Perspectives

Engineering the future through synthetic biology

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Abstract

The last two decades have witnessed tremendous progress in synthetic biology. Despite the technological advances, the maturing field has yet to transition from fundamental study to translational practice. In this perspective article, I discuss my vision to enable this transition. With this vision, our next generation will solve global problems through synthetic biology.

Keywords

Synthetic biology; global problems; future generation; EBRC; predictable engineering

Main

Synthetic biology is an engineering discipline that focuses on creating or modifying biological systems for practical applications. This exciting field tries to solve global problems, including climate crisis, sustainable biomanufacturing, noninvasive diagnostics, therapeutics, and food inequality. This is a two-decade-old field although the discovery of the DNA structure could be considered to be the start of an incubation period for synthetic biology. Typically, the year 2000 is considered to be the beginning of synthetic biology with three seminal papers that demonstrated a toggle switch [1], an oscillator [2], and a negative feedback circuit [3]. The synthetic biology framework and workforce have been formed systematically from 2006 to 2016 when the US Synthetic Biology Engineering Research Center (SynBERC) maintained, encouraging similar centers to be formed in other countries. The efforts of SynBERC to advance the field continued in the United States for 10 years, followed by those of the Engineering Biology Research Consortium (EBRC). Since 2016, EBRC has provided the visions of engineering biology to educate funding agencies and researchers all over the world. Multiple roadmap documents have been written, and they are freely available on the website (ebrc.org). The climate roadmap will be available in September 2022, on the same website.

Synthetic biology is becoming a maturing field [4]. The discovery of the DNA structure can be seen as the beginning of learning languages. In other words, we saw the four letters ATGC with the discovery of the DNA helix structure and the base-paring rule 70 years ago. We then learned how to read the words, sentences, and paragraphs using DNA sequencing. Now, we are writing poems that describe the truth in life using DNA synthesis technology. In the future, masterpieces will be created by our imagination and synthetic biology tools, including CRISPR-based genome editing tools [5-7]. EBRC is providing the vision to solve global problems using synthetic biology.

The next decades will witness great advances in computational biology adopting machine learning, forward engineering for building programmable genetic circuits, and predictable

bioengineering assisted by directed evolution. Computational algorithms such as AlphaFold [8] and Rosetta [9] will facilitate protein design to create new enzymes, transcription factors, and transporters [10]. The screening of protein variants will be facilitated by combining directed evolution with such protein structure prediction programs even if the crystal structure is unavailable [11]. The prediction of 3-dimensional structures of RNA and its dynamic interactions will be possible by combining molecular simulation technology and experimental analysis such as SHAPE-seq [12, 13]. Machine learning will make biology better predictable [14, 15]. Genetic circuit building will be more systematic using an extensive genetic part library, easy-to-use circuit design programs (e.g., Cello [16]), and an iterative cycle of design-build-test-learn.

Synthetic biology will move from fundamental research to translational practice. Understanding the dynamics of microbiota and developing synthetic biology tools for consortium engineering will lead to engineering the entire microbiomes, as opposed to manipulating a single strain at a time [17]. Probiotics will be engineered to be used for diagnostic and therapeutic applications [18]. Paper-based diagnostics will continue to be developed [19]. Stem cell therapy and cancer immunotherapy will be realized using synthetic biology tools [20]. Metabolic engineers will continue to produce high-value chemicals and materials [21] as well as commodity compounds and biofuels [22]. Soil microbiotas will be engineered to reduce greenhouse gases and serve as a huge bioreactor [23]. Plastic upcycling will enable the circular economy and reduction of plastic pollution [24]. Microbes will be used to extract rare earth elements from the environment [25]. The space exploration will require more roles of synthetic biology, including studies of the impact of microgravity and radiation on organisms and development of photosynthetic organisms that survive and produce necessary chemicals and materials under harsh conditions in the Moon and Mars [26]. Sustainable bioproduction will reduce our dependance on petroleum-based products and contribute to solving the climate crisis [27]. Synthetic biology would solve the food inequality using nitrogen fixing bacteria, better crop species, safer ways to kill insects and plant pathogens, and alternative foods such as plant-based proteins and microbially-produced foods [28].

Translational applications of synthetic biology should consider ethical, safety, security, and societal impacts. For environmental applications of genetically engineered organisms, biocontainment strategies must be developed further and improved to meet the regulatory guidelines [29]. The consequence of genetically engineered microbes (GEMs) in the environment should be studied before their deployment [30]. DNA synthesis companies need to screen for potentially malicious or dangerous DNA sequences before synthesizing requested DNA [31]. CRISPR-based genome engineering should consider ethical implications [32]. The public should be better educated to make people better understand the new technology and make a reasonable decision.

We should educate and nurture our future leaders. Our next generations will implement and execute the vision that I discuss in this article. Because of our passionate and ambitious young researchers, our future is bright despite many global problems, including climate crisis, decreasing resources, pollution, food inequality, and the pandemic. Our future workforce will solve these global issues using synthetic biology. Young researchers' imagination is our limit. Dream high. Nothing is impossible.

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