Synthetic biology as a breakthrough direction in the creation of biological systems

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Abstract. Synthetic biology as a scientific direction appeared at the beginning of the 21st century on the basis of the accumulated scientific and technological base and discoveries in the fields of systems biology, biotechnology, molecular biology, bioengineering and genetic engineering. The formation of synthetic biology as a separate area fell on the period of 2000–2010, when the first discoveries were made related to the standardization of DNA parts, combinatorial synthesis of the genetic network, synthetic schemes that promote the penetration of bacteria into tumor cells, etc., and the first scientific - research centers and teams (Craig Venter Institute and the Center for Synthetic Biology and Innovation at Imperial College London), the first international conference on synthetic biology Synthetic Biology 1.0 was held. Since 2010, there has been an intensive development of this direction, as well as an increase in the number of developments with applied applications (creation of the first synthetic cell, artemisinin synthesis, the first computer-generated genome, etc.). One of the main factors in the development of synthetic biology has been the expansion of data analysis and modeling capabilities, the active digitalization of research and the development of interdisciplinary areas, such as bioinformatics. Today, the areas of application of synthetic biology are actively expanding (medicine, pharmaceuticals, food industry, agriculture, cosmetics, textile industry, energy, etc.), which leads to an increase in its role in ensuring economic growth.

1 Introduction

Biotechnological methods are associated with revolutionary changes in biology, which, as a leader in natural science, has reached the molecular and subcellular levels. Biotechnological methods involve the use of biological systems and processes in solving various problems: diagnosis and treatment of oncological diseases, lack of clean water and nutrients (especially proteins), environmental pollution, lack of raw materials and energy resources, etc. (Table 1).

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Table 1. Directions of biotechnology that determine the development of areas of science

Direction of biotechnology	Technology object	An example of a method and its use in science
genetic engineering	Recombinant DNA	CRISPR/CAS is a method for editing the genomes of higher organisms, as well as a research tool in embryology [9]; Method for creating an artificial genome; Method for creating designer plant and animal organisms; RNA interference is a method for suppressing gene expression in the presence of short RNA fragments; Sequencing.
tissue engineering	Organs and tissues of living organisms	3D printing is a method for creating artificial organs and tissues
Biocatalysis	Enzymes, whole microbial cells	Methods for obtaining amylolytic and proteolytic enzymes used in the chemical, food and other industries
Immunology	Monoclonal antibodies	CAR-T method of treatment with genetically modified T-cells of oncological diseases
Fermentation technology	Food, biologically active substances, waste	Fermentation methods in the food industry: meat softening, curdling of milk in cheese making, clarification of juices, etc.
Biomedicine, biopharmaceutics	DNA, drugs	GWAS is a statistical method that determines the significance differences in the selected gene region (SNP snip) between groups of sick and healthy people, determines the relationship between gene variants and phenotypic manifestations; DNA microarrays (small plates on which DNA molecules are applied and attached, complementary RNA studied genes); Drag design - a method of designing drugs; Quantum dots (fluorescent semiconductor nanocrystals) - a method using a nanomaterial with special spectral characteristics; Optogenetics is a method of controlling nerve and muscle cells of a living organism with the help of light; Sequencing is a method for determining the complete nucleotide sequences; Organ chips - a method of organ modeling, followed by drug testing;

Synthetic biology is today an interdisciplinary scientific field that is formed at the intersection of different areas of biology, mathematics, information technology, chemistry and engineering (see Figure 1)[1] . The development of synthetic biology is associated with one of the most ambitious tasks of mankind - to learn how to reproduce life: to synthesize a cell, its components and create biological systems with desired properties. Engineering approaches and principles are fundamental for the development of synthetic biology, since to obtain products of new properties that allow solving new problems and challenges in various industries, full-cycle engineering (including design, assembly, testing, data analysis) of a large number of biological sequences is required. [2] The areas of application of synthetic biology are not limited only to the field of Life science and include a number of industries - the food industry (synthesized foodstuffs, various food components grown in a bioreactor), bioenergy (biofuel), pharmaceuticals and medicine (new methods of drug delivery, new antimicrobials, new generation gene vaccines), industry (new types of materials) [3] . Synthetic biology contributes to the transformation of production chains, a significant reduction in the cost of products and the timing of their production compared to existing analogues. In general, synthetic biology is an exclusively applied scientific field: any synthesized biological object is created not by itself, but for a specific branch task, this is one of the main ideas of synthetic biology.

2 Research Methodology

One of the clearest examples of the application of synthetic biology in the food industry is the production of cultured cellular meat. The production cycle of cultured cell meat is reduced to four phases - collection and preparation of cellular material (as a rule, stem cells, muscle cells, hormones and nutrients are extracted from animal tissues), preparation of a nutrient medium for growing tissues, tissue production by placing cells in a nutrient medium in a bioreactor and subsequent mass production of meat [5]. From 1 gram of muscle tissue, up to 10 thousand kilograms of cell mass can be obtained. The entire process takes up to four weeks in total. While with the traditional method of animal husbandry, the time for obtaining the finished meat product is measured in two years. Another argument in favor of cultivated meat is the rapid reduction in the cost of its production (4 times in 6 years - from $400/kg of beef meat in 2013 to $110/kg in 2019 and potentially to $10/kg by 2024 .). The main challenge for this type of production in the future is the use of fully synthesized cells, rather than editing animal cells, as is the case today.

Methods and approaches to study the development of synthetic biology includes various methods:

1. Synthetic biology researchers create new biological systems by changing the genetic code of organisms or creating an entirely new organism with desired properties.

2. Gene Engineers: With the help of CRISPR-Cas9 technologies and other tools that allow you to edit genetic information in reverse, it allows you to create organisms with certain characteristics.

3. The biological analogue of electronic circuits for controlling biological processes is synthetic circulation.

4. The collected data on changes in genetic information and the functioning of organisms are analyzed with the support of bioinformatics.

5. The use of mathematical models and computer simulations to predict the behavior of biological systems, as well as to evaluate the effectiveness of created structures.

6. Creation of ethical foundations for the creation and use of synthetic biological systems, as well as the development of safety standards is one of the areas of bioethics.

7. Networking and knowledge sharing: In the field of synthetic biology, it is useful to team up with experts who have experience in different fields of knowledge (biology, engineering or computer science) in order to achieve meaningful results.

Developments in synthetic biology are in constant development. The latest methods and approaches appear along with a deepening understanding of biological processes, as well as the development of technologies.

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 [6].

3 Results and Discussions

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 the engineering intervention in individual elements of the cell (see fig.1). Scientists and researchers, instead of thinking about how to design a cell, are concentrating on questions, for example, how to learn how to synthesize plasmids that encode 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 [7]. The original hypothesis of synthetic biology, 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.

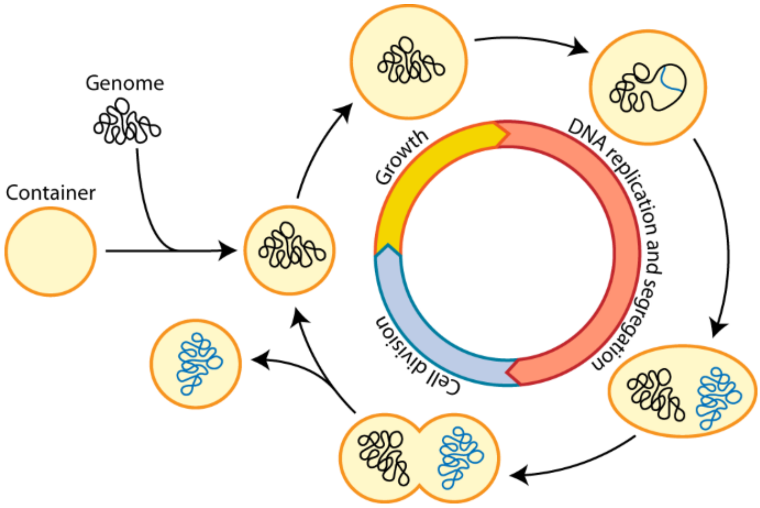

Fig. 1. Towards a synthetic cell cycle

The original idea of synthetic biology was as follows - when mastering the synthesis and understanding 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. Source: Report preparation interview with I. D. Klabukov dated November 2, 2021 Leading Russian research centers in the field of synthetic biology include [8]: 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, IPTP RAS, IBCh RAS. One of the main applications 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 rate of patients will be higher, the degree of radiation complications will be lower, the effectiveness of treatment will be higher due to the possibilities of a higher dose of radiation.

A typical cycle of biological engineering consists of four stages: in silico design, in vitro assembly of synthetic structures and their testing, in vivo implementation of synthetic structures and their testing, data analysis (see Figure 2).

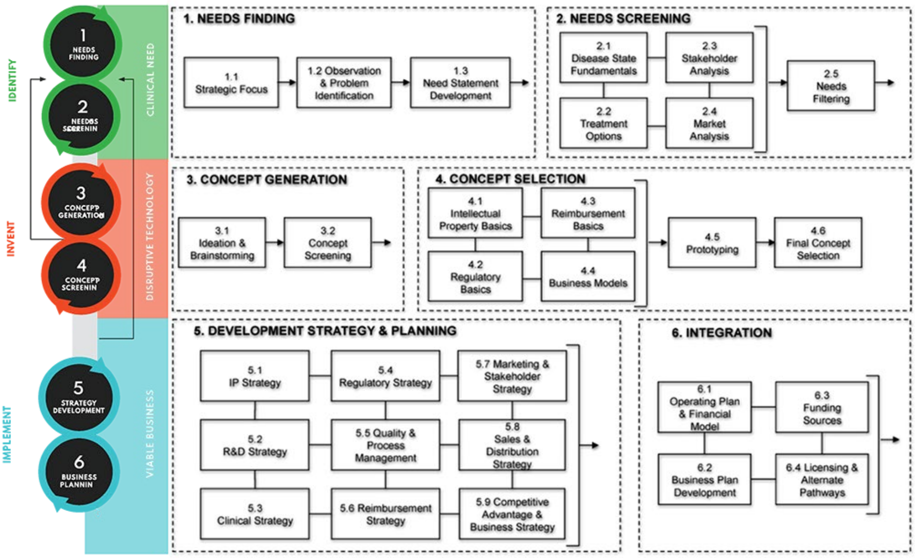

Fig. 2. Innovation Biodesign Process

The design stage involves the design of new nucleotide sequences, incl. selection of approaches to design and selection of a package of necessary software tools [9]. The subsequent assembly step is associated with the combination of DNA sequences, collection and storage of new strains. This is followed by the stage of testing the obtained strains and collecting data as a result of the tests [10]. The final stage of the bioengineering cycle is the analysis of the data obtained as a result of the tests, and the use of the results of the analysis to form new research hypotheses and start a new cycle of bioengineering.

4 Conclusions

The implementation of the bioengineering cycle in synthetic biology involves the creation of a single instrumental platform that provides the ability to detect and analyze thousands of nucleotide fragments, synthesize or edit DNA and RNA sequences, as well as genomic and proteomic constructs, analyze and predict the biological properties and functions of newly synthesized biological objects.

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