Synthetic bio/techno/logy and its application

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ABSTRACT
Synthetic Biology, which began in the 1970s, is a rapidly growing, multidisciplinary field that aims at improving our capacity to design, assemble or develop biological molecules. Nowadays, instead of mapping a particular gene and transferring it to a deficient cell, scientists are building life from scratch in the absence of societal debate and regulatory oversight. This mini-review outlines the explanations and principles, genome minimization techniques, application and ethical considerations.

Introduction
Synthetic biology (SB) is a scientific area that uses science and technology to build or redesign existing biological systems or new organisms, such as enzymes, genetic circuits and cells [1]. It emerges from various fields of science including biology, engineering and computer science. SB differs from conventional genetic engineering in terms of the complexity of organisms or systems created by researchers. The aim is to design and build biological systems at each level of organization through genetic networks and entire organism cooperation rather than focusing on the expression of individual genes or gene components [1]. Modification of an organism’s genome can cause unpredictable effects and increase the complexity of the genome.

SB aims to build or reform new organisms in human services [2]; produce highly sought products in medicine, energy, the environment and agriculture. It also has a high potential for creating new jobs, boosting the global economy [3] and offering solutions to environmental challenges. This paper provides brief information about the advantages, risks, applications and ethical concerns in SB.

Historical origins
Synthetic biotechnology recently emerged in the 1970s [2], and it has a long-standing history of genome-scale engineering (Figure 1). The emergence of recombinant DNA technology has created a new biotechnology era [3], known as SB, which was developed at the beginning of the twenty first century. Synthetic genomics merged with advanced methods for synthesizing DNA sequences and allowing scientists to build genetic material, which was impossible with previous biotechnological approaches [5]. Nowadays, the entire genome of an organism can be synthesized [6].

Principle and methods
Synthetic biologists might use synthetic genomics to partially or wholly synthesize genes of restructured or completely novel life forms (Figure 2) with the aims to create life forms that are substantially different from those that already exist [8,9]. To achieve their goal, synthetic biologists pursue several visible projects, like building the library for the biological parts and devices with known functions or features. In addition, synthetic biologists have attempted to develop microbial pathways for the production of chemical compounds. These areas aim to produce biological systems as biochemical plants using energy, industry and medicine [10].

Genome minimization
Genome minimization is a method and tool for maximizing the efficiency of biotechnology. This helps to understand the basic evolutionary processes. Genome
minimization combines genetic design with genetic engineering to change and construct biological systems and then evaluate the effects of genetic modifications [11,12]. Instead of establishing a lower life from the beginning, genomes may contain many non-essential genes with little or no importance to the organism [13]. Any organism genome can be reduced by top-down or bottom-up frameworks, which cover several genetic, metabolic or protein synthesis mechanisms [14]. Genome minimization also provides insights into the metabolism of more complex organisms by better understanding how a single genome encodes different types of cells. Minimization can be used to identify genes essential in all cell types as well as genes essential for specific cell types only [15,16]. Several approaches can be used to identify minimum genomes. It includes comparing different old lines of the minimal genome in silico (in vivo and in vitro) or large-scale gene inactivation. In recent times, scientists have developed a mathematical model for the hypothetical cell with the lowest gene quantity necessary to grow and divide in optimal conditions [17]. Reports have shown 20% genome reduction achieved for Escherichia coli (reviewed in 18), Bacillus subtilis and Mycoplasma genitalium [19].
approaches for the design and construction of artificial cells in SB, the top-down and bottom-up approaches, are illustrated in Figure 3.

The top-down approach (Figure 3) aims to shorten the genome by identifying the lowest number of genes needed in laboratory conditions to survive [21]. It develops a genetically stable, metabolically robust platform with low energy to carry out tasks and generate less unwanted waste products. In this approach researchers identify and isolate specific chemical processes performed easily by metabolically active bacteria. The genes responsible for this chemical process are sequenced or synthesized and inserted into yeast cell. Then, highly productive modified yeast cells will be produced and these modified yeast cells perform new or enhanced chemical processes and functions [22]. This is done either by stripping or replacing the genomes as shown in Figure 3 [20]. Thus, only a small number of cells is enough to fulfill a limited set of physiological functions. However, most of these cells will have low environmental persistence and will only survive under specific laboratory conditions [23,24].

The bottom-up method (Figure 3) is to create new kinds of self-reproducing minimal cellular life. It increases the complexity of the biological system by assembling various non-living components [20]. In other words, a bottom-up approach can cause the engineering of novel minimal biological systems with desired properties [25]. It uses raw materials, which are not necessarily natural (non-living) but mimic the properties of natural molecules [26]. Based on biological knowledge, life can be chemically constructed with suitable intermediate organisms. Recent advances have resulted in reforming the organisms with entire synthetic genomes with DNA synthesis and computation. Technical improvements in the assemblage of large pieces of DNA have also led to several milestones. These included de novo DNA virus synthesis, the re-assembly into the bacterial genome of chemical-based DNA segments and mail-order DNA poliovirus regeneration [27].

The protocell is the final bottom-up creation, which mimics certain functions of cells. It is a polypeptide-like or membrane-like structure that separates the inner and the outer world [28]. Protocell systems are chemical systems which are designed to imitate cell behaviour and emerging properties via their component interactions [29]. Protocells have potential biotechnological applications. Protocells could be used for synthesis and processing of biotechnological products with high efficiency in mass scale and reduced cost of production [29].

Application of synthetic bio/techno/logy

SB is a technology applied in all sectors, such as agriculture, food, health, chemical and industrial production [30]. It is used widely in nearly all science areas (Figure 4).

Health applications

Synthetic biology techniques based on rapid design, with iterative prototyping of the gene circuits, have enabled the creation of several innovative diagnostic approaches. Many of these solutions are ongoing and show the growing maturation of the field for critical biomedical issues [32]. SB offers potential benefits for immunoassay development, diagnosis, drug screening, new antibiotics generation, drug production and sensor-effector therapeutic development [33]. Diagnosis of communicable and non-communicable diseases including cancer, coronary artery disease, Ebola, Zika, tuberculosis, malaria, HIV, SARS-CoV-2, routine blood test quantification, and water quality monitoring has been successfully performed using SB [32, 34]. Recent work in animal models for human diseases has shown that the use of sensor effectors and mammalian cell reprogramming may soon pave the way for genetic and cellular therapies [35].
Agricultural applications

Synthetic biology also delivers major outcomes for agriculture [36]. It can increase crop-based sustainable fuel production [37,38]. Producing plant hormones with SB will provide opportunities to manipulate crop nutrient uptake and reduce nutrients applied as fertilizers [39]. This technology has an important role in bringing long term agricultural transformation through biosensors, synthetic speciation, microbial metabolic engineering, multiplexed mammalian CRISPR and new anti-microbial substances production [36]. SB will generate products to reduce farm waste and provide methods to convert them into methane and other economically significant products [40]. Specifically, synthetic biology promises to deliver benefits that increase productivity and sustainability across primary industries, underpinning the industry’s prosperity in the face of global challenges [36, 39]. The SB technology introduces organisms, processes and products that were thought not possible a decade ago [41]. Some research institutes and companies work on microbes to optimize their synthetic metabolic pathways, biofuel production, enzyme production and the development of engineered microbes. Engineered cyanobacterial organisms and eukaryotic alga could be used for making valuable industrial compounds like biofuels and other chemicals [42].

Environmental applications

SB’s contributions to environmental protection include biosensing systems that convert environmental signals into unique cellular events [43]. Other research efforts have concentrated on the engineering of micro-organisms to remediate a few of the most hazardous environmental pollutants [44]. Heavy metals and pesticides could be remediated by natural
bio-degradative pathways [45]. Engineering several networking microbial communities ignited the curiosity of remediation and other environmental protection [46]. Synthetically designed microbial groups have been developed to investigate their potential in health, environment, industry and evolution. A synthetic ecosystem between mammalian and bacterial cells could facilitate the study and mimic fundamental coevolution forms in nature. Symbiosis, parasitism, and predator-prey relationships are examples of these [33].

**Ethical considerations**

SB offers significant benefits to humanity. All responsible governments and a socially conscious industry are very interested in using these new technologies, in a way that does not transform products into hazardous substances [47]. However, it also raises some significant concerns. These include, for instance, worries about laboratory biological safety, the worsening of inequities, and challenges to existing intellectual property law systems [48]. Despite their benefits, the advances in synthetic genomics have led to an ethical debate on the synthesis of naturally dangerous pathogens to improve their virulent properties [9, 49]. After the first Obama Presidential Commission report in bioethics, the ethical value of SB became clear [3]. An issue in SB is that it can lead to the creation of organisms between the living and the machinery [50]. The other concern about SB was the possibility of intentional misuse of its knowledge [51]. The de novo synthesis of human pathogens poliovirus and Spanish influenza virus has been reported as a ground breaking study in the last decade [52]. Engineered organisms can be made from several structures which are artificially simulated and synthesized into one organism. SB raises problems relating to the scope and efficiency of patent law [53, 54].

**Data access statements**

Data sharing does not apply to this article as no new data were created or analyzed in this study.

**Disclosure statement**

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**Ethical declarations**

No need for an ethical declaration.

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