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Synthetic Biology: The design and construction of biological parts and systems for various applications, such as biotechnology, biofuels, and medical devices

Aiša Galijatović [1*],
[1] Genetics and Bioengineering, International University of Sarajevo

*Corresponding author: aisatrebo@hotmail.com

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Abstract

Synthetic biology, as a multidisciplinary field, including biology, computer science, and engineering, has an aim to crate/modify current biology systems or other organisms such as enzymes, genetic circuits, and cells. In comparison to the conventional genetic modifications, synthetic biology differs and has the aim of developing functioning devices, systems, and organisms. What makes synthetic biology special is how scientists from very different areas of knowledge share their ideas and collaborate on how to expand their knowledge and innovations. Additionally, the application of synthetic biology is reflected in the usage of S. cerevisiae or Cyanobacteria with synthetic biology methods to produce biofuels. However, the fast expansion of this discipline gives rise to the benefits but also ethical concerns. Benefits of synthetic biology are numerous, though it can change many aspects of everybody's life, while on the other hand, it poses a risk to the environment, limitation of the difference between life and non-life, or general alterations to genes. Throughout this report, diverse applications of synthetic biology are explained, including methods used in medicine, specifically in observation of human well-being, to the novel treatment of infectious diseases, diabetes, and the production of vaccines.

Keywords: synthetic biology, DNA, cells, scientists, bioparts, biological systems, chassis, genetic circuits

1. Introduction

The intersection of biology and engineering has led to a multidisciplinary field termed synthetic biology in the context of scientific study. By the first definition, synthetic biology (SB) is a scientific field that employs science and technology to create or modify current systems of biology or other organisms like enzymes, genetic circuits, and cells [1].

It is a multidisciplinary discipline that combines biology and engineering [2] and is different compared to conventional genetic modification when it comes to the complexity of organisms or systems built by scientists [1]. The purpose of synthetic biology is to develop and construct functioning devices, systems, and organisms with established, practical, and unique features that are not present in the environment, employing concepts from engineering to genetics through the DNA code. Along these definitions, key events of SB are termed as the creation of novel biological components, tools, and systems, the practical modification of already-existing, natural biological systems, and the use of science, technological advances, and engineering to develop, produce, and/or modify biological material in living organisms more quickly and easily [2]. As already mentioned, SB differs from conventional biology, which explores the interior of organisms. On the other hand, SB uses molecular building blocks to create linked biological circuits and pathways, regardless of the origin of the building blocks [3]. Additionally, the primary distinction between synthetic biology and traditional biology is the fact that in synthetic biology, scientists can modify organisms' DNA by changing its architecture or functionality. In classical biology, scientists may only conduct studies on the organism's current architecture [4]. By using those methods and DNA synthesis, it has provided several practical benefits in numerous fundamental industries [3]. Additionally, it has forced academics from a variety of fields to collaborate and to create international networks of individuals who share knowledge and collaborate cooperatively [5]. In the same way that synthesis revolutionized chemistry and the development of chips transformed computers, biologists have used developments to convert biology from a scientific field to an engineered subject. When hardware engineers create novel integrated circuits and microprocessors according to the physical characteristics of resources, biologists are able to develop syn-bio systems that enable corporations improve their goods, procedures, or both [6]. Enough advancements in the underlying technology were required for the discipline to become established. Through the Human Genome Project of the 1990s, the method for sequencing DNA evolved. The area of systems biology, which has adopted a "complete" approach towards comprehending the way cells and organisms' function, that is, looking at connections of relationships or systems in their entirety instead of focusing on a few parts, has advanced alongside mathematical modelling and the "omics" tools, such as transcriptomics, proteomics, and metabolomics [5]. This project will explain the history of synthetic biology, its application in general to diverse fields of human's everyday aspects of life, the basis of synthetic biology, current projects and future, and its benefits, ethical risks, and threats.

2. Main part

2.1. History of synthetic biology

Waclaw Szybalski, a prominent geneticist, initiated the word back in 1970. Throughout the 1970s, basic research was conducted that would set a path for the growth of DNA sequencing and synthesis methods. From that point, it only got more expensive [7]. The foundation for modern synthetic biology was laid by the 1960s finding of mathematical reasoning in gene regulation (e.g., the lac operon) and the 1970s pioneering work in genetic engineering (e.g., recombinant DNA technology) [8]. Two gene-synthesis companies were founded in the 1990s: GeneArt and Blue Heron Biotech. The first-ever synthetic biology meeting took place at MIT. Shortly thereafter, the BioBricks Foundation emerged (an organization for nonprofit purposes that classifies synthetic biology components). Back in 2013, the sixth synthetic biology symposium was held in London, while in 2016, a team of prominent researchers suggested an enormous synthetic biology work, giving rise to Human Genome Project-Write (HGP-Write). That has resulted in the birth of a massive number of genome synthesis initiatives [7]. Not anything in science has sparked a greater degree of scientific, intellectual, administrative, and business curiosity than the double helix and recombinant DNA breakthroughs. This particular topic has resulted in a sufficiently wide range of secondary sources regarding the way it might affect every aspect [9]. Furthermore, in 2016, synthetic biology resulted in the identification of a unique immunologic cell engineering approach that increased the recovery percentage in life-threatening blood malignancies by almost 50%. The procedure is successful in individuals who have breast cancer that has advanced [10].

2.2. What made synthetic biology develop so quickly, and what makes it so special?

What exactly characterizes synthetic biology and what is so special about it is that SB is the result of joint work across disciplines and is a synthesis of concepts from numerous professions. The discipline has various distinguishing characteristics, which include the representation of a novel strategy for biological research, the use of methods from engineering to manipulate systems of living things, work with informal frameworks for innovation and research, and the understanding of the significance of community variables in the progress of the subject [11]. However, synthetic biology in its widest meaning seeks to employ the central dogma's emerging features for scientific and humanistic purposes. While even artificially created biological circuits connect with the cell's preexisting central dogma machinery, this overview of the area is broad. In this sense, synthetic biology technologies utilize the central dogma process's diversity in a deterministic and intentional way. Three levels comprise this network: the extrinsic physical and chemical surroundings of the cells, the internal mechanisms that regulate within the cells, and the central dogma units (transcription and translation). Though shown individually, the above three layers are intricately linked because of the complexities of biology. However, due to its level of complexity, synthetic biologists can develop a wide range of access points, or nodes [12].

2.3. The relationship between system biology and synthetic biology

There are many similarities between the two fields of study; the most significant is that the researchers operating within each field's concepts agree that organisms are composed of functional units that are partially self-sufficient and arranged in systems. On the other hand, synthetic biology is focused on more useful advancements, while systems biology tries to characterize this modular arrangement [13]. Synthetic biology is employing mechanistic insights that systems biology provides into the functioning of biology at the level of molecular structure to drive biology in novel guidelines: from employing biology to synthesize compounds to creating entirely novel kinds of biological reality. Systems biology is important in the setting of synthetic biology since it is necessary to comprehend the functioning of such fundamental mechanisms in addition to creating something entirely novel and predicting its behavior. In the framework of systems biology, synthetic biology emerges as a more potent instrument that offers techniques for evaluating computer simulations of biological processes in laboratory conditions [14].

2.4. Basis of synthetic biology

Synthetic biology is the study of reorganizing defined and identified biological parts methodically and reasonably to develop and construct working biological designer products, structures, and organisms with expected, practical, and innovative elements. This is achieved through the application of fundamental engineering concepts regarding biology. Synthetic biology involves employing technology that allows for the analysis, synthesis, assembly, modification, and passage of genetic material into live organisms, in addition to a database of biomolecular materials accumulated for more than fifty years of molecular biological and functional genomic studies [15].

The inclusion of engineering concepts in biology is what characterizes synthetic biology. It facilitates logical building for industrial purposes by employing engineering concepts such as standardization, modularity, and abstraction. A biological part, or "biopart," is made up of DNA fragments. Biological systems are formed by the integration and fusion of biological equipment. The design phase is the first stage in creating a new biological system. This might require constructing a detailed computer model and doing thorough in silico testing of the system. More information can be gathered from the differences between what is observed and what is predicted throughout the Test phase (the Learn phase). With the newly acquired information, the model can be refined and modified in a new Design stage. It could require numerous runs of this process to obtain the necessary new biology. The Synthetic Biology Open Language (SBOL) information norm was developed to promote the exchange of concepts and material among those in the synthetic biology profession. Biological patterns can be modeled in silico with the assistance of this collection. The goal is to improve the efficiency of sharing information between scientists. A cell's surroundings are required for various bioparts, technologies, and biological systems to operate properly. The cell is particularly necessary to organize outside stimuli and deliver energy to the biopart. The cellular surroundings in synthetic biology may be built from a freely accessible common element termed the chassis [5]. The genomes and biochemical pathways of chassis are well-known, allowing for the quick generation of platform strains [16].

2.5. Tools in synthetic biology

To give cells autonomy, genetic circuits are frequently built to be orthogonal to the host, guaranteeing that the control components driving these genetic circuits aren't found in the host's signaling systems [17]. The use of genetic circuits to improve chemical manufacturing is commonplace. Furthermore, microbial development toward enhanced biochemical synthesis can be accelerated by the application of evolving genetic circuits [18]. Induction of genetic circuits - LacI and TetR, both bacterial repressor proteins, represent two such instances. By attaching such regulatory proteins to transcriptional regulating areas, they were transformed into effective gene expression regulators in mammalian cells [17]. Sequence-specific DNA binding domains (DBDs) have been found, and their structure–function relationships have been clarified. This has led to the creation of modular synthetic transcription regulators, which are essential resources for creating synthetic gene circuits since they can be tailored for targeting nearly any portion of DNA [19]. Since synthetic biologists proceed to enhance their methods for controlling cell behavior, numerous are looking at typical transcriptional networks inside cells to learn the way cells regulate these pathways, as well as intrinsic inducers that trigger genetic circuits. Zinc finger proteins (ZFs) and transcription activator-like effectors (TALEs) represent two forms of DNA-targeting proteins that identify and attach to DNA to change transcription in host cells. Combining numerous ZF protein domains allows the creation of synthetic ZF proteins, enabling particular sequences in the genome to be addressed. Such synthetic components are crucial for the construction of genetic circuits that track and respond to endogenous variations in natural transcription that govern cell and tissue integrity. Cellular computation and memory - Cells contain an automatic capacity to detect a variety of signals in their surroundings, carry out calculations, maintain details, and conduct actions according to this data. Numerous synthetic biologists are working to exploit these characteristics to gain biological oversight of cells for future medicines, testing, and biological production purposes. Multiple techniques were used to create synthetic memory, involving genetic switches with feedback loops and memory states that correlate to the prevalence of one repressor. Scientists are employing synthetic memory in cells to transform transient cellular actions into identifiable memories stored in the genome to discover how minor variations more accurately in cellular phenotypes, such as cell fate decisions and molecular changes throughout the disease's development and time frame, may be explained for the transforms in cellular phenotype [17].

2.6. Application of synthetic biology

Promising methods for creating novel biological systems or modifying already-existing ones for practical uses are provided by synthetic biology. It can be considered a transformative breakthrough at the core of the Bioeconomy, likely to provide fresh approaches to issues affecting industry, medical treatment, the agricultural sector, and environmental issues. As an example, biomedicine is making tremendous strides thanks to synthetic biology, and these developments will drastically enhance medical care. Individuals have already benefited from the known CAR (chimeric antigen receptor) technological advances, which modify the patient's T cells to identify and fight cancer cells [20]. Plant synthetic biology offers a fresh perspective on how to address important plant biology issues. Biosystems can be reprogrammed to support sustainable agriculture using plant synthetic biology. Improved nutritional value, reliable crop engineering, inventive material development, and the production of diverse biological products are just a few of its many uses [21]. More and more, synthetic biology is being used to enhance the balance, solubility, and binding capacity of proteins, as well as to produce vaccines and treatments based on cells. Drug target recognition and deconvolution, biosynthesizing products from nature, target finding, genetic circuits, and therapies based on cells are among the areas in which synthetic biology continues to be used in drug development [22].

2.7. Application in medicine

Synthetic biology for medical testing enables continuous surveillance of human well-being and the accurate assessment of disease intensity by changing the genomes of cells or microbes, establishing them with the ability to recognize abnormal cells and abnormalities inside the human system. The CRISPR-Cas9 technology, for instance, may be utilized to build biological circuits inside cells that selectively detect critical protein molecules in intracellular cancer signal networks, allowing for more exact assessments of cancer cell location and condition development [23]. As an application in *immunotherapy,* malignancy immunotherapy serves as one of the many interesting possibilities for the transplantation of cells. Tumor investigations reveal that immune cells, particularly T lymphocytes particular for tumor-derived peptides, infiltrate the tumor. During the first research, scientists separated, grew, stimulated, and injected tumor-infiltrating lymphocytes (TILs) into individuals, but results were inconsistent. This technique has been improved by targeting patient-derived cells with tumor-specific T-cell receptors (TCRs) with increased impact to boost anticancer efficacy. Chimeric antigen receptors (CARs), which are made up of high-affinity binding domains that attach to tumor antigens on cell surfaces and signaling domains that trigger T-cell antitumor capabilities, demonstrated improved effectiveness if injected into individuals' T cells and utilized to treat malignancies [24]. Another application of SB in medicine is the *HEK-β cells used for diabetes treatments*. Within pancreatic islets, beta cells generate and release insulin. Being the major location of insulin production in mammals, β cells monitor blood sugar levels via a signal transduction route that includes glycolysis and the stimulus-sensing-secretion coupling mechanism. The next stages comprise the release of insulin. The blood sugar is carried to β cells and processed by glycolysis within the cell, leading to cell membrane depolarization, production of energy, and the closure of K+ATP channels, which triggers the calcium channel Cav1.3 and promotes calcium influx along with the release of insulin granules. Increased blood sugar levels in individuals with diabetes are caused by a lack of insulin-producing cells in the form of type 1 diabetes or a lack of insulin responsiveness in body cells in type 2 diabetes. In one of the researchers, human kidney cells were modified HEK-293-β to monitor blood sugar levels for insulin release utilizing a synthetic biology-based multi screening method [25].In diabetic medication, the layout integrates automatic diagnosis and medication. Overexpression of Cav1.3 offered a mechanism for the formation of a -cell-like glucose-sensing course in somatic cells, according to the scientists. The pairing of Cav1.3-controlled calcium and a synthetic Ca2+-inducible promoter enabled sugar concentrations to be monitored in vivo via a regulated transcriptional reaction. The cell line HEK-293-β for glucose-response insulin generation, which retained the equilibrium of glucose for more than 3 weeks upon placing the cells through the abdomen in mice, additionally auto-corrected diabetic high blood sugar levels throughout 72 hours in T1D mice in the present research. The benefits of HEK-293-β cells are obvious. HEK-293-β cells proved more effective than primate pancreatic islets in regulating postprandial glucose metabolism in T1D mice. Furthermore, HEK-β cells are easier to cultivate in vitro. It is believed that the engineered cells from humans will be generated readily, economically, and effectively, in accordance with up-to-date pharmaceutical industry standards and norms, enabling the development of prepared-for-use advertisements with excellent attributes for product simplicity, security, and excellence. This very inventive synthetic cell offers the idea of deliberately reprogramming any kind of cell to obtain specific skills like managing blood sugar levels [25]. While bacterial antibiotic resistance becomes a growing concern, synthetic biology is returning to a nearly century-old idea of employing bacteriophages to combat bacterial diseases. The formation of biofilms, which are surface-associated colonies in a hydrated network of extracellular polymers, is an example of bacterial immunity to drugs and human responses. Engineering T7, an E. coli-specific phage, to express dispersin B (DspB) enzyme for biofilm breakdown is an instance of creating a bacteriophage with higher bactericidal capabilities. In an additional investigation, the M13 phage was modified to improve the effectiveness of antibiotics in phage-drug mix treatment. The phage was engineered to excessively express LexA3, an SOS repressor in E. coli [26]. Additionally, in the United Kingdom, studying at Imperial College has resulted in the engineering of designer cell which had might be helpful in the advancement of illness therapy. Researchers in the Departments of Chemical Engineering and Chemistry invented a method for engineering artificial cells that respond similarly to biological cells when exposed to external variations. A group of synthetic biologists has discovered a mechanism for imitating the dynamic properties of natural sub-compartments in engineered cells, which may be present whether within or outside the cell [27]. Synthetic biology might be applied to produce yeast to manufacture pharmaceuticals more effectively and cheaply on an extensive basis. Artemisinin, a malaria medication, was the first medicine synthesized in this manner. It is naturally generated by sweet wormwood. Pharmaceutical corporation Sanofi has established the biochemical route that produces artemisinin's precursor, artemisinic acid, in *Saccharomyces cerevisiae*. The output of artemisinin was increased by redesigning yeast cells to include the genes required for the mechanism [5].

2.8. Application of synthetic biology in vaccination

Synthetic biology has greatly assisted in pushing vaccine advancement outside of the conventional boundaries, aiding in designing of novel biological systems with improved effectiveness and security in addition to accelerating vaccine manufacturing processes [28].

Vaccinations constitute essential parts of the healthcare system, helping to reduce mortality and death from a variety of illnesses. The basic objective of teaching the human immune system how to react strongly to a pathogen despite triggering serious sickness entails two key stages: (a) choosing an antigen and (b) getting it into the body. Present vaccines employ complete (deactivated or live attenuated) microorganisms or viruses or chosen portions that are administered into the body by different means [29]. COVID-19 synthetic RNA vaccines (Pfizer-BioNTech, Moderna) - The nucleoside-modified RNA that encodes for the spike protein antigen and is coated in lipid nanoparticles forms the basis of synthetic RNA vaccines for SARS-CoV-2. The plasmid vector into which an entirely synthetic SARS-CoV-2 S gene had been cloned provided the template for the in vitro production of the RNA vaccine. The pattern of the translated protein was altered to maintain it in the prefusion form [30].

2.9. Application of synthetic biology in genetics

Synthetic biology can improve gene stability. Blazejewski et al. developed a computational tool, Constraining Adaptive Mutations using Engineered Overlapping Sequences (CAMEOS), that can restrict and shield synthetic biology structures against mutations. CAMEOS considers both point mutations and indels, which influence protein coding and mutations that alter long-range connections. It emphasizes the overlapping nature of genes and analyzes whether a mutation may be handled by several proteins generated from the same sequence statistically. This is significant since host cells possessing a mutation in the synthetic gene design can expand and overwhelm the population, resulting in an alternate or less productive ultimate product. Although gene flow can enhance genetic diversity, if the synthetic gene intersects with an important gene, the identical mutation will die off rather than taking over the population [31].

2.10. Application of synthetic biology in biofuel production

It has sped strain engineering to the extent where sample strains that may be evaluated for industrial usage have been generated, heavily advancing biofuel manufacture. Considering it has a long history of manufacturing biofuel, especially ethanol, plus has been fitted with different synthetic biology approaches, yeast *S. cerevisiae* is a commonly used chassis that has been explored for the bioproduction of a number of chemicals. The synthetic biology design stage for production of biofuel includes model development, data mining, synthetic promoter, terminator, and enzyme sequence design, metabolic pathway and metabolism design, and cell production and fermentation process design [13]. Approaches for producing first-generation biofuels: First-generation biofuels rely on oilseed crops to produce triacylglycerols, which can then be chemically changed to biodiesel, or else they rely on crops as biomass to produce sugar or starch from corn, wheat, or barley, which is then fermented and distilled into ethanol. Second-generation biofuel study methods: Instead of food crops, synthetically designed replacements, or second-generation biofuels, rely on the changed microbial cell as the foundation of biofuel production [32]. Additionally, the investigation of several more possible organisms is expected to enhance research on the manufacturing of synthetic biofuels considerably. *Cyanobacteria* appear to be encouraging at the beginning. Because *cyanobacteria* can convert carbon dioxide and solar energy into biofuel particles, they may serve as an exceptionally efficient organic system for the manufacture of biofuel. *Synechocystic sp. PCC 6803* represents one such bacterium [33]. This application of synthetic biology, which involves producing chemicals and fuels, is expanding quickly. The most complicated aspect of microbial genetic engineering is the construction of synthetic microbial hosts [34].

2.11. Benefits of synthetic biology

How we produce nutrition, the things we consume, and from where we get resources and medications will all change as a result of synthetic biology [35]. People's comprehension of the biological components' mechanisms for functioning and the complex framework that regulates organisms is enhanced by the integration of synthetic biology and engineering. Significant progress has been made in the genetic engineering of living beings, including the treatment of diseases. However, this also raises the possibility of bio-risks related to safety concerns, security of life, and even cyber biosecurity [36]. The development of synthetic biology holds great potential for the creation of vaccines. One crucial benefit of creating and producing mRNA vaccines is that they can be used as a completely synthetic foundation approach for many targets. This will be a crucial component in developing an eventual industry that is successful. The process of optimizing the product for a particular virus spread might then be simpler. Synthetic biology's logical methodology would strengthen vaccine development [37]. The mRNA COVID-19 vaccines were developed using synthetic biology, making them among the initial vaccinations to employ synthetic biology on such an extensive basis [38]. No matter the individual use, the utilization of synthetic biology demonstrates the rapid speed of technical discovery and acceptance through extremely fruitful collaborations between academics and industries [29].

2.12. Ethical risks of synthetic biology

The enthusiastic principle appears troubling from a moral point of view, particularly considering that the advantages and disadvantages of synthetic biology might not be distributed evenly among all economic classes and countries. Synthetic biology has been predicted to likely have similar effects to technological breakthroughs, which have historically benefited the wealthy at the expense of those living in poverty. Because such nations have far fewer resources for treatment and less opportunity to purchase and administer vaccinations, a worldwide outbreak of an infectious disease brought on by bioterrorism will probably have far more consequences. Consequently, there's good reason to act with concern if a particular innovation in synthetic biology raises the possibility of a transmissible illness breakout, even though it has a chance to greatly improve life for specific segments of the world's population [39]. Furthermore, the goals of synthetic biology are not always met. Artificial life forms are typically created in accordance with human interests or needs, yet they may also be an expedited version of natural development. However, the creation and result of synthetic organisms are not always going according to our plans because of the limitations of our understanding of life codes. Along with other important considerations, including academic and professional safety evaluations and legal frameworks, family, legitimate, acceptable, and faith-based factors should also be taken into account [9].

2.13. Synthetic biology and future perspectives

Regarding the future predictions about synthetic biology, it is believed that by 2030, every person will have consumed, worn, implemented, or received treatment with something that was derived from synthetic biology. Also, it is expected to make a great contribution to the world, as seen by the enormous amount of funding it has received in recent years. According to reports, the industry got over $7.8 billion in funding in 2020 from both the public and private sectors. This is more than twice as much money as the industry received in 2019 and

2018. Moreover, it is projected that the value of the worldwide synthetic biology industry will surpass $14 billion by 2026 [5]. Accordingly, biology will no longer be primarily an analytical study but rather a prescriptive one in which accurate functioning hypotheses are generated and put into reality. Synthetic biology requires resources, personnel that is skilled in its involvement, and widespread support in order to live up to its vision of an innovative bioeconomy.

3. Conclusions

Synthetic biology is an innovative field with a great promise for future discoveries at the intersection of biology, engineering, and technological advancements. As it combines science and technology to create or modify current biological systems, organisms, enzymes, or cells, it has a purpose to make a functional and operating device that will have established features that are not able to be found today. While being applicable in diverse areas of life, the benefit of synthetic biology is also reflected in the efforts of many scientists and academics all around the world, based on sharing knowledge and ideas, and implementing the same to create novel devices. Since synthetic biology can be applied in health care, medicine, agriculture, or the environmental industry, it can be seen how scientists are able to observe human health or how to cure diverse health issues by changing the genomes of specific cells. While on one hand,e there is full potential of this discipline, on the other hand, it can also be applied to finding the solution for current and future environmental issues. As all of these are listed as benefits of synthetic biology, like every other field, it also has its own risks. If not designed in the way it is wanted, synthetic biology can go in the wrong direction. By some, it is believed that synthetic biology may disrupt the line between life and non-life. In terms of the future perspective of synthetic biology, this discipline is still under expansion. As a part of today's world, we can only be witnesses of technological innovation when combined with diverse scientific fields. With the right and skilled team, educated personnel, synthetic biology will have a promising future.

Declaration of competing interest

The authors declare that they have no known financial or non-financial competing interests in any material discussed in this paper.

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