Developing platforms for biological engineering

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The fundamental goal of synthetic biology is to make the process of engineering biology easier. To date, much of the work in the field has centered around translating lessons from the development of other engineering disciplines to biological engineering. Standardization, abstraction, collections of reusable parts, reference standards, device datasheets, CAD tools and other engineering practices have all found uses in various synthetic biology design efforts.

Today, the challenge in synthetic biology is no longer just the invention new tools to support the engineering of biology but also the compilation of those tools into an integrated pipeline capable of producing engineered organisms on significantly shorter timescales. Due to the huge capital investments and uncertain development timeframes, engineered organisms are only a viable manufacturing option for products with very largest markets such as fuels and bulk chemicals. Yet these products only scratch the surface of what biology is capable. In order to make engineered organisms a viable solution for global challenges faced in energy, manufacturing, food and health and medicine, we need to make the overall process of engineering organisms more reliable and faster.

In common acknowledgement of this challenge in synthetic biology, several groups are working on platforms for synthetic biology. Some, like that of JCVI and Synthetic Genomics, focus on genome sequencing and synthesis. Others focus on modeling tools for the forward, predictive design of biochemical pathways (Palsson, Karp). Still others concentrate on CAD tools to design and optimize genetic programs (Densmore/Beal/Weiss, Peccoud).

We argue that there is no single "silver bullet" solution to rapid and reliable organism engineering. Rather, transforming biological engineering from an ad hoc artisanal craft to a rigorous, robust engineering process requires integration of software, hardware and "wetware" (biology) tools that span design, construction and testing (see Figure). Furthermore, each component of the platform must be designed with the overall platform such that throughput matches across the design, build and test steps and such that the wetware, hardware and software are tightly integrated into a cohesive pipeline. As a first example of this principle, we have designed and demonstrated a novel, one-pot DNA assembly process that is optimized to be performed at scale via automation. Unlike other one-pot DNA assembly methods, our approach can assemble standardized, genetic parts and requires no custom oligos or reaction conditions—key features of any automated DNA construction process. We now run this process routinely on off-the-shelf liquid handling robots using custom computer-aided manufacturing (CAM) software at Ginkgo.

	Wetware	Hardware	Software
Design	Standardized parts & gene databases	Computational power and data storage	CAD & LIMS
Build	Biochemical reactions for DNA construction	Liquid-handling robotics	CAM & LIMS
Test	Selections, (Bio) chemical tools etc.	Analytical instruments	Data analysis tools