

# Synthetic Biology Innovation Will Spur More Efficient Chemical Engineering

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## Abstract

Synthetic biology is a new tool in chemical engineering that has already shown success in developing bio-based alternatives to chemicals typically derived from petroleum. A recent technical advance in synthetic biology stands to make this the design and development method of choice for chemical engineers.

## Introduction

In the last few years, chemical engineers have begun to take advantage of a promising new approach known as synthetic biology. This emerging method most often uses rational design to genetically modify an organism to produce bio-based components critical to building chemicals, offering the industry a tantalizing new path to chemical processing that reduces reliance on petroleum-based materials. However, progress in this area has been limited by tedious, manual methods for generating the synthetic DNA needed to enable this research and development. But recently a new, industrial-scale synthetic DNA technology is enabling rapid, large-scale experimentation to develop chemicals rationally, efficiently, and effectively.

Early synthetic biology-driven successes in the chemical engineering field have sparked a great deal of interest and, more tangibly, research investment into this area. Small startup companies are teaming up with big players in chemical processing to make the most of the tremendous potential.

Just this year, for example, a startup company called Genomatica announced the first commercial-scale production of bio-based 1,4-butanediol (BDO), a high-value chemical used as a solvent and in the manufacture of plastics and fibers such as Spandex. The company used a fermentation process with a biologically engineered version of *E. coli* to manufacture the chemical. In five weeks, the company which has partnered with DuPont Tate & Lyle produced 5 million pounds of BDO, worth nearly \$5 million. The annual demand for BDO, which is typically manufactured with petroleum, is in the billions of pounds. Converting to a bio-based form of the chemical offers not just a significant market, but also the opportunity to dramatically lessen the related use of petroleum.

Another small company, Cobalt Technologies, recently completed a production campaign of bio-based n-butanol, a product commonly used in surface coatings like paints. The chemical was processed at a fermentation scale of more than 100,000 liters and at lower cost than comparable production of petroleum-based n-butanol. Crucial to the process is the selection of the optimal microbial strain to perform the fermentation step; the company was able to test various strains for efficient sugar utilization to find the one best-suited to the task at industrial scale.

This type of microbial screening can be performed rapidly and effectively by using synthetic biology, which allows engineers to investigate factors in designing, building, and testing chemical production. Currently, however, scientists working on projects using

synthetic biology are hindered by limitations of the gene synthesis technology required to build DNA constructs involved in these efforts. Existing methods for stitching pieces of DNA together to form longer constructs are error-prone and tedious. Moreover, the process is not scalable, which keeps costs and the need for manual intervention high.

To address these limitations, academic scientists developed a new approach to gene synthesis that improves the quality, accuracy, and length of synthetic DNA. Based on research from George Church at Harvard, Drew Endy at Stanford, and Joseph Jacobson at MIT, this next-gen gene synthesis combined microchip oligosynthesis [1,2], high-fidelity amplification from complex DNA pools [3-5], enzyme-mediated error correction and assembly [6]. Gen9, a startup company based in Cambridge, Mass, is continuing to advance this technology by improving error correction and assembly to enable more diverse gene synthesis at longer lengths. Moreover, Gen9 is commercializing this biofabrication platform for massively parallel gene synthesis, offering lower-cost, more accurate DNA constructs.

Unlike other means of building DNA, the Gen9 manufacturing process permits additional capacity at an exponential scale. This BioFab<sup>®</sup> platform can generate tens of thousands of DNA constructs each year; the company currently offers clonal, base-perfect 3 kilobase constructs and plans to extend this range to 10 kilobases by the end of 2013. This capacity will enable chemical engineers to use longer, higher-accuracy, lower-cost gene constructs for testing genetic designs from genes to whole engineered pathways than can be done with current gene synthesis technologies.

This next-generation gene synthesis, and the corresponding radically increased capacity, will serve as a powerful turning point in synthetic biology. Ready access to long, reliable DNA constructs will allow chemical engineers to conduct rapid building followed by high-

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throughput testing and subsequent redesigning of microbes to identify the best performers for any given process. With this new innovation, engineers will be able to introduce synthetic biology at an industrial scale to pipelines dedicated to developing bio-based chemicals.

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