Rethinking the Way of Life —Synthetic Biology

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Abstract. Synthetic biology is a rapidly developing field which stems from normal genetic engineering, and benefiting from the advances of chemical and physical experimental technology. In doing so, scientists can artificially create or predict certain traits of a creature. Serving as a tool to manipulate gene expression and genome sequence, synthetic biology has multiple applications such as for studying microorganisms, agriculture, environmental conservation, and economy. In the orthodox belief, people are not capable of intervening with inherent gene traits, but as breakthroughs in synthetic biology are constantly made, rethinking of the way of life is needed. Challenges and opportunities always appear simultaneously. Not only were the scientific thoughts shown through the development of synthetic biology invaluable, but people shall consider further topics of life. That is, what can be done with synthetic biology, for humankind and for the world. A brief introduction about this field will be given, and the applications and prospect about synthetic biology will also be discussed. In conclusion, all the advancements in this field have greatly enhanced scientists’ ability to manipulate genomes and have deepened their understandings about the way of life.

1. Introduction
Even though the creation of synthetic biology cannot be traced back to a couple of decades ago, this nova in the field of biology has its roots in various kinds of studies, including genetic engineering, biochemistry, and bio-informatics. The development of this technology is especially dependent on the improvements made in specific physical and chemical techniques in DNA sequencing—both typical and new, like Sanger, Shotgun, and Next Generation sequencing.

Currently, experimenting with microorganisms is a major part of synthetic biology. The study of yeast has opened up a toolbox for synthetic biologists. Furthermore, real world applications are also made, from mammalian cells to crops’ resistance to disease; the contributions of synthetic biology are irrefutably true. Technologically speaking, major problems with the experiments focus on correct methods and the right use of techniques. People’s dexterity in experimenting can still be enhanced. Now every decision made by scientists is not exclusive, because life on Earth is the collective result of all species. Correspondingly, consideration of what role humans can play in the development even in the evolution of life is necessary, since illness, animal behavior, and interrelationship of species are already under control due to GE and synthetic biological approaches.

2. Literature Review
Regarding the studies of pioneer scientists, the ambition to synthesize artificial life is realized in the field of synthetic biology. Through decades’ of efforts, scientists have made a number of breakthroughs, such as synthesizing large genomes, editing inherent traits, and revealing intricate mechanisms.
The first successful trial of synthetic biology, or in other words, artificial life, was achieved by Craig Venter and his colleagues around the year 2010. There were three major steps in this experiment: the synthesis of minimal genome, the synthesis of the larger bacterium genome, and the transplantation into living cells. In addition, relevant studies in yeast also brought scientists many benefits. Finding it convenient, comparatively simple, and controllable, scientists have widely expanded the methods to regulate gene expression through experiments on yeast. Furthermore, synthetic biology has begun to have practical use in the real world. By editing the genome sequences of kelp, crops, and mammalian cells, certain traits are successfully brought to these creatures. In prospect, synthetic biology has raised up a whole new way to consider the relationship and the manipulation of lives on Earth.

3. Analysis

3.1 Experimental material

3.1.1 CRISPR/Cas technology
Synthetic biology is greatly facilitated by genome engineering tools. Recently, CRISPR/Cas system has been proven to have great utility. Not long ago, scientists had already developed such technologies, such as TALEN and ZINC finger. Though considered a huge step forward, these two strategies were very costly to use, only medium in efficacy, and may have detrimental effects- due to their low accuracy. Luckily, CRISPR/Cas system was discovered.

This was initially found to be a kind of primitive immune system within prokaryotic cells. Considering its ability to recognize and manipulate certain gene sequences, scientists tried to develop it to be a toolbox in genome engineering.

Fig. 1. Multiplex Genome Engineering Using CRISPR/Cas Systems
Fig. 2. Multiplex Genome Engineering Using CRISPR/Cas Systems

The experiment led by Le Cong investigated the ability of CRISPR system to perform multiplex genome engineering. Focusing on vivo experiments, the scientists discovered the fusion complex of crRNA and tracrRNA could guide Cas protein to target sequences. Also, they found some redundant complexes could be eliminated from the system, such as RNaseIII. As a result, this novel way of genome editing was put forth, and later became one of the most useful toolboxes in synthetic biology.

3.1.2 Model species

E. coli and S. cerevisiae—a type of Yeast—are two types of host microorganisms used to test the functionality of certain synthesized genomes. The intricate mechanisms of specific molecular pathways in S. cerevisiae had been extensively studied in the former decades, making S. cerevisiae an optimal model species for biological engineering and synthesizing experiments.

There are three major reasons which make S. cerevisiae an ideal platform performing synthetic experiments. First, it has great, unmatched homologous recombination abilities, namely that it allows the joining of long length DNA fragments. Additionally, it can be readily manipulated. With certain genetic engineering tools having been developed, such as tools for over expression and knockouts, S. cerevisiae provides biologists with great manipulability. Considering the inherent advantage of eucaryon, S. cerevisiae has multiple organelles that meet the need of different environment to perform different synthetic experiments respectively. Last but not least, S. cerevisiae exhibits great tolerance against common toxic hydrolysates in cellular environment. Regarding these natural advantages of S. cerevisiae, S. cerevisiae has long been adopted as a useful tool to produce biofuel and certain chemicals.

3.1.3 Experimental techniques

As previously mentioned, synthetic biology has its roots in traditional fields. Therefore it can greatly benefit from genetic engineering and biochemical techniques. Two important technologies will be included in the discussion, DNA assembly and genome editing.

The aim of DNA assembly is to artificially create and transplant long length genomes into the reading frame of the experimented creatures. Collectively, there are three types of DNA assembly: techniques based on constrained sequences, editions depending on homologous recombination, HR, and de novo DNA synthesis. Interestingly, considering S. cerevisiae is naturally more capable of being manipulated through HR-dependent means compared to E. colis, the direct utilization of HR offers
biologists great convenience. Complementarily, genome editing techniques for yeast are developed. Relevant intricate chemical interactions are considered through such development, but with the help of previously mentioned techniques, some genetic toolbox has already been made for the yeast. Every step involved in creating a protein can be modified now, including the modifications made to promoters, mRNA, and translated proteins.

Additionally, in order to acquire desirable phenotypes, a large variety of biochemical techniques have been devised in order to promote the selection among libraries of countless mutations and potential traits.

All in all, the advanced techniques have now allowed synthetic biologists to manipulate functions of the yeast much more conveniently.

3.2 Applications

3.2.1 First laboratory trial
Craig Venter began with the synthesis of minimal genomes in microorganisms-the possession of the minimum number of genes needed for life by an organism [4]. Resorting to finding more efficient alternative method in the synthesis of mini genomes, Venter utilized the assembly of polymerase, but not involving the commonplace primer in excess to a template. In so doing, Venter created the first synthesized genome of a virus.

Moving on from virus genomes to bacterium, Venter carried the final assembly of the genome in yeast—a more stable form than that in viruses. After transplantation of this artificial genome into living cells, Venter’s team utilized several biochemical approaches to overcoming the inherent challenges caused by restrictive enzymes within these cells. Hence, Venter’s venture of a synthetic organism was proved to be successful, paving the road for future development of synthetic biology. Besides the advancements made in technology, the greater legacy of this first trial is the courage and inspirations in exploring the new field of synthetic biology.

3.2.2 Protecting the environment
As the destruction to the natural world becomes more and more severe day after day, scientists have already put their attention on using the newly developed synthetic biology technology to address this crisis. As far as the biology community progressed, such technology has been used in the conservation of kelp forests [5].

![Fig. 3. Harnessing synthetic biology for kelp forest conservation](image)

Kelp forests are vital to the biodiversity surrounding them, so the loss of such forests has caused a cascade of destruction to the natural environment. Nowadays, with synthetic biological techniques, biologists can effectively conserve the kelp forest either by directly manipulating kelp genomes or helping kelp combat its competitors, inhibitors, or other harmful environmental factors.

Direct intervention can be effective: the improvement of genes within kelps forestalls the impact of detrimental factors. The enhancement of several genes which perform a certain function, for example,
heat or pollution tolerance, will have obvious improvement in the kelp’s survival against unfavorable conditions. However, directly changing genomes of kelp is still a controversial issue, both technologically and ethically, which needs further investigation for support.

Correspondingly, indirect approaches are more feasible and workable. Basically, the genomes of microorganisms, like bacterium and virus, are much smaller and easier to edit through synthetic means compared to the intricate structure and function of the kelp genome. Even though concerns about specific impact on kelp still remains, scientists can more easily to seek solutions and implement the strategies in generating microbiomes to help kelp conservation. For instance, the engineered microbiomes will have limited impacts on the kelp. Thus they can help the kelp tolerate heat waves or severe weather conditions caused by global warming. In addition, efforts other than engineering microorganisms have been made. Historically, environmental cues like overfishing have led to the unbalanced increase in sea urchin population, causing much grazing pressure on the kelp. Through genetic engineering, the populations of some sea urchins are constrained in an area to reduce grazing pressure on kelp.

Lastly, engineered crops also made many contributions. With enhanced nitrogen fixation, the engineered crops have less dependence on nitrogen fertilizer. Causing less water run-off, these crops can reduce the impact on the kelp which relies on nitrogen to grow healthily. Moreover, some engineered crops can be harvested as the alternative of sea urchin predators-certain types of fish, because after engineering, these crops can offer valuable nutrition like omega 3, which is typically found in sea fish. The feedback result of this strategy, which is controlling sea urchin population, prohibits the recurrence of trophic cascades-the destruction of kelp caused by grazers.

Challenges emerge as new technology appears, but for the global goal of protecting the environment, the science community shall never give up trying. The conservation of the kelp is an excellent start, and new breakthroughs will be continuously made.

3.2.3 Bolstering agricultural and economical development

One of the most severe problems brought about by overpopulation is the shortage of food. Being farmed as a main source of food for thousands of years, crops are essential to this problem. However, viruses and pathogens constitute a great challenge to the healthy growth of crops. Considering that it is possible to add virus and pathogen resistant traits to crops by transplanting synthesized genomes in to them, scientists have found that a solution may be found through synthetic biology means. Already, two potential solutions have been proposed [6]. The first one is to identify specific genes essential to disease resistance within natural plants’ cells and then endow those features to crop by transplanting. The second is the production and installation of a synthetic chloroplast genome, a synplastome, for broad pest resistance. Though both feasible, these two proposals still need to be further tested and refined. Despite unsure proposals, by the same token, scientists have already succeeded in some types of plants by recoding codons in a cell.

3.2.4 Potential energy source

With the mounting population on Earth, the ever growing energy consumption is a major concern to the science community. Sought to help with the energy crisis faced by the whole world, biologists have come up with the idea of producing biofuels, which are renewable biomass [7].

Initially, yeast was used to create quite simple molecules, such as sugar. However, with more advanced synthetic biological technology, ambitious experiments have been focused on creating complicated biomass-biofuels. To maximize the utility of synthesized Yeast, scientists are also trying to develop specific pathways in the generation of biofuels, like editions to ensure that yeast is able to tolerate the toxic hydrophobic productions of the fuels.

Efforts have been made to address the existing problems respectively. Gene editions and protein engineering to regulate catalytic activity have been proved to be effective in controlling the productivity of biofuels. Additionally, reconstituted metabolic pathways are designed to meet the need for different types of fuels. As a consequence of biofuel production, toxic chemicals may accumulate
to thwart the productivity of yeast. However, the phenotype of toxic resilience is controlled by intricate genes, thus the enhancement in tolerance still needs future investigations.

4. Discussion: Consideration of the Way of Life

4.1 Contemplation of the development of synthetic biology

Beginning with traditional laboratory experiments, the utilities of synthetic biology methods and tools have been expanded to a worldwide scope. Ranging from conserving biodiversity on the planet, to finding cure for diabetes and cancers with available synthetic biology tools, this new field of biology is bringing more and more advantages to creatures all over the world.

More than merely the practical applications, the development of synthetic biology has brought people new insights into the consideration of the way of life. Today, humans no more have to be subject to natural selection, for people have established their own societies to sustain the livelihood of billions of lives. Furthermore, now people can even play the role of natural selection- with innumerable synthetic biology tools to modify protein within cells, to regulate DNA/RNA expression, to create gene circuits artificially, and to give man made selection pressure on experimental creatures. More resources are brought to humans in this way, including energy sources, medical cures, and more powerful crops.

The trend is apparent. Step by step, humankind is becoming the master of all the creatures, and gradually, is getting skillful at creating their own phenotypes, and even species. With such an ability in their hands, more attention can be paid to the entire situation of creatures in the world, and then help with the conservation of endangered species, bolstering energy production, and maintenance of humans’ safe livelihood.

4.2 Advantages and precautions

Every powerful technology has its inherent advantages and potential drawbacks. Synthetic biology is enabling humans to do things they have never conceived before—helping people to save lives and save the environment. Although synthetic biology is now widely used for beneficial products, it’s possible to produce biological weapons-weapons that are based on the toxic microorganisms- since people can already regulate genomes within bacterium, viruses, and single cell creature readily. For the brighter future of mankind and other creature, governments, scientists, and every citizen have the duty to weigh the pros and cons to synthetic biology on important issues.

Presently, there are mainly two measures to help establish the coordinated development of synthetic biology-scientific methods, and legal regulations. First of all, in pursuit of better control, scientific abilities ought to be enhanced, for instance, enriching biological toolbox, searching for more pathways, and figuring more complex mechanisms of gene expression within creatures. In so doing, risks due to negligence can be circumvented and scientific experiments can be monitored more comprehensively. Secondly, laws need to be established to prevent the overuse of synthetic biology. With the collaborative help of governments and international courts, the balanced development in the field of synthetic biology is achievable.

4.3 Prospect for future advances

Up to now, a great number of technological problems have been addressed in the field of synthetic biology, also bringing us the enhancement in our scientific ability to manipulate genomes and monitor gene expression. The ultimate goal of all kinds of biological sciences is to help with human lives. For now, the biggest crisis to human health is arguably cancer. Even though potential medicine has been sought and extracted among plants, the utility is still not influential enough to promote the cure rate of cancer though out the world. Regarding this, one of the major issues for synthetic biologists to solve is going to be the search for a powerful cure for cancers.

In order to achieve this, people should first learn from the history of synthetic biology in medicine. Natural substances in plants have been used to cure diabetes [8], so among the variety of species in the
plant kingdom, there shall also be chemicals that may help with cancers. Cancer cells have their own biological features, so it is practical to influence their growth and spread by introducing chemicals that intervene with their cellular metabolism.

Moreover, the emergence of cancer cells is always due to abnormal mutations of two types of genes-oncogene and tumor-suppressor gene. Because the aim of synthetic biology is to redesign genomes within living cells and to regulate their expression, relevant tools and technology can be adopted to manipulate the expression in embryonic cells to help preserve cancers. Also, through marrow transplantation, it’s possible to incept healthy cells into cancer patients to help them fight their illnesses.

5. Conclusion
According to the beliefs of post modern era scientists, synthetic biology is an innovative way to revolutionize the use of biotechnology by applying it on a wider range of issues. By constructing novel genomes or redesigning already existing entities in living cells, synthetic biologists can promote the development of low cost drugs, vaccines, antibiotics, production of chemicals and energy, detection through biosensors, transformation, bioremediation or biodegradation through engineered bacteria. At the same time, there are still technological challenges in this field, for the intricate nature of all biochemical responses in living cells has not been completely demystified now. A lot more efforts in the basic study of inherent traits of specific genomes and pathways are still needed. All in all, synthetic biology has greatly boosted the science in biology, for the inspirations brought by the study of synthetic biology are various: the discovery of better chemical assays, the more rapidity on the regulation of genomes, and eventually-the rethinking of the way of life on Earth.

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