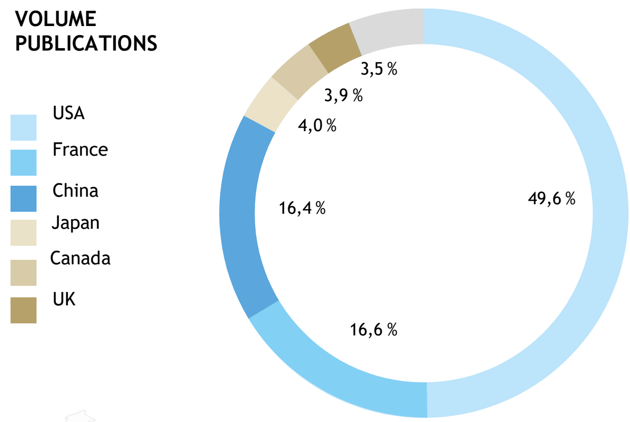
54 — 82 707

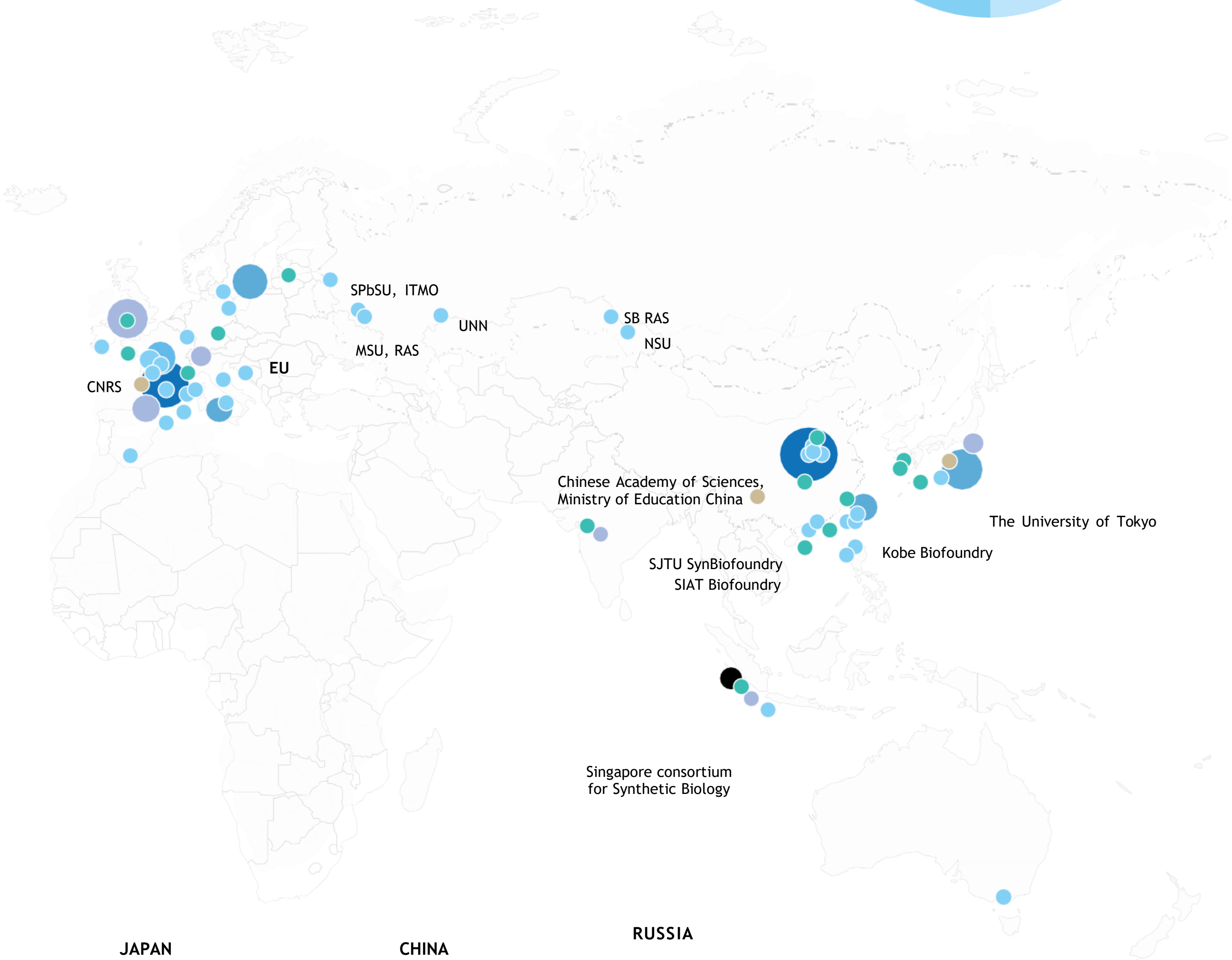
UK

- 5 R&D-centres (University of Cambridge, University of Oxford)
- 36 start-ups (Cargill, Synpromics Ltd, Bento Bioworks)
- 5 BioFoundries (GeneMill, SYNBIOCHEM, London BioFoundry ICL, EdinburghGenome Foundry)

FRANCE

- 5 R&D centres (Inserm, CNRS Centre National de la Recherche Scientifique, etc.)
- 11 start-ups (Algama, Sartorius, etc.)
- 1 company (Ynsect (agriculture)





JAPAN

- 3 R&D centres (The University of Tokyo, etc.)
- 6 start-ups (Kyocera, Genewiz, etc.)
- 1 BioFoundriy (Kobe Biofoundry)
- 1 company (Spiber (synthetic materials industry)

CHINA

- 15 R&D centres (Chinese Academy of Sciences, Chinese Ministry of Education, Fudan University, etc.)
- 5 BioFoundries (Tiajin University Biofoundry,SIAT Biofoundry, SJTU SynBiofoundry)
- 1 company (XtalPis (software development))

RUSSIA

Start-ups: Planta, Light Bio

6 REGULATION OF SYNTHETIC BIOLOGY IN THE WORLD

countries' leadership in developing synthetic biology markets is determined not only by scientific and technological competencies and access to dedicated infrastructure, but also by regulatory issues, which can be a key barrier to entry into these markets. countries that fail to put in place a comprehensive set of mechanisms and regulatory frameworks will lag behind.

At the international level, the regulation of synthetic biology is based on the United Nations Convention on Biological Diversity, the Cartagena Protocol and the Nagoya Protocol. Within the European Union, the majority of synthetic biology research under GMO legislation relates to genetic engineering. European Union legislation is based on Directive 90/219/EC (governing genetic modification of micro-organisms and their cultivation, storage, transport, destruction and utilization) and Directive 2001/18/EC (governing the deliberate release of GMOs).

However, regulation of synthetic biology technologies is not limited to genetic engineering, biotechnology and biodiversity. Although traditionally support programmes for synthetic biology have been an integral part of biotechnology sector development programmes, synthetic biology is now becoming a separate priority of federal S&T development programmes and a regulatory area in its own right in most developed countries. Most often, such programmes are administered by ministries, national academies of science, and Councils of state for the purposes of science and technology..

Specific programmes to support synthetic biology, for example, have been established in the UK and the US. The UK, in particular, is one of the first countries to actively develop the synthetic biology sector, both at the infrastructure and programme-strategy level. In 2012, the UK published a strategic roadmap for synthetic biology, based on the concept of realising the potential of synthetic biology with a focus on economic success, exploiting cutting edge science and clear societal benefits. In 2015, the UK Synthetic Biology Strategic Plan was published, focusing on accelerating the commercial delivery of new products and services and the need for responsible research and innovation, proportionate and adaptive regulation [34].

Table 5 provides basic information on government support programmes for synthetic biology.

34 Keiper F, Atanassova A. Regulation of Synthetic Biology: Developments Under the convention on Biological Diversity and Its Protocols. Front Bioeng Biotechnol. 2020. doi:10.3389/fbioe.2020.00310.

Country	Document	Status	Year	Budget	Programme operators	The place of synthetic biology (CO)
China	National programme of basic research (Programme 973) Sub-section «Synthesis and Advanced Studies»	State programme at the national level	1998	0,75-1,125 million dollars	Ministry of Science and Technology Chinese Academy of science	Funded by individual CO projects including for energy, agriculture, health care, etc.
EU	Framework programmes on STDs the 6th Programme - Natural Sciences, Genomics and Biotechnology for health 7th programme - Food, Agriculture, Biotech 8th programme - Biotechnology	Open international programme support	2005	491,4 million dollars	EU Council, European Parliament	Funded by individual CO projects within the priority for biotechnology development
Germany	Biotechnologie 2020+	Departmental industry programme of the ministry	2010	143 million dollars	Ministry of Education and Science	Funded by individual CO projects MaxSynBio, Fraunhofer Society: Biomolecules off the assembly line, Bio/Synthetic multifunctional micro production units
France	Investments for the Future programme	State programme at the national level	2010	24 billion dollars during the period from 2021 to 2026	National Research Agency-	Funded by individual projects CO
UK	Synthetic Biology for Growth Programme	Programme non-government public body	2012	141 million dollars	Biotechnology and Life Sciences Research Council	The specialised programme is entirely dedicated to CO
USA[35]	Living Foundries Program: ATCG Living Foundries: 1000 Molecules	Departmental sectoral programmes	2011-2014 2013 - n.a.	35 million dollars 110 million dollars	US Department of Defence (Office of Advanced Research Projects)	Specialised programmes are fully dedicated to CO
Canada	Collaborative Research and Training Experience	Departmental Federal agency programme	2018	1,65 million dollars	Natural Sciences Council and Engineering Research	Funded by individual teams and projects on CO themes

Table 5.
Programmes to support the development of synthetic biology around the world

Sources: Ministry of Science and Technology of the People´s Republic of China; Asia — Pacific Biotech; CORDIS; Bioökonomie.DE; ANR; Biotechnology and Biological Sciences Research Council; DAPRA, Global Biodefence; Natural Sciences and Engineering Research Council of Canada, Concordia

35 Si, Tong & Zhao, Huimin. (2016). A brief overview of synthetic biology research programs and roadmap studies in the United States. Synthetic and SystemsBiotechnology. 1. 10.1016/j. synbio.2016.08.003.

The main trends related to the regulation of synthetic biology are listed below.

1 There is a large group of public investors in the world (USA, China, France, Germany, UK) funding research in synthetic biology and expanding support mechanisms through the creation of special funds and grant programmes. These countries (including the most important Asian states for Russia) are the ones that will put pressure on industry regulation in the future. For example, the European Commission actively supports synthetic biology research - €38.9 million were allocated to European centres for synthetic biology projects in 2020 (€9.4 million in 2011).

2 Emergence of national biodata storage systems (including banks of standardised biological components) [36] as key objects of synthetic biology will require special regulation in this area. Access to large amounts of biological data is one of the main conditions for the development of synthetic biology. The growing production of biological data not only requires developing the infrastructure of bio-data banks (which allow continuous access to updated bio-data, thereby accelerating research[37]), but also their security and ethical use (more details in 3 and 4) - an issue of national importanceIn addition, to speed up and cheapen research and production in synthetic biology, banks of standardised biological parts will need to be established[38]. Standard setting involves, on the one hand, a decision at the level of the research community, which should define the main standard parts and processes of biological systems [39]. On the other hand, regulation by the state can be an additional driver for the standardisation process, including the introduction of special regulations to support the establishment of standards and their implementation in research centres and production facilities [40].

3 Tightening policies related to biosafety. The rapid advances in synthetic biology and the rapid integration of digital technology are contributing to the rise in biosecurity issues. The growing number of users with access to biological data complicates the ability to control their use. This exacerbates the problem of producing dual-use technologies and biological weapons through the use of synthetic biology and genetic engineering technologies. Existing regulations in the area of genetic information protection (e.g. the Genetic Information Non-Discrimination Act, GINA) do not cover all aspects of apparatus infrastructure and cloud software security. The importance of biodata in biosafety issues is also not fully taken into account in the Dual Use Research of concern (DURC) policy. The scope of regulation of this policy is limited to individual agents, which does not entail the regulation of new organisms created by synthetic biology [41, 42].

36 Examples of biodata repositories are: European Genome-Phenome Archive (EGA), European Nucleotide Archive (ENA), three-dimensional protein and nucleic acid database (PDB), functional genomics database (ArrayExpress).

37 Stephen K. Burley, Charmi Bhikadiya, Chunxiao Bi, Sebastian Bittrich, Li Chen, Gregg V. Crichlow, RCCO Protein Data Bank: powerful new tools for exploring 3D structures of biological macromolecules for basic and applied research and education in fundamental biology, biomedicine, biotechnology,bioengineering and energy sciences, Nucleic Acids Research, Volume 49, Issue D1, 8 January 2021.

38 Decoene T., De Paepe B., Maertens J., et al. Standardization in synthetic biology: an engineering discipline coming of age. Crit Rev Biotechnol. 2018;38(5). doi:10.1080/07388551.2017.1380600.

39 One example of an approach to the standardisation of synthetic biology is the creation of the Biobricks Foundation and the Registry of Standard Biological Parts. This approach has evolved around the idea of developing and providing standardised genetic parts, called "BioBricks", which can be used to build complex systems.

40 Zhao H., & Medema M. H. (2016). Standardization for natural product synthetic biology. Natural product reports, 33(8). doi.org/10.1039/c6np00030d.

41 Dieuliis, Diane. (2018). BiodataRisks and Synthetic Biology: A Critical Juncture. Journal of Bioterrorism & Biodefense. 09. doi:10.4172/2157-2526.1000159.

42 Li J., Zhao H., Zheng L. andAn W. (2021) Advances in Synthetic Biology and Biosafety Governance. Front. Bioeng. Biotechnol. doi: 10.3389/fbioe.2021.598087.

4

Ethical regulation and popularisation of synthetic biology. Discoveries in biotechnology and synthetic biology raise ethical concerns about the need to control interference with the genome, the secrecy of genetic information, etc., as well as the legal and social implications of such research (Ethical, Legal and Social Implications, ELSI)[43]. According to Cambridge University, public interest in bioethics has grown significantly since 2017. To a large extent, bioethics issues focus on preventing the use of advanced technologies for biological weapons [44]. Bioethics education is being actively promoted in developed countries (bioethics is at the core of special educational programmes in Europe and the United States). States and the international community are taking gradual steps toward institutionalising bioethics issues. At the state level there are established such structures as the Presidential Council on Bioethics (USA), National Advisory Council on Ethics (France). At the international level, the United Nations (UNESCO), the Council of Europe, the International Bioethics committee, etc. are involved in policy-making on issues of bioethics. Ethics in synthetic biology has two main functions. On the one hand, it is an academic discipline that studies the value and normative issues that synthetic biology raises. On the other hand, ethical issues regulate research and production in synthetic biology in order to prevent harm, reduce risks and control conflicts of interest[45]. Discussion of ethical and social issues is long represented in the agenda of synthetic biology. For example, they have been discussed in different formats at international meetings of the Biobricks Foundation.

43 ARNASON, G. (2017). Synthetic Biology between Self-Regulation and Public Discourse: Ethical Issues and the Many Roles of the Ethicist. Cambridge Quarterly of Healthcare Ethics, 26 (2). doi:10.1017/S0963180116000840.

44 Maria Belén Paredes, Maria Eugenia Sulen. An overview of synthetic biology. DOI. 10.21931/RB/2020.05.01.14 URL: revistabionatura.com/files/2020.05.01.14.pdf (accessed: 16.01.2022).

45 HÄYRY, M. (2017). Synthetic Biology and Ethics: Past, Present, and Future. CambridgeQuarterly of Healthcare Ethics, 26(2). doi:10.1017/S0963180116000803.

7 THE POTENTIAL OF RUSSIA

In Russia, synthetic biology has only just begun to emerge as an independent sector of science and the economy. The slow pace of development is primarily caused by the lack of a systemic order for this kind of research in the country both from the state and from business, although individual developments in this area are certainly underway and business is already investing in them (for example, «EFCO» in the field of food industry). In addition, there are infrastructural constraints (lack of suppliers of the necessary equipment, software and reagents for scientific experiments), a low level of R&D cooperation and an underdeveloped regulatory system for the industry. The insufficient speed of removal of these barriers limits Russia's capabilities, which are particularly sensitive to the development of its economy under sanctions restrictions. Synthetic biology can provide strategic solutions to a range of problems in the healthcare, food industry, agribusiness, energy and ecology. This new branch of science could become a centre of attraction for a large number of researchers, generating patents in socially important areas of the economy.

Below are the barriers to be overcome by synthetic biology as a promising scientific discipline and a new economic sector in Russia.

Firstly, there is a barrier of low research and publication activity to be overcome. In terms of scientific publications Russia is still far behind the leading countries. The share of Russian publications by Scopus on synthetic biology (by the keyword "Synthetic biology") in the period 2000-2021 is 0.86% (249 articles), Web of Science is 1.83% (1503 articles). During the same period, the US publication volume was 10,918 articles by Scopus (38%), 30,531 articles by Web of Science (37.3%); the publication volume of China had a publication volume of 3,562 Scopus articles (12.4%), 10,424 Web of Science articles (12.7%). Although quantity is not always equal to quality, Russia needs to increase its activity in this area. The positive thing here is that Russia has shown an increase in the volume of publications throughout the observed period, especially since 2016[46]. There are some strong competences in the country. First and foremost is the area of bioinformatics and data management. In terms of the compound annual growth rate of publications in bioinformatics (in the period 2010-2020) Russia is ahead of the USA and China. The indicator was 23.9% for publications in Scopus (USA - 5.7%, China - 12%) and 15.5% for publications in Web of Science (USA - 4.2%, China - 9.1%). However, the share of Russian publications is only 1.38% (Scopus) and 1.49% (Web of Science) [47].

Secondly, there is the challenge of overcoming the insufficient level and pace of development of the necessary research and innovation technology infrastructure, research cooperation in synthetic biology in the presence of strong accumulated capacity:

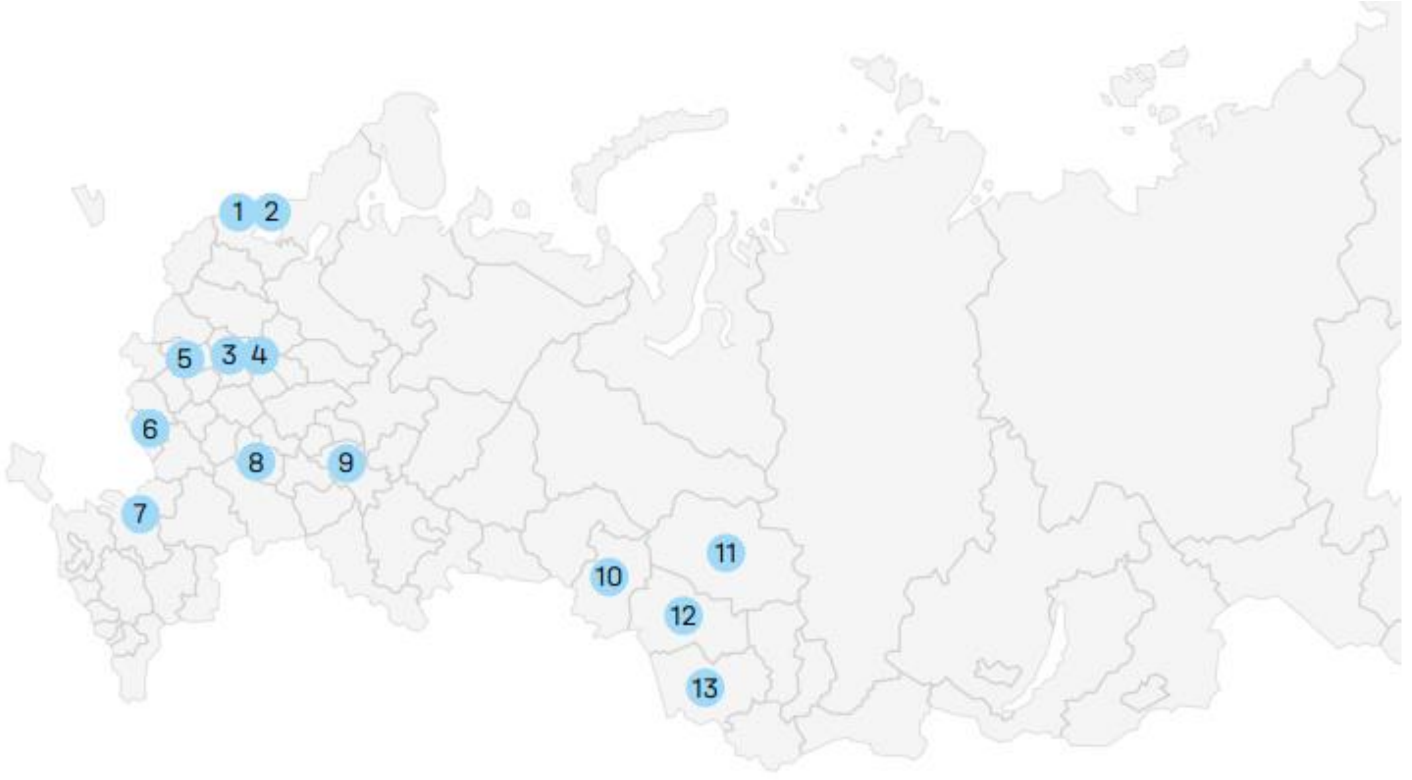
- There are strong centres with competencies in biological, chemical, bioengineering and related fields. The centres are gradually building up laboratories, experimental research groups aimed at solving research problems in synthetic biology. These include IBCh RAS, Federal Centre of Biotechnology RAS, Institute of Biochemistry. A. N. Bach, The K. G. Skryabin Institute of Bioengineering, Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences, Engelhardt Institute of Molecular Biology of Russian Academy of Sciences and others, which together ensure the leadership position of the RAS

46 CSR North-West according to Scopus, Web of Science.

47 CSR North-West according to Scopus, Web of Science; CSR North-West according to materials of interviews with Shityakov S.V. (15.10.2021), Gusev O. A. (25.10.2021).

In Russia in terms of the volume of publications in Scopus, Web of Science in the field of synthetic biology, the leader is MSU (Faculty of Biology - departments of Bioengineering, Biochemistry and Synthetic Biology, Faculty of Bioengineering and Bioinformatics, School "Molecular Technology of Living Systems and Synthetic Biology"), SPbSU - Institute of Chemistry (Laboratory of Biohybrid Technology), ITMO — Infochemistry Research Center, Bioinformatics Institute, KFU — Institute of Fundamental Medicine and Biology (Regulatory Genomics Research Centre), NSU — «Synthetic biology», implemented as part of Project 5-100 Lobachevsky State University of Nizhny Novgorod.

13 clusters implement activities in the fields of biotechnology, biomedicine, biopharmacology and agro-biotechnology, which contribute to accelerating the development of the biotechnology market in general, forming and strengthening technological competences and creating new products in emerging markets, which include synthetic biology in particular (see Figure 16).



1. Cluster of Medical, Environmental Instrumentation and Biotechnologies (St. Petersburg)
2. Cluster of medical, pharmaceutical industry, radiation technologies (St. Petersburg)
3. Cluster "Medical industry, new chemistry and biotech" (Moscow)
4. Biotechnical innovative territorial cluster Pushchino (Moscow Oblast)
5. Cluster "Pharmaceutics, biotechnology and biomedicine" (Kaluga Oblast)
6. Cluster "Biopharmaceuticals" (Belgorod Oblast)
7. "Biotechnologies" (cluster for deep processing of grain in the Millerovsky district of the RO) (Rostov Oblast)
8. Engineering and production "Biomed" (Penza Oblast)
9. Territorial and sectoral cluster of «AGROBIOPROM» (Republic of Tatarstan)
10. Agrobiotechnological industrial cluster (Omsk Oblast)
11. Innovative territorial cluster "Pharmaceuticals, medical equipment and information technologies of the Tomsk Oblast"
12. Innovative cluster of information and biopharmaceutical technologies in the Novosibirsk Oblast
13. Altai Biopharmaceutical cluster (Altai Territory)

Figure 16.
Geography of Russian biotechnology clusters and CCPs in 2021

Source: CSR North-West according to Map of Russian clusters. URL: map.cluster.hse.ru,

- Support programmes for biotechnology start-ups are available. For example, Skolkovo assists participants in entering the market and actively supports startups in the field of biomedicine (there is a mentoring programme aimed at training in preaccelerating projects, grant support in the form of micro grants, technological R&D services, Go-To-Market Department helps Skolkovo startups to enter international markets and attract funding, etc.).The Russian Venture company (RVC) uses various investment tools to support entrepreneurship and includes separate structures related to research in the field of biotechnology: "RVC seed Fund", "RVC Infrastructure Investments" (RVC Infrafund), "RVC Biopharmaceutical Investments" (RVC Biofund), "Bioprocess Capital Ventures"[48]. The presence of such programs contributes to the growth of Russian start-ups in the field of biotechnology. The Skolkovo Biological and Medical Technologies Cluster alone includes 612 biotechnology companies (startups) at various stages of development. The largest number of startups in Russia today relates to biomedicine and agricultural biotechnologies. There are separate technological projects in the field of synthetic biology, for example, scientists from the Russian-British startup Planta, a Skolkovo resident, have created luminous plants using the genes of fungi [49].

- In recent years, large Russian companies operating in the fields of biotechnology, food technology, and biomedicine have been launching special projects and allocating a budget (usually by creating special funds to support new projects in advance) for research and experiments in the field of synthetic biology. In 2019, "EFKO" created an early-stage venture fund called Fuel For Growth to invest in food tech. "EFKO" plans to launch the production of meat from vegetable protein in the Belgorod Oblast, for which it has invested 100 million rubles in the project, and by 2022 it plans to produce up to 40 thousand tons of artificial meat and cover about 0.4% of meat production in Russia [50]. В 2019 г. In 2019, the Ochakovo Food Ingredients Plant reported on its first "lean" minced meat cutlet. Its weight was 40 grams and 900 thousand roubles were spent on development. "Miratorg has opened an innovative genomic breeding centre, which is a Skolkovo resident and will become one of the top five genetic veterinary laboratories in the world; it will solve the most complex tasks of genome evaluation and genotyping of all types of farm animals [51].

In addition to the positive aspects and the accumulated potential, there are a number of problems, mainly related to the lack of a systematic approach to the development of research and technology infrastructure and the scientific community in the field of synthetic biology.

- There is a closure of the infrastructure at individual research institutes and universities, which leads to the dispersal of the necessary equipment, often the inability to use the resources of other research organizations [52]. In the world, this problem is solved due to the previously mentioned Biofoundries format, when large R&D tasks in synthetic biology are decomposed and distributed among various research centers, including taking into account the infrastructure available in these centers.
- In Russia, scientific consortiums in the field of synthetic biology and related scientific fields have not yet been formed. This leads to a decrease in cooperation between research groups, the lack of a unified R&D agenda and large research tasks. The development and functioning of scientific teams in synthetic biology occurs to a greater extent in isolation, within the framework of individual research centers.

48 Russian Venture Company (RVC). URL:biotech2030.ru/ instrumenty-gos-podderzhki/ fondy/rvk/ (accessed: 16.01.2022).

49 Scientists create glowing plants using mushroom genes. URL: theguardian.com/ science/2020/apr/27/scientists-create-glowing-plants-using-mushroom-genes (accessed: 16.01.2022).

50 EFKO is our answer to Beyond Meat. Release meat from sunflower protein. URL: quote.rbc. ru/news/article/5f60f5c69a794 702558a49fb (accessed: 16.01.2022).

51 Miratorg opened an innovative center for genomic selection. URL: miratorg. ru/press/news/miratorg-_ otkryl_innovatsionnyy_tsentr_ genomnoy_se/ (accessed: 16.01.2022).

52 CSR North-West based on interviews with K.S. Sarkisian (28.10.2021).

At the same time, world practice shows that the creation of consortiums is one of the key opportunities for the development of synthetic biology. For Russia after the events of 2022, it is important to decide on the configuration of such consortiums, apparently building a configuration of a “new openness” of science towards Asian partners and not forgetting to ensure its own technological stability and even autonomy (in the most significant critical nodes).

There is a shortage of suppliers of components and equipment necessary to support the development of synthetic biology (in the areas of SynBio Stack (see Figure 13), including suppliers of special software for biodesign, equipment, chemicals and reagents for experiments), which leads to industry dependence on imports[53]. This problem is already evident in the Russian biotechnology market as a whole - thus, according to Abercade Consulting, in 2018, imports dominated the biotechnology market (82% of the market volume)[54]. Large-scale software and hardware re-engineering programmes should be launched to address this deficit.

Thirdly, the barrier of low readiness of the regulatory system for the development of synthetic biology should be removed. In Russia, it is necessary to develop regulatory legal acts and specialised programs for the development of synthetic biology. This will open up new possibilities for this field of knowledge, as at present, only in general terms, synthetic biology falls under the scope of documents for the program-strategic regulation of biotechnologies (Comprehensive Program for the Development of Biotechnologies in the Russian Federation for the period up to 2020, Action Plan (roadmap) “Development of Biotechnologies and Genetic Engineering” for 2018 -2020, Federal Law "On biomedical cell products", "Biotechnologies. Classification of biotechnological products»), genetic engineering (Federal Scientific and Technical Programme for the Development of Genetic Technologies for 2019-2027, Federal Law "On State Regulation in the Field of Genetic Engineering Activity", Federal Law "On Biological Safety in the Russian Federation"), as well as ensuring biological safety.

It is necessary to ensure the focus of government grants and funding programs in a special way, shifting it from a general focus on the biotechnology market as a whole and support for its development towards a more focused topic, including synthetic biology. At the same time, it is necessary to increase the volume of investments from budgetary and non-budgetary sources for the corresponding development goals. So far, only the Russian Foundation for Basic Research has approved targeted grants for synthetic biology in Russia. The maximum grant amount is 6 million rubles. for a three-year project, which is a low value compared to investments in foreign start-ups [55]. Nevertheless, this is a good basic and foundation for the further development of this branch of knowledge. In the future, the volume of support for synthetic biology will have to be significantly scaled up.

53 CSR North-West based on based on the materials of interviews with Sarkisyan K.S. (28.10.2021), Tennikova T.B. (01.11.2021).

54 Overview of the biotechnology market in Russia and worldwide. Barriers and prospects for development. September 2019. URL: biotech2030. ru/wp-content/uploads/2019/09/Orlova-N-V.pdf (accessed: 16.01.2022).

55 Nature under the editorship. Development of synthetic biology in Russia is hindered by lack of money. URL: dp.ru/a/2019/02/12/Priroda_pod_redakciej (accessed: 16.01.2022).

Nikitin I.A., Head of the Department of Food Biotechnology from Plant and Animal Raw Materials, K.G. Razumovsky Moscow State Technical University

Source: Interview as part of the report preparation with Nikitin I.A. dated 06.04.2022

“Synthetic biology will be one of the drivers of the food industry in the future. Synthetic food products are a transformation of the food supply system as a whole: new rules of the game, new economic indicators, a complete paradigm shift. When the synthetic power system is built, it will be more efficient than the one we currently have. Synthetic biology will reduce the cost product value, meet the ever-increasing demand. I believe that we, as humanity, have no other choice. Synthetic products are the products of the future, and genetic engineering is just one step towards that. The sooner we understand this, the better. Another question is that there are moral aspects, long-term consequences, but all this is calculated, and relative harmlessness has already been proven.

In Russia, all this will be scaled up for a long time, because the country has a huge number of resources, unlike Europe. That's why neither the state nor business is interested in synthetic biology yet. However, the current crisis may spur the development of the industry, will stimulate the search for new opportunities to reduce the cost of food production, for import substitution of a number of lost links in production chains.

There is also personalised nutrition - an approach to compiling a diet and regulating eating habits, taking into account the genetic characteristics of a person, etc. Personalised nutrition is based on the achievements of modern science and stands on several whales, one of them is digital technology. With the help of them, we can collect and digitise data about a person. It is then possible to predict and identify the impact of particular nutritional factors on performance. And then, thanks to synthetic biology, we can control the properties and composition of food whereby each digital doppelganger will be matched with the synthetic food they need. So, one of the major challenges of synthetic biology is to regulate the precise nutrient content of the food to the needs of the individual end user.

Under the current situation, we see an exodus of foreign players who have been involved in the food industry. As a result, there is a shortage of necessary components for production. To avoid a state of vacuum, on the one hand we have to look for partners who still remain, like China, for example. On the other hand, the situation can be used to develop our own production facilities, we have backlogs in the field of computer design, we have strong schools. In this sense, synthetic biology will also contribute to this process. With its help, it is possible to recover missing components for the food industry. Of course, restoring the missing links in production will take years, something we won't be able to be able to recover. With its help, we can restore the missing components for the food industry. Of course, it will take years to restore the missing links of production, and we will not be able to restore something at all. But simple components, fructose, for example, its production is not such a complicated process - you can organise it in a month, but no one has done it yet ».

Sarkisian K.S., Head of the Synthetic Biology Group, Biomolecular Chemistry Department, IBCh RAS

Source: Reporting interview with K.S. Sarkisian, dated 28.10.2021

«When we talk about synthetic biology, this is a research field that is determined not by an object, but by an approach - engineering. Synthetic biology is biology whose goal is the engineering of living organisms. Today, the leading centers of research in the field of synthetic biology are MIT, Harvard University, Imperial College London.

In Russia, there is a rather complicated attitude towards editing organisms or transgenic organisms. If we compare the volume of patents in countries with similar bans - Europe, and in countries with a flexible attitude - the United States, we can see a sharp decline in patents after the introduction of regulatory bans, as was the case in Europe in the late 1990s. Before the bans, they were at the same level, but the introduction of bans greatly affects the activity of investors. In Russia, the situation is similar to Europe, and for the development of the biotechnology sector, it is necessary to revise the legislation in the field of regulation of transgenic and genetically modified products.

Russia has the prerequisites for the development of synthetic biology - there is the necessary infrastructure for conducting and developing such research, a developed IT sector and medicine. However, legislation hinders this process. In terms of the environment for synthetic biology startups in Russia, all goes well. «Skolkovo»and other sites provide real development support. The main deficits are in human resources and investment. Additionally: Russia still lacks good incubators for startup development.

An important problem in the development of synthetic biology is the lack of a mechanism for technology transfer from the state to the private sector. Intellectual property that is created within universities belongs to the universities and, consequently, to the state. The issue of alienation of state property in favour of researchers is very problematic. This significantly complicates the implementation of projects and the attraction of funding.

Critical for Russia in the development of synthetic biology are 2 directions: changing the legislation in the field of regulation of transgenic organisms and creating effective mechanisms for the transfer of scientific technologies from scientific organizations to business.

Gusev O. A., Director, Regulatory Genomics Research Centre, Institute of Fundamental Medicine and Biology, KFU; Professor of Medicine, Yuntendo University (Japan)

Source: Interview with O. A. Gusev as part of the preparation of the report dated October 25, 2021

“Russia will not be noticeable in the field of synthetic biology for a very long time. This is primarily due to the fact that the prerequisites for prerequisites for development. The main problem for the development of synthetic biology in Russia is the considerably stretched path from idea to experimental activities. This is related to Russia's dependence on imports of such technologies, as well as the lack of mechanisms to quickly provide research teams. There is also no competitive opportunity to test and implement ideas, and there are no systematic and global projects that could form the basis for companies.

On the other hand, Russia has a very strong segment of bioinformatics. Russian specialists are not inferior to foreign ones, but bioinformaticians and systems biologists rely on available global data, which are rapidly becoming obsolete, and their concepts cannot be picked up by scientific groups. In general terms, Russia can develop "dry" synthetic biology - emphasizing computational aspects and realizing the potential in bioinformatics. The second way is the "marginalisation" of synthetic biology: the search for fundamentally new objects for research in directions that do not yet exist".

Decisions on further development of synthetic biology in Russia will be linked to the development of priority application sectors. The choice of sectors will be dictated by their maturity, availability of necessary resources, components, infrastructure and competencies, as well as availability of reagents and equipment in the open markets of the country.

For Russia, taking into account socio-economic and political consequences of the crisis at the beginning of 2022, pharmaceuticals, medicine and chemistry are likely to take the lead in the fields of application of synthetic biology technologies. The role of synthetic biology in pharmaceuticals and medicine will increase in view of higher costs and the need to substitute imported drugs, the need to create your own innovative medicinal biopreparations. For the chemical industry, adapting synthetic biology solutions will potentially make production processes cheaper and replace substances and chemical components that are being phased out due to trade restrictions.

According to experts, the application of synthetic biology technologies in the food industry, bioenergy, decarbonisation or pollution abatement in Russia will, on the contrary, fall by the wayside in the short term. Individual pilot projects will continue in these areas, but there will not be any major changes. For example, the adaptation of alternative protein solutions and the establishment of new food production facilities on their basis will presumably be postponed, as they require considerable investment and the existing organisation of production and farming methods are currently more cost-effective.

Despite existing barriers, constraints and limitations, Russia has the potential and opportunity to build a synthetic biology industry, particularly in cooperation with Asia-Pacific countries, to address its own public health, food, biological and environmental security challenges.

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Appendix 1

Leading Research Centres in Synthetic Biology

The table presents a list of synthetic biology S&T fronts ranked by the volume of Scopus scientific publications for the period 2015-2020. For each S&T frontier, the global and Russian research centres that are the leaders in terms of Scopus publications in this area are given. This list makes it possible to identify the key scientific players, assess the geography of synthetic biology research concentration, as well as identify the deficit areas of Russian synthetic biology research.

№	Science and technological frontiers	In the world	In Russia
1	**Bioinformatics**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Harvard Medical School (USA), National Institutes of Health NIH (USA), Shanghai Jiao Tong University (China), Fudan University (China), Inserm (France), Central South University (China), Zhejiang University (China)	RAS, MSU, IC&G SB RAS, SB RAS, NSU, MIPT, SPbU, Vavilov Institute of General Genetics RAS, IBCh RAS
2	**Gene expression**	Harvard Medical School (USA), Inserm (France), National Institutes of Health NIH (USA), Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Howard Hughes Medical Institute (USA), University of California (USA), The University of Tokyo (Japan), University of Toronto (Canada)	RAS, MSU, Ministry of Health of the Russian Federation, SB RAS, IC&G SB RAS IBCh RAS, Sechenov University, NSU, SPbU, Engelhardt Institute of Molecular Biology RAS
3	**Biomarkers: cancer markers, markers of ageing**	Chinese Academy of Sciences (China), Inserm (France), CNRS Centre National de la Recherche Scientifique (France), National Institutes of Health NIH (USA), Harvard Medical School (USA), University of California (USA), The University of Tokyo (Japan), University of Toronto (Canada), Baylor College of Medicine (USA), Albert Einstein College of Medicine of Yeshiva University (USA)	RAS, MSU, Ministry of Health of the Russian Federation, Sechenov University KFU, Pirogov Medical University, SPbU
4	**Polymerase chain reaction**	Ministry of Education China (China), Chinese Academy of Sciences (China), Inserm (France), Universidade de São Paulo (Brazil), CNRS Centre National de la Recherche Scientifique (France), Harvard Medical School (USA), Fudan University (China), Chinese Academy of Agricultural Sciences (China), Sun Yat-Sen University (China), Nanjing Medical University (China)	RAS, Ministry of Health of the Russian Federation, MSU, Sechenov University, SB RAS, Pirogov Medical University, IC&G SB RAS, KFU, SPbU
5	**Obtaining the target metabolites**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Harvard Medical School (USA), Universidade de São Paulo (Brazil), Inserm (France), Zhejiang University (China), Chinese Academy of Agricultural Sciences (China), Ministry of Agriculture of the People's Republic of China (China)	RAS, MSU, Sechenov University, SB RAS, Ministry of Health of the Russian Federation, FEB RAS, SPbU, Pirogov Medical University, KFU, PIBOC FEB RAS

№	Scientific and technological frontiers	In the world	In Russia
6	**Cell and tissue culture technologies**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (China), Harvard Medical School (USA), Inserm (France), National Institutes of Health NIH (USA), Universidade de São Paulo (Brazil), University of Chinese Academy of Sciences (China), Zhejiang University (China), Consiglio Nazionale delle Ricerche (Italy)	RAS, MSU, Ministry of Health of the Russian Federation, Sechenov University, SB RAS, SPbU, IBCh RAS, KFU, NSU, Pirogov Medical University
7	**Machine Learning In biology**	Carnegie Mellon University (USA), Dalian University of Technology (China), Wuhan University (China), Hong Kong Polytechnic University (China), Harvard Medical School (USA), ETH Zurich (Germany), Google LLC (USA), Beijing Normal University (China), Huazhong University of Science and Technology (China), Fudan University (China)	ITMO, MIPT, HSE University, Skoltech, MSU, Yandex LLC, Innopolis University, Sechenov University, KFU, TPU
8	**Protein synthesis and mutation**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Harvard Medical School (USA), Inserm (France), National Institutes of Health NIH (USA), Zhejiang University (China), Universidade de São Paulo (Brazil), Consejo Superior de Investigaciones Científicas (Spain)	RAS, MSU, SB RAS, SPbU, IBCh RAS, Sechenov University, NSU, KFU, Ministry of Health of the Russian Federation, MIPT
9	**Protein-protein interactions**	CNRS Centre National de la Recherche Scientifique (France), Harvard Medical School (USA), National Institutes of Health NIH (USA), Inserm (France), Howard Hughes Medical Institute (USA), Ministry of Education China (China), Chinese Academy of Sciences (China), University of Toronto (Canada), University of California (USA), University of Cambridge (USA)	RAS, MSU, SB RAS, Institute for Biological Instrumentation RAS, IBCh RAS, NSU, Institute of Cytology RAS, IBMC
10	**Bioreactors**	Chinese Academy of Sciences (China), Wageningen University (Netherlands), National University of Singapore (Singapore), Harbin Institute of Technology (China), The State Key Laboratory of Bioreactor Engineering (China), Chongqing University (China), Hohai University (China), Arizona State University (USA), Delft University of Technology (Netherlands), KU Leuven (Belgium)	MSU, ITMO, Timiryazev Institute of Plant Physiology RAS, Sechenov University, ZIOC RAS, KFU, Engelhardt Institute of Molecular Biology RAS, Center for Theoretical Problems of Physical and Chemical Pharmacology RAS, IBMC, TIPS RAS
11	**Mathematical modelling in bioengineering**	Massachusetts Institute of Technology (USA), KU Leuven (Belgium), Virginia Polytechnic Institute and State University (USA), Harbin Institute of Technology (China), Harvard T. H. Chan, School of Public Health (USA), Imperial College, London (UK), Wuhan University of Technology (China), Alma Mater Studiorum Universita di Bologna (France), China University of Mining and Technology (China), Yonsei University (South Korea)	MSU, MIPT, Bauman MSTU, SPbU, ITMO, Sechenov University, Skoltech, UrFU, TPU, National Research Lobachevsky State University of Nizhni Novgorod

№	Scientific and technological frontiers	In the world	In Russia
12	**Protein folding (predicting protein structure)**	CNRS Centre National de la Recherche Scientifique (France), Chinese Academy of Sciences (China), Ministry of Education China (China), National Institutes of Health NIH (USA), University of Cambridge (USA), University of Chinese Academy of Sciences (China), Inserm (France), Harvard Medical School (USA), Consiglio Nazionale delle Ricerche (Italy), Howard Hughes Medical Institute (USA)	RAS, MSU, Institute for Biological Instrumentation RAS, Institute of cytology RAS, IBCh RAS, SPbU, SB RAS, Institute of Protein Research RAS
13	**Microfluidics**	Chinese Academy of Sciences (China), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), Tsinghua University (China), Massachusetts Institute of Technology (USA), University of Chinese Academy of Sciences (China), Harvard Medical School (USA), Zhejiang University (China), ETH Zürich (Switzerland), Harvard University (USA)	RAS, MSU, SB RAS, Sechenov University, ITMO, Kutateladze Institute of thermophysics SB RAS, NSU, SIBFU, TPU, Institute for Analytical Instrumentation RAS
14	**Genome sequencing**	Chinese Academy of Sciences (China), Harvard Medical School (USA), Ministry of Education China (China), National Institutes of Health NIH (USA), CNRS Centre National de la Recherche Scientifique (France), Wellcome Sanger Institute (UK), Massachusetts Institute of Technology (USA), University of Cambridge (UK), Inserm (France), Broad Institute (USA)	RAS, SPbU, MSU, SB RAS, IC&G SB RAS, NSU, VIGG RAS, Sechenov University, MIPT, KFU
15	**Protein network engineering**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Zhejiang University (China), Harvard Medical School (USA), Massachusetts Institute of Technology (USA), Shanghai Jiao Tong University (China), Ministry of Agriculture of the People's Republic of China (China), Sichuan University (China)	RAS, MSU, SB RAS, SPbU, IBCh RAS, KFU, Sechenov University, MIPT, NSU, ITMO
16	**Obtaining secondary plant metabolites**	Chinese Academy of Sciences (China), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Universidade de São Paulo (Brazil), Chinese Academy of Agricultural Sciences (China), Ministry of Agriculture of the People's Republic of China (China), Consiglio Nazionale delle Ricerche (Italy), Zhejiang University (China), King Saud University (Saudi Arabia)	RAS, MSU, SB RAS, FEB RAS, SPbU, FEFU, PIBOC FEB RAS, Sechenov University, KFU, All-Russian Institute of Plant Protection
17	**Site-directed mutagenesis**	Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of Toronto (Canada), University of Pittsburgh (USA), University of Wisconsin-Madison (USA), University of Pennsylvania (USA), Cornell University (USA), ETH Zurich (Switzerland), University of Oxford (USA), Aarhus Universitet (Denmark)	MSU, IBCh RAS, Kurchatov Institute, IBMC, SPbU, NSU, Institute of Biochemistry and Physiology of Plants and Microorganisms RAS, IEPhB RAS, KFU, IC&G SB RAS

№	Scientific and technological frontiers	In the world	In Russia
18	**Cheaper personalised medicine**	Harvard Medical School (USA), CNRS Centre National de la Recherche Scientifique (France), Columbia University (USA), Charite Universitatsmedizin Berlin (Germany), German Cancer Research Center (Germany), Massachusetts General Hospital (USA), University College London (UK), University of California (USA), University of Pennsylvania (USA), University of Washington (USA)	Pirogov Medical University, MSU, SPbU, TSU, SibMed
19	**Omics technology**	Chinese Academy of Sciences (China), Ministry of Education China (China), Harvard Medical School (USA), CNRS Centre National de la Recherche Scientifique (France), Inserm (France), University of Chinese Academy of Sciences (China), University of California, San Diego (USA), National Institutes of Health NIH (USA), Københavns Universitet (Denmark), Imperial College London (UK)	RAS, MSU, Sechenov University, IBMC, SPbU, MIPT, SB RAS, IBCh RAS, IC&G SB RAS
20	**Extraction of genetic material**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Chinese Academy of Agricultural Sciences (China), Universidade de São Paulo (Brazil), Ministry of Agriculture of the People's Republic of China (China), Zhejiang University (China), Inserm (France), Københavns Universitet (Denmark)	RAS, MSU, SB RAS, SPbU, KFU, IBCh RAS, FEB RAS, Sechenov University, MIPT, Vavilov Institute of General Genetics Russian Academy of Science
21	**Targeted delivery of biologics, medicines**	Ministry of Education China (China), Chinese Academy of Sciences (China), Harvard Medical School (USA), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Sichuan University (China), Fudan University (China), Zhejiang University (China), Shanghai Jiao Tong University (China), Inserm (France)	RAS, MSU, Sechenov University, SB RAS, KFU, IBCh RAS, SPbU, Ministry of Health of the Russian Federation, «MISIS», ITMO
22	**CRISPR-Cas9 (since 2013)**	Chinese Academy of Sciences (China), Harvard Medical School (USA), Ministry of Education China (China), Howard Hughes Medical Institute (USA), Massachusetts Institute of Technology (USA), University of Chinese Academy of Sciences (China), National Institutes of Health NIH (USA), CNRS Centre National de la Recherche Scientifique (France), Broad Institute (USA), University of California, San Francisco (USA)	RAS, SB RAS, MSU, IC&G SB RAS, NSU, Institute of Chemical Biology and Fundamental Medicine SB RAS, Ministry of Health of the Russian Federation, Institute of Gene Biology RAS, Sechenov University, Institute of Immunology of the Federal Medical and Biological Agency
23	**Metagenomics**	Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of California, San Francisco (USA), Ministry of Education China (China), University of California, San Diego (USA), U.S. Department of Energy Joint Genome Institute (USA), Københavns Universitet (Denmark), Lawrence Berkeley National Laboratory (USA), Massachusetts Institute of Technology (USA), University of California, Berkeley (USA)	RAS, MIPT, SPbU, MSU, SB RAS, Institute of Immunology of the Federal Medical and Biological Agency, S. N. Vinogradsky Institute of Microbiology RAS, Bioengineering Centre RAS, KFU, Limnological Institute SB RAS

№	Scientific and technological frontiers	In the world	In Russia
24	**Cybersecurity**	Chinese Academy of Sciences (China), Carnegie Mellon University (USA), Amrita University (India), Chengdu University of Information Technology (China), Arizona State University (USA), Austrian Institute of Technology (Austria), Delft University of Technology (Netherlands), Imperial College London (UK), The University of Arizona (USA), Universiteit Twente (Netherlands)	NRNU MEPHI, Peter the Great St. Petersburg Polytechnic University, ITMO, ETU «LETI»», SPbU, TPU, Institute of Control Sciences RAS, Innopolis University, Bauman MSTU, TUSUR University, SPCRAS
25	**Biobank of biodiversity and genetic resources**	Harvard Medical School (USA), University of Oxford (UK), University of Oxford Medical Sciences Division (UK), Karolinska Institutet (Sweden), King's College London (UK), University College London (UK), University of Cambridge (UK), Imperial College London (UK), Inserm (France), The University of Edinburgh (UK)	RAS, Sechenov University, MSU, Ministry of Health of the Russian Federtion
26	**Analysis of the biotechnological potential of rare extremophilic micro-organisms, plants, fungi**	Chinese Academy of Sciences (China), Chinese Academy of Agricultural Sciences (China), Central South University (China), Wageningen University (Netherlands), China Agricultural University (China), Jiangnan University (China), Tsinghua University (China), Consiglio Nazionale delle Ricerche (Italy), Centre de Biotechnologie de Borj Cedria (Tunisia), Delft University of Technology (Netherlands)	A. N. Bach Institute of Biochemistry RAS, MSU, KFU, FRC “Fundamentals of Biotechnology” RAS, Kurchatov Institute, S.N. Vinogradsky Institute of Microbiology, Institute of Biochemistry and Physiology of Plants and Microorganisms RAS, IBCh RAS, IBMC, TSU
27	**Cell factory**	Danmarks Tekniske Universitet (Denmark), Ministry of Education China (China), Chinese Academy of Sciences (China), Novo Nordisk Foundation (International Foundation), Chalmers University of Technology (Sweden), CNRS Centre National de la Recherche Scientifique (France), Jiangnan University (China), University of Chinese Academy of Sciences (China), National Institutes of Health NIH (USA), Consejo Superior de Investigaciones Científicas (Spain)	MSU, RAS, Institute of Gene Biology RAS, SPbU, Vavilov Institute of General Genetics RAS, Irkutsk National Research Technical University, Sechenov University, Kabardino-Balkarian State University named after H. M. Berbekov, Russian Research Institute for Agricultural microbiology
28	**Descriptive analysis of microbial genomes**	Chinese Academy of Sciences (China), Wellcome Sanger Institute (UK), Imperial College London (UK), University of Cambridge (UK), University of Oxford (UK), CNRS Centre National de la Recherche Scientifique (France), National Institutes of Health NIH (USA), University of Melbourne (Australia), The University of Sydney (Australia), The University of Edinburgh (UK)	RAS, SPbU, NWSMU, The Institute of Experimental Medicine, N. F. Gamaleya Federal Research Center for Epidemiology & Microbiology, UB RAS, UFU, Saint-Petersburg Pasteur Institute, St.Petersburg Institute of Bioregulation and Gerontology
29	**Neurogenesis and therapy of neurodegenerative diseases**	Harvard Medical School (USA), Inserm (France), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), Chinese Academy of Sciences (China), University of Toronto (Canada), National Institutes of Health NIH (USA), Massachusetts General Hospital (USA), Karolinska Institutet (Sweden)	RAS, MSU, Sechenov University, Center Institute of Cytology and Genetics SB RAS, SPbU, Ministry of Health of the Russian Federation, SB RAS, Pirogov Medical University, NSU, IHNA&NPh RAS

№	Scientific and technological frontiers	In the world	In Russia
30	**Genetic editing, creating plants with 'pre-programmed' properties**	Tianjin University (China), Stanford University (USA), The University of Tokyo (Japan), Southeast University (China), Jiangsu University (China), Arizona State University (USA), Carnegie Mellon University (USA), Cornell University (USA), NC State University (USA), Technical University of Munich (Germany)	MSU, SPbU, Vavilov Institute of General Genetics RAS, Skoltech, NSU, UrFU, SUSU, TPU, SFEDU
31	**The search for new 'targeting' in medicine**	Charite Universitatsmedizin Berlin (Germany), University of California (USA), Stanford University School of Medicine (USA), Capital Medical University (China), Baylor College of Medicine (USA), Anhui Medical University (China), Beth Israel Deaconess Medical Center (USA), Case Western Reserve University (USA), Centro de Investigacion Biomedica en Red de Enfermedades Hepaticas y Digestivas (Spain), Graduate School of Medicine (Japan)	Sechenov University, Institute of Molecular Genetics RAS, Pirogov Medical University, KFU, Institute of Cytology RAS, KRASGMU
32	**Production of biopreparations**	Harvard Medical School (USA), Inserm (France), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), Chinese Academy of Sciences (China), Baylor College of Medicine (USA), Anhui Medical University (China), University of Toronto (Canada), National Institutes of Health NIH (USA), The University of Tokyo (Japan)	Pirogov Medical University, MSU, Sechenov University, Institute of Molecular Genetics RAS, KFU, Engelhardt Institute of Molecular Biology RAS, Institute of Chemical Biology and Fundamental Medicine SB RAS
33	**Viral delivery vectors**	National Institutes of Health NIH (USA), CNRS Centre National de la Recherche Scientifique (France), Ministry of Education China (China), Chinese Academy of Sciences (China), Inserm (France), Harvard Medical School (USA), University of Oxford (UK), University of Florida (USA), Chinese Academy of Agricultural Sciences (China), University of Pennsylvania (USA)	RAS, MSU, State Research Center of Virology and Biotechnology VECTOR, Sechenov University, SB RAS, Ministry of Health of the Russian Federation, NSU, IBCh RAS, KFU, Institute of Chemical Biology and Fundamental Medicine SB RAS
34	**RNA synthesis**	National Institutes of Health NIH (USA), CNRS Centre National de la Recherche Scientifique (France), Inserm (France), Harvard Medical School (USA), Howard Hughes Medical Institute (USA), The University of Tokyo (Japan), Chinese Academy of Sciences (China), Ministry of Education China (China), University of California, San Francisco (USA), University of Wisconsin-Madison (USA)	RAS, MSU, SB RAS, Institute of Chemical Biology and Fundamental Medicine SB RAS, NSU, IBCh RAS, Engelhardt Institute of Molecular Biology RAS, Skoltech, IC&G SB RAS, Sechenov University
35	**Fag libraries**	Fudan University (China), Albert Einstein College of Medicine of Yeshiva University (USA), Huazhong Agricultural University (China), Forschungszentrum Julich (FZJ) (Germany), Genentech Inc. (USA), Harvard Medical School (USA), Imperial College London (UK), German Cancer Research Center (Germany), Hanyang University (South Korea), Harbin Medical University (China)	RAS, IBCh RAS, MSU, National Research Lobachevsky State University of Nizhni Novgorod, State Research Center of Virology and Biotechnology VECTOR, Institute of Protein Research RAS

№	Scientific and technological frontiers	In the world	In Russia
36	Molecular machines	Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Ministry of Education China (China), Massachusetts Institute of Technology (USA), Harvard Medical School (USA), University of Cambridge (UK), The University of Tokyo (Japan), University of California, San Diego (USA), Howard Hughes Medical Institute (USA), Stanford University (USA)	RAS, MSU, MIPT, Skoltech, KFU, Sechenov University, ITMO, «MISIS», IBCh RAS, HSE University
37	Cellular interactions	Harvard Medical School (USA), Inserm (France), CNRS Centre National de la Recherche Scientifique (France), National Institutes of Health NIH (USA), Chinese Academy of Sciences (China), Howard Hughes Medical Institute (USA), Ministry of Education China (China), University of California, San Francisco (USA), University of Toronto (Canada), University of California, San Diego (USA)	RAS, MSU, SB RAS, IBCh RAS, SPbU, Sechenov University, NSU, MIPT, Ministry of Health of the Russian Federation, KFU
38	Scaffold protein	CNRS Centre National de la Recherche Scientifique (France), Massachusetts Institute of Technology (USA), Colorado State University (USA), Duke University (USA), Graduate School of Medicine (Japan), Osaka University (Japan), Consiglio Nazionale delle Ricerche (Italy), University of Chinese Academy of Sciences (China), Shandong University (China), The University of North Carolina at Chapel Hill (USA)	Center Institute of Cytology RAS, MSU, Institute for Analytical Instrumentation RAS, IBCh RAS, KFU, Institute of Chemical Biology and Fundamental Medicine SB RAS, IBMC, TPU
39	Molecular tools	Harvard Medical School (USA), Inserm (France), CNRS Centre National de la Recherche Scientifique (France), Chinese Academy of Sciences (China), University of Cambridge (UK), The University of Tokyo (Japan), Howard Hughes Medical Institute (USA), Stanford University (USA), Imperial College London (UK), Tianjin University (China)	MSU, IBCh RAS, Pirogov Medical University, Engelhardt Institute of Molecular Biology RAS, Institute of Chemical Biology and Fundamental Medicine SB RAS, Institute of Gene Biology RAS, Mendeleev University of Chemical Technology, NSU, KFU
40	The regulation of synthetic biology	Chinese Academy of Sciences (China), Jiangnan University (China), University of Washington (USA), Chalmers University of Technology (Sweden), ETH Zurich (Switzerland), China Academy of Chinese Medical Sciences (China), Chinese Academy of Agricultural Sciences (China), Academy of Scientific and Innovative Research (India), Centre for Applied Synthetic Biology (Canada), Sorbonne Universite (France)	MSU, NSU, SPbU, Ajinomoto-Genetika Research institute, Skoltech, TSU, A. N. Bach Institute of Biochemistry Russian Academy of Sciences RAS, Pirogov Medical University, Kurchatov Institute, SPCPU
41	Marker-mediated selection	Chinese Academy of Agricultural Sciences (China), USDA Agricultural Research Service (USA), Ministry of Agriculture of the People's Republic of China (China), United States Department of Agriculture (USA), Ministry of Education China (China), Chinese Academy of Sciences (China), Northwest A&F University (China), Indian Council of Agricultural Research (India), ICAR — Indian Agricultural Research Institute, New Delhi (India), Huazhong Agricultural University (China)	Vavilov Institute of General Genetics RAS, IC&G SB RAS, SB RAS, RAS, All-Russian Research Institute of Agricultural Biotechnology RAS, RSAU - MTAA named after K.A. Timiryazev, NSU, SPbU, Timiryazev Institute of Plant Physiology RAS, Vavilov Institute of General Genetics RAS

№	Scientific and technological frontiers	In the world	In Russia
42	**The "one health" concept**	Harvard Medical School (USA), University of Toronto (Canada), National Institutes of Health NIH (USA), Ministry of Education China (China), University of Melbourne (Australia), Chinese Academy of Sciences (China), Inserm (France), University College London (UK), The University of Sydney (Australia), Karolinska Institutet (Sweden)	Ministry of Health of the Russian Federation, RAS, Sechenov University, MSU, Pirogov Medical University, SB RAS, SPbU, KFU, RUDN University, HSE University
43	**Production of chimeric proteins (containing the activity of two or more target proteins)**	Chinese Academy of Sciences (China), Harvard Medical School (USA), National Institutes of Health NIH (USA), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), Inserm (France), University of Pennsylvania (USA), University of Pennsylvania Perelman School of Medicine (USA), University of Texas MD Anderson Cancer Center (USA), University of California, San Diego (USA)	RAS, MSU, IBCh RAS, Sechenov University, NSU, Ministry of Health of the Russian Federation, Engelhardt Institute of Molecular Biology RAS, SPbU, Institute of Chemical Biology and Fundamental Medicine SB RAS
44	**Synthesis of nutrient media for cell cultivation**	Beijing University of Chemical Technology (China), Chinese Academy of Sciences (China), Friedrich-Alexander-Universitat (Germany), Adolphe Merkle Institute (Switzerland), Amgen Inc. (USA), Bristol-Myers Squibb (USA), ETH Zurich, (Switzerland), University College London (UK), Consiglio Nazionale delle Ricerche (Italy), Universidade do Porto (Portugal)	MSU, Institute of Chemical Biology and Fundamental Medicine SB RAS, Center Institute of Cytology RAS, Timiryazev Institute of Plant Physiology RAS, IBCP RAS, N. F. Gamaleya Federal Research Center for Epidemiology & Microbiology, KFU, Mendeleev University of Chemical Technology, SPbU, FEFU
45	**Organisms with modified DNA/RNA**	Chinese Academy of Sciences (China), Ministry of Agriculture of the People's Republic of China (China), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), Chinese Academy of Agricultural Sciences (China), China Agricultural University (China), Wageningen University & Research (Netherlands), Universiteit Gent (Belgium), Harvard Medical School (USA), Consejo Superior de Investigaciones Científicas (Spain)	RAS, MSU, IBCh RAS, SB RAS, SPbU, NSU, All-Russian Research Institute of Agricultural Biotechnology RAS, IC&G SB RAS, Sechenov University, Ministry of Health of the Russian Federation
46	**Biosurfactants**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Universiteit Gent (Belgium), Universidade Catolica de Pernambuco (Brazil), University of Massachusetts Amherst (USA), Universidade de São Paulo (Brazil), Consejo Nacional de Investigaciones Científicas y Técnicas (Argentina), University of Chinese Academy of Sciences (China), Ulster University (Ireland)	RAS, Institute of Ecology and Genetics of microorganisms SB RAS, PSU, MSU, UFRC RAS, KFU, Institute of Biochemistry and Physiology of Plants and Microorganisms RAS, S.N. Vinogradsky Institute of Microbiology, UB RAS, SB RAS
47	**Cultivated skin**	Chinese Academy of Sciences (China), Ministry of Education China (China), Tsinghua University (China), University of Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Harvard Medical School (USA), National University of Singapore (Singapore), Massachusetts Institute of Technology (USA), Zhejiang University (China), Shanghai Jiao Tong University (China)	RAS, MSU, Sechenov University, Ministry of Health of the Russian Federation, ITMO, SB RAS, MIPT, Kurchatov Institute, National Medical Research Centre for Transplantology and Artificial Organs named after Academician V.I. Shumakov, TPU

№	Scientific and technological frontiers	In the world	In Russia
48	**Human cell editing (blood cells, stem cells and others)**	Harvard Medical School (USA), Massachusetts Institute of Technology (USA), Broad Institute (USA), University of California (USA), Center for iPS Cell Research and Application (Japan), Central South University (China), Charite Universitatsmedizin Berlin (Germany), Children's Hospital Boston (USA), Seoul National University (South Korea), China Pharmaceutical University (China)	MSU, IBCh RAS, Pirogov Medical University, Engelhardt Institute of Molecular Biology RAS, Institute of Chemical Biology and Fundamental Medicine SB RAS, E.N. Meshalkin National Medical Research Centre, Institute of Gene Biology RAS, Research Centre for Medical Genetics, NSU, KFU
49	**Human cell editing (blood cells, stem cells and others)**	University of California (USA), Ministry of Agriculture of the People's Republic of China (China), University of WiscoBnsin-Madison (USA), South China Agricultural University (China), Nanjing Agricultural University (China), Tohoku University (Japan), Ruhr-Universitat Bochum (Germany), University of Pretoria (South Africa), Huazhong Agricultural University (China), University of Wisconsin-Madison (USA)	MSU, IBCh RAS, SPbU, All-Russian Research Institute of Agricultural Biotechnology RAS, Sechenov University, All-Russian Research Institute of Agricultural Microbiology, Kurchatov Institute, Skoltech, Research Centre for Medical Genetics
50	**A study of glioblastoma, the mechanism of transmission blockage**	Harvard Medical School (USA), German Cancer Research Center (Germany), Capital Medical University (China), Columbia University (USA), Beijing University of Chinese Medicine (China), Anhui Medical University (China), Arizona State University (USA), Baylor College of Medicine (USA), Beijing University of Chinese Medicine (China), Karolinska Institutet (Sweden)	MSU, NSU, Institute of Cytology RAS, Institute of Chemical Biology and Fundamental Medicine SB RAS, SFEDU
51	**Creating recombinant proteins**	Ministry of Education China (China), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), National Institutes of Health NIH (USA), Inserm (France), Harvard Medical School (USA), Chinese Academy of Agricultural Sciences (China), Jiangnan University (China), Universidade de São Paulo (Brazil), Ministry of Agriculture of the People's Republic of China (China)	RAS, MSU, IBCh RAS, Sechenov University, Ministry of Health of the Russian Federation, SB RAS, SPbU, FRC “Fundamentals of Biotechnology” RAS, KFU, Kurchatov Institute
52	**Bioprinting of organs**	Ministry of Education China (China), Harvard Medical School (USA), Chinese Academy of Sciences (China), Nanyang Technological University (China), Tsinghua University (China), Massachusetts Institute of Technology (USA), Brigham and Women's Hospital (USA), Zhejiang University (China), School of Mechanical and Aerospace Engineering (UK), Wake Forest School of Medicine (USA)	Sechenov University, RAS, MSU, Federal Research Centre "Crystallography and Photonics” RAS, Ministry of Health of the Russian Federation, Institute of Chemical Biology and Fundamental Medicine SB RAS, Peter the Great St. Petersburg Polytechnic University, Moscow Polytechnic University
53	**Biodata**	Biocomplexity Institute of Virginia Tech (USA), Chinese Academy of Agricultural Sciences (China), Geisel School of Medicine at Dartmouth (USA), Harvard Medical School (USA), Wageningen University (Netherlands), University of Pennsylvania (USA), University College London (UK), Universitat Bielefeld (Germany), University of California (USA), University of Cambridge (UK)	IBMC, MSU, MIPT, Skoltech, Sechenov University, Vavilov Institute of General Genetics RAS, Institute for Information Transmission Problems RAS, Institute of Gene Biology RAS, Pirogov Medical University, Institute of Mathematical Problems of Biology RAS

№	Scientific and technological frontiers	In the world	In Russia
54	**Networked biolaboratories**	Ministry of Education China (China), Chinese Academy of Sciences (China), University of Chinese Academy of Sciences (China), Tsinghua University (China), Shanghai Jiao Tong University (China), Zhejiang University (China), CNRS Centre National de la Recherche Scientifique (France), Peking University (China), Beijing University of Posts and Telecommunications (China), Huazhong University of Science and Technology (China)	RAS, MSU, MIPT, NSU, NRNU MEPHI, LPI RAS, Institute for Theoretical and Experimental Physics, IHEP
55	**Cell cultivation**	Chinese Academy of Sciences (China), Shandong University (China), State Oceanic Administration China (China), Istituto Di Chimica Dei Composti Organometallici (Italy), Rice University (USA), Chinese Academy of Agricultural Sciences (China), Universiteit Maastricht (Netherlands), University of Kalyani (India), Westfalische Wilhelms-Universitat Munster (Germany), University of Minnesota Twin Cities (USA)	A. N. Bach Institute of Biochemistry RAS, Vavilov Institute of General Genetics RAS MSU, NSU, IC&G SB RAS
56	**De novo obtaining cells through genomic editing**	Chinese Academy of Sciences (China), Ministry of Education China (China), Ministry of Agriculture of the People's Republic of China (China), Chinese Academy of Agricultural Sciences (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Nanjing Agricultural University (China), USDA Agricultural Research Service (USA), Huazhong Agricultural University (China), University of California, Davis (USA)	RAS, SPbU, MSU, SB RAS, Vavilov Institute of General Genetics RAS, NSU, IC&G SB RAS, IBChRAS, SIBFU, Skoltech
57	**Treatment methods for orphan diseases**	Harvard Medical School (USA), Broad Institute (USA), Children's Hospital Boston (USA), KU Leuven (Belgium), Fudan University (China), Columbia University (USA), Inserm (France), Harvard Stem Cell Institute (USA), Hopital Gui de Chauliac (France), Medizinische Universitat Wien (Austria)	Pirogov Medical University, Pavlov University, Sechenov University, Research Institute of Public Health, Medical Research Centre for Child Health, Research Centre for Medical Genetics, SPbU, Tomsk National Research Medical Center RAS, National Medical Research Center of Cardiology, UrFU
58	**Production of alternative proteins**	University of Oxford (UK), University of Chinese Academy of Sciences (China), Yale University (USA), Washington University (USA), University of Toronto (USA), Zhejiang University (China), Westfalische Wilhelms-Universitat Munster (Germany), Vanderbilt University (USA), Weizmann Institute of Science Israel (Israel), University of Wisconsin-Madison (USA)	RAS, MSU, IBCh RAS, Skoltech, Sechenov University, Institute of Cytology RAS, MIPT, SPbU, NSU
59	**Analysis of thermophilic micro-organisms**	Central South University (China), NC State University (USA), Universidade de Vigo (Spain), Oak Ridge National Laboratory (USA), Chinese Academy of Sciences (China), Indian Institute of Technology Banaras Hindu University (India), Huazhong Agricultural University (China), University of Tehran (ИRAS), Kobenhavns Universitet (Denmark), Arizona State University (USA)	MSU, Vinogradsky Institute of Microbiology, Institute of Physical, Chemical and Biological Problems of Soil Science RAS, Institute of General and Experimental Biology SB RAS, IC&G SB RAS, FRC “Fundamentals of Biotechnology” RAS, Limnological Institute SB RAS, IBCh RAS, ISU

№	Scientific and technological frontiers	In the world	In Russia
60	**Editing micro-organisms for bioremediation**	Chinese Academy of Sciences (China), Collaborative Innovation Center of Chemical Science and Engineering (China), Jiangnan University (China), Massachusetts Institute of Technology (USA), Technical University of Denmark (Denmark), NC State University (China), CSIC — Centro Nacional de Biotecnologia (CNB) (Spain), Huazhong Agricultural University (China), Qingdao Institute of Bioenergy and Bioprocess Technology (China), Institute of Plant Physiology and Ecology (China)	MSU, All-Russian Research Institute of Agricultural Biotechnology RAS, Engelhardt Institute of Molecular Biology RAS, IC&G SB RAS, Kurchatov Institute, Mendeleev University of Chemical Technology, Skoltech
61	**Bacterial cell transformation**	Chinese Academy of Sciences (China), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), Ministry of Agriculture of the People's Republic of China (China), Consejo Superior de Investigaciones Científicas (Spain), Zhejiang University (China), Chinese Academy of Agricultural Sciences (China), Nanjing Agricultural University (China), Tsinghua University (China)	RAS, MSU, SB RAS, Institute of Biochemistry and Physiology of Plants and Microorganisms RAS, IBCh RAS, KFU, FEB RAS, Vavilov Institute of General Genetics RAS, SPbU, RAMS
62	**Identifying the ecological roles of symbiotic of micro-organisms**	Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Ministry of Education China (China), Consejo Superior de Investigaciones Científicas (Spain), University of Chinese Academy of Sciences (China), Consejo Nacional de Investigaciones Científicas y Técnicas (Аргентина), Universidade de São Paulo (Brazil), Sorbonne Universite (France), Wageningen University & Research (Netherlands), Københavns Universitet (Denmark)	RAS, All-Russian Research Institute of Agricultural Biotechnology RAS, MSU, SPbU,SB RAS, Limnological Institute SB RAS, KFU, Vinogradsky Institute of Microbiology RAS, Institute of Biochemistry and Physiology of Plants and Microorganisms RAS
63	**Genetic libraries**	National Institutes of Health NIH (USA), Harvard Medical School (USA), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Howard Hughes Medical Institute (USA), Ministry of Education China (China), Massachusetts Institute of Technology (USA), Inserm (France), The University of Tokyo (Japan), University of California, San Francisco(USA)	RAS, MSU, SPbU, NSU, IBCh RAS, SB RAS, Engelhardt Institute of Molecular Biology RAS, KFU, Vavilov Institute of General Genetics RAS, Pirogov Medical University
64	**Digital modelling in biodesign**	Capital Normal University (China), Yale University (USA), Tsinghua University (China), Politecnico di Milano (Italy), Urban Environmental Processes and Digital Modeling Laboratory (China), Technical University of Munich (Germany), Sapienza Universita di Roma (Italy), University of Chemistry and Technology (Czech Republic), Southeast University (China), Korea Advanced Institute of Science and Technology (South Korea)	Institute of Mathematical Problems of Biology RAS, Peter the Great St. Petersburg Polytechnic University, Moscow State University of Civil Engineering, Bauman MSTU, Mendeleev University of Chemical Technology
65	**Digitisation of consciousness and Wetware for transferring consciousness**	University of Oxford (UK), University of Toronto (Canada), University College London (UK), Monash University (Australia), University of Melbourne (Australia), The University of Sydney (Australia), Helsingin Yliopisto (Finland), University of Michigan, Ann Arbor (USA), The University of British Columbia (Canada), Aarhus Universitety (Denmark)	RAS, SPbU, MSU, KFU, HSE University, Peter the Great St. Petersburg Polytechnic University

№	Scientific and technological frontiers	In the world	In Russia
66	**Chimera animals**	Harvard Medical School (USA), National Institutes of Health NIH (USA), Chinese Academy of Sciences (China), Inserm (France), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), University of Pennsylvania (USA), University of California, San Diego (USA), University of Pennsylvania Perelman School of Medicine (USA), University of Melbourne (Australia)	RAS, MSU, IBCh RAS, SB RAS, Sechenov University, NSU, Ministry of Health of the Russian Federation, Engelhardt Institute of Molecular Biology RAS, SPbU, Institute of Chemical Biology and Fundamental Medicine SB RAS
67	**Storing information with the help of microorganisms (since 2010)**	University of California, Berkeley (USA), Imperial College London (UK), The University of Edinburgh (UK), Harvard University (USA), National University of Singapore (Singapore), - Chinese Academy of Sciences (China), Bharath Institute of Higher Education and Research (India), Osaka Prefecture University (Japan), University of Toronto (Canada), National Research Centre (Egypt)	MSU, FRC “Informatics and Management control" RAS, MIPT
68	**AI platforms in bioengineering**	Carnegie Mellon University (USA), Rheinisch-Westfalische Technische Hochschule Aachen (Germany), Shandong University (China), Tsinghua University (China), University of Chinese Academy of Sciences (China), University of Surrey (UK), Wayne State University (USA), School of Computer Science and Engineering (Singapore), RMIT University (Australia), Technische Universiteit Eindhoven (Netherlands)	KIAM RAS
69	**Creating artificial nucleic acids**	National Institutes of Health NIH (USA), Harvard Medical School (USA), Chinese Academy of Sciences (China), CNRS Centre National de la Recherche Scientifique (France), Howard Hughes Medical Institute (USA), Massachusetts Institute of Technology (USA), Inserm (France), The University of Tokyo (Japan), Massachusetts College of Pharmacy and Health Sciences (USA), Tsinghua University (China)	IBMC, MSU, Vavilov Institute of General Genetics RAS, Engelhardt Institute of Molecular Biology RAS, Institute of Chemical Biology and Fundamental Medicine SB RAS
70	**Creating new drug platforms**	Houston Methodist (USA), Fudan University (China), Tulane University (USA), Universitat Ulm (Germany), Universita degli Studi di Torino (Italy), Universite de Montpellier (France), Zhejiang University School of Medicine (China), IMT School for Advanced Studies Lucca (Italy), Wuhan University (China), Universite de Tunis El Manar (Tunisia)	Not available
71	**Chimeric micro-organisms**	Harvard Medical School (USA), National Institutes of Health NIH (USA), Chinese Academy of Sciences (China), Inserm (France), Ministry of Education China (China), CNRS Centre National de la Recherche Scientifique (France), University of Chinese Academy of Sciences (China), University of California, San Diego (USA), University of Pennsylvania Perelman School of Medicine (USA), University of Melbourne (Australia)	Not available

№	Scientific and technological frontiers	In the world	In Russia
72	**Personalised veterinary diagnostics (since 2010)**	VA Medical Center (USA), West Virginia University (USA), The University of Tampa (USA), Pennsylvania State University (USA), Harvard University (USA), Texas State University (USA), Syracuse University (USA), Ontario Veterinary College (Canada), The University of Queensland (Australia), Massachusetts College of Pharmacy and Health Sciences (USA)	Not available
73	**Research on dark RNA for use as biomarkers in personalised medicine (since 2016)**	Westfalische Wilhelms-Universitat Munster (Germany), University of Miami Leonard M. Miller School of Medicine (USA), St. Laurent Institute (USA), Oregon State University (USA), Brown University (USA), Harvard Medical School (USA), Cornell University (USA), Fudan University (China), Max Planck Institute for Evolutionary Biology (Germany), Istituto Nazionale di Genetica Molecolare (Italy)	IBMC, Vavilov Institute of General Genetics RAS
74	**Microbiome, metagenomics, metabolomics (since 2017)**	Northwest University (China), Ministry of Agriculture of the People's Republic of China (China), Central South University (China), Sorbonne Universite (France), Wake Forest School of Medicine (USA), China Pharmaceutical University (China), Guangzhou University of Chinese Medicine (China), University of Alberta (Canada), Universite d'Ottawa (Canada), University of Luxembourg (Luxembourg)	Not available
75	**Synthesis of new vaccine platforms**	Harvard Medical School (USA), National Institutes of Health NIH (USA), Chinese Academy of Sciences (China), Inserm (France), Zhejiang University (China), University of Chinese Academy of Sciences (China), Shandong University (China), Massachusetts Institute of Technology (USA), University of Cambridge (UK), Baylor College of Medicine (USA)	Not available

Table 6.
Programmes to support the development of synthetic biology around the world, 2015-2020, according to Scopus

The report was preceded by a foresight session 'Fronts in the New Sciences', organised by the Centre for Strategic Research North-West in cooperation with the St Petersburg Foundation for Innovation and Youth Initiatives, with support from the St Petersburg Government and the Russian Ministry of Education and Science.

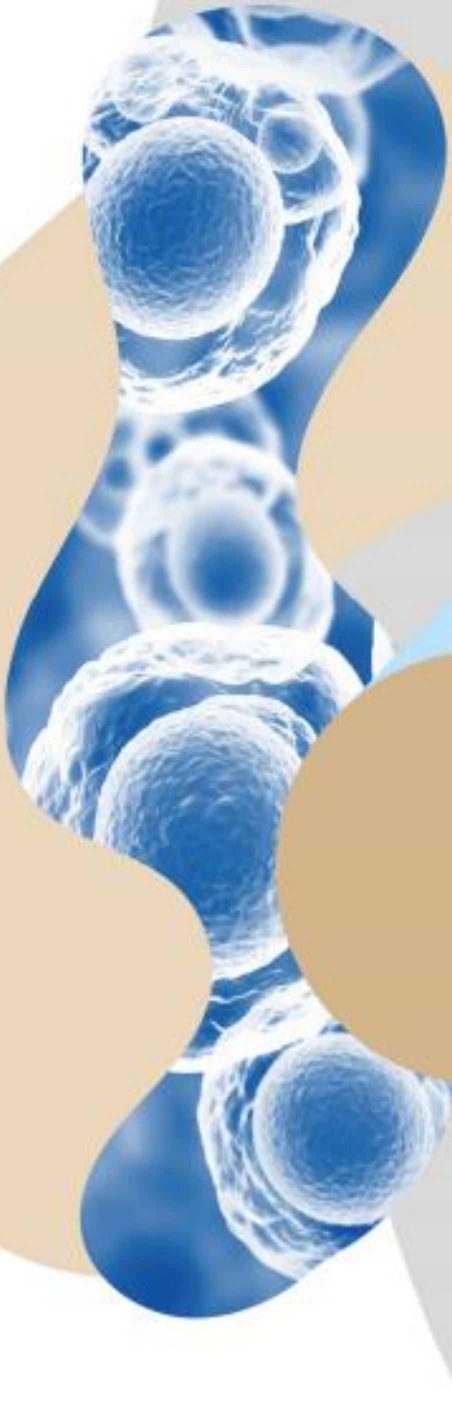
Date: 9-10 November 2021.

Format: Conference and collaborative group work according to areas of focus

Areas: new chemistry, SYNTHETIC BIOLOGY, artificial intelligence in industry, green transition in industry and cities

Participants: 168 participants representing Russian universities from 19 regions of the Russian Federation

Results for each area:
- trends in the development of research topics up to 2030 and 2050 are identified;
- the most relevant topics for BlueSkyResearch are identified;
- training programmes for key researchers of the PI school are designed.



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ПРАВИТЕЛЬСТВО САНКТ-ПЕТЕРБУРГА

ЦЕНТР СТРАТЕГИЧЕСКИХ РАЗРАБОТОК СЕВЕРО-ЗАПАД

ФОНД ИНИЦИАТИВ САНКТ-ПЕТЕРБУРГА