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Challenges and opportunities in synthetic biology for chemical engineers

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HIGHLIGHTS

- Main challenges and opportunities for chemical engineers in synthetic biology are discussed.
- Standardization of biological parts represents a key challenge in synthetic biology.
- Chemical engineers play a leading role in engineering cellular factories.

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ABSTRACT

Synthetic biology provides numerous great opportunities for chemical engineers in the development of new processes for large-scale production of biofuels, value-added chemicals, and protein therapeutics. However, challenges across all scales abound. In particular, the modularization and standardization of the components in a biological system, so-called biological parts, remain the biggest obstacle in synthetic biology. In this perspective, we will discuss the main challenges and opportunities in the rapidly growing synthetic biology field and the important roles that chemical engineers can play in its advancement.

1. Introduction

Synthetic biology focuses on the design and construction of biological systems that draws on principles elucidated by biologists, chemists, physicists, and engineers. The term synthetic biology is almost as old as the term genetic engineering. However, synthetic biology has recently become a field of its own, mostly driven by the advances in DNA synthesis and sequencing and systems biology (Liang et al., 2011). Synthetic biology has broad applications in agriculture, medical, chemical, and food industries. Examples of landmark accomplishments include microbial production of artemisinic acid, a key precursor of the commonly used antimalarial drug artemisinin (Martin et al., 2003; Ro et al., 2006), commercial manufacture of bio-derived 1,3-propanediol, an industrial chemical with a variety of applications in solvents, adhesives, resins, detergents, and cosmetics (Nakamura and Whited, 2003; Tang and Zhao, 2009) and the reconstruction of a complete microbial genome by the J. Craig Venter Institute (Gibson et al., 2010).

The key challenges in synthetic biology exist on two main levels. One is the modularization and standardization of biological parts, while the other is the integration of these biological parts into devices with desired functions. Modularization and standardization of biological parts are analogous to modularization and standardization of electronic parts such as inverters, switches, counters, and amplifiers. By doing so, any part can be easily combined with others and reused in genetic devices (Bio FAB Group et al., 2006). Many experimental and computational tools have been developed to address these challenges, creating numerous scientific and technological opportunities. In this perspective, we will briefly highlight these main challenges and opportunities in the rapidly growing synthetic biology field for chemical engineers.

2. Challenges in synthetic biology

Luis Serrano, a systems biologist at the Centre for Genomics Regulation in Barcelona, Spain, recently said: "We are still like the

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Wright Brothers, putting pieces of wood and paper together" (Kwok, 2010). This statement aptly describes the current state of the synthetic biology field. Challenges are manifested at every step in the process of improving an existing biological functionality or creating a new one, ranging from the standardization of the "wood and paper" to the integration of these pieces at the system level.

2.1. Modularization and standardization of biological parts

By snapping together various pieces of different colors, shapes and sizes from a Lego® box, a multitude of structures with different functions such as a boat, a car and a building can be readily built. In the world of synthetic biology, biological parts such as genes, promoters and terminators are treated as building blocks in an analogous manner. Improved and novel structures and functions of cells are created by a growing community of scientists who develop and use these building blocks. However, many of the parts are still undefined and incompatible; the circuitry is unpredictable; the complexity is unwieldy; and variability crashes the system sometimes (Kwok, 2010).

All biological parts are encoded by the 4-letter DNA code: ATGC, which can be anything from a gene sequence encoding a specific protein to a promoter sequence regulating gene expression. In 2003, the Registry of Standard Biological Parts was established at the Massachusetts Institute of Technology. Relatedly, in 2004, the BioBricks Foundation (BBF) was established and the International Genetically Engineered Machine (iGEM) competition was started. Numerous new biological parts have been generated through these coordinated efforts for synthetic biology applications. However, most of them are not well characterized. This is mainly because there are many different interactions under various cellular backgrounds between most of the biological parts, and many of these interactions are not understood. For example, transferring a particular gene with known function in a heterologous host to confer new abilities is often not guaranteed. Similarly, even if particular enzymes are known to catalyze certain reactions, the naturally occurring enzymes are often incompatible or suboptimal for use in a non-native environment. They may lack desired substrate specificity or may be insoluble in desired reaction conditions (Martin et al., 2009). Thus, it is critical to improve the quality of the standard parts and increase the number of reusable parts (Collins, 2012; Grunberg and Serrano, 2010; Martin et al., 2009; Pleiss, 2011).

In addition to small biological parts mentioned above as genes or promoters, some larger parts are also included in the synthetic biology toolkit such as pathways or even whole cells. Not surprisingly, the standardization problem dwells in those parts too. For pathways, the main aim is to create novel or improved biological routes for the production of natural or unnatural compounds. Therefore, one key challenge is the construction and optimization of highly efficient pathways. Because a pathway contains so many genes, promoters, and terminators as well as other regulatory elements that are not well characterized, it becomes very challenging to reliably construct a target pathway with desired features. On the other hand, as a standardized part, a target pathway should be transferable between different hosts. However, most of the known pathways cannot meet this requirement because of the difference in the genetic backgrounds of hosts.

2.2. Integration of biological parts at the system level

Similar to the standardization challenge, integration of various biological parts into a functional biological system has also met many challenges. One challenge is related to the compatibility issue because different biological parts have evolved to fit different contexts. Moreover, the same biological parts may behave differently in different cellular backgrounds. Therefore, reprogramming cells using synthetic biology requires the interrogation and understanding of the living system's organizational principles (Bashor et al., 2010).

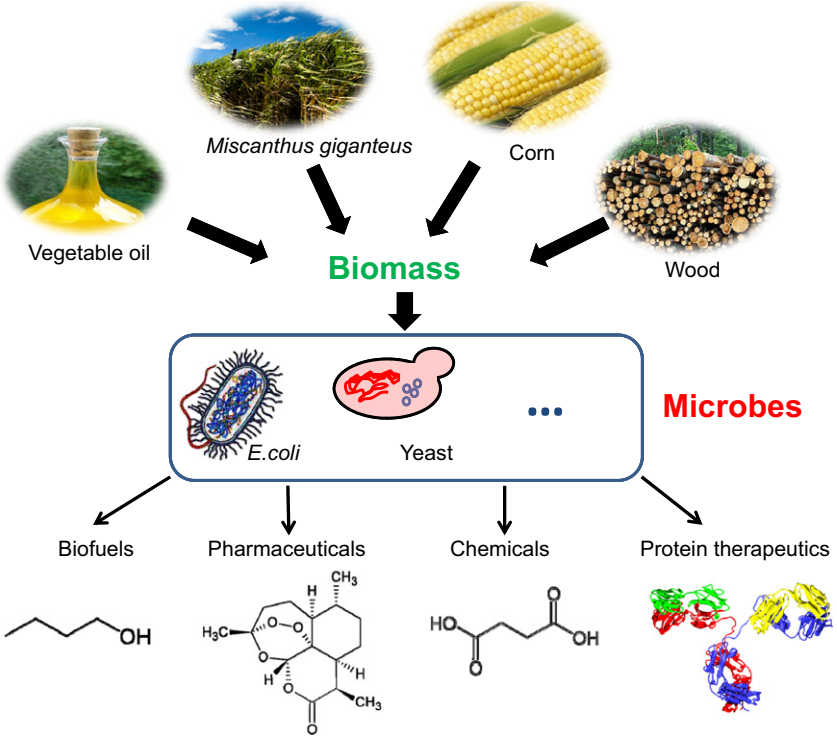

Fig. 1. Conversion of plant biomass to value-added products using recombinant microbes engineered by synthetic biology tools.

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