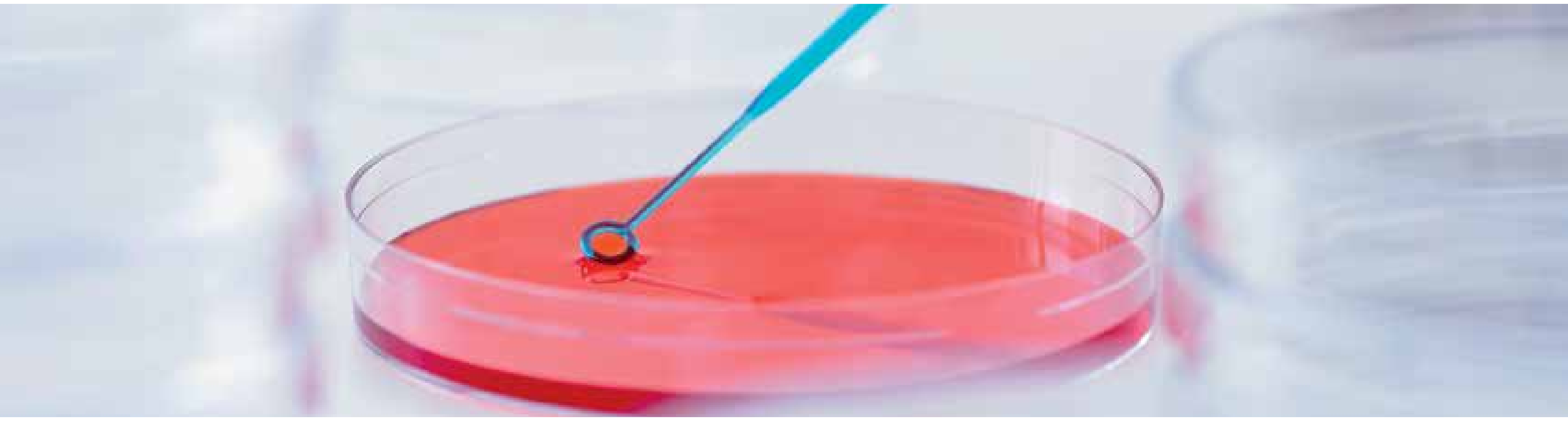

Exploring SynBio's potential for semiconductor players

Synthetic biology has the potential to disrupt trillion-dollar industries, and semiconductor players could help make it happen.

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The disruptive potential of synthetic biology (SynBio) is as compelling today as the transformative effect of the first transistor in the era of vacuum tubes. Both technologies appear to share similar growth trajectories, beginning with rapid innovations in basic sciences and moving quickly through process development to commercial reality. We also see signs that the semiconductor industry could play an enabling role for SynBio and in the process capture a portion of the value that this technology generates.

SynBio is poised to disrupt several trillion-dollar industries. The businesses emerging from this technology have the potential to revolutionize end markets in the agriculture, chemical, energy, and health-care sectors. And semiconductor players, if they capitalize on this momentum, might help usher in the era of SynBio-enabled cellular computing and capture adjacent market opportunities as the industry matures.

What is synthetic biology?

SynBio is the science of "programming" organisms (typically simple cells or microbes) with synthetic or artificial DNA that biologists develop by conducting metabolic engineering or otherwise modifying bacteria to deliver a specific function, system, or product. Scientists can, for example, program bacteria to convert biological feedstock into specific chemicals or biofuels.

Similarly, biotech companies can program bacteria or yeast with synthetic DNA to generate specific proteins that the industry can then use in the production of biologic remedies. SynBio entrepreneurs have begun to envision innovative new applications for the technology. One start-up, for example, used the peer-to-peer funding site Kickstarter to raise capital to produce a synthetically engineered light-emitting plant that it says could lead to a new source of lighting.

A 2013 McKinsey Global Institute (MGI) analysis of disruptive technologies identified SynBio as one of the top technologies that could cause massive economic disruptions between now and 2025. MGI expects next-generation genomics, including SynBio, to generate between $700 billion and $1.6 trillion of combined economic impact in 2025, disrupting major industries such as agriculture, energy production, and health care.[1]

Scientists focused first-generation SynBio research on the basic evolution of cells as they attempted to find the most productive applications. The second generation—currently under way—concerns designing these cells to make a more productive biological factory. For example, in the energy industry, first-generation applications concentrated on evolving existing yeast strains for more efficient ethanol production. Second-generation research focuses on designing and engineering the yeast to produce long-chain hydrocarbons that offer much higher performance and value than ethanol as fuel (for example, high-purity diesel or jet fuel) or to create advanced polymers.

A number of sectors have already adopted SynBio, but the industry remains vertically integrated and depends on the so-called scale-up model to organize the SynBio ecosystem and value chain. Specifically, organizations that use this model undertake each step on the path individually, from lab-based research to demonstration to piloting and scale-up, and, ultimately, to commercial production. The challenge with the scale-up model is that companies need to make significant investments in process engineering and development for this approach to work, and both capital and operating expenses can be crippling for relatively small and early-stage companies. These themes recall the early days of Silicon Valley, when companies dealt with the challenge of both designing and making semiconductors at scale.

We believe that SynBio will achieve its true potential only if the industry can develop a scale-out model that enables companies to use a set of standardized tools and technologies across industries to develop innovative new applications. The semiconductor industry advanced using a similar approach, ultimately evolving into a scale-out value chain that allows systems companies to innovate using standardized components.

If perfected, the scale-out model could make the process of modifying organisms as simple as writing computer code, and evidence already exists for applications in science and business. For example, a research team at Ginkgo BioWorks in Boston is developing the biological equivalent of a high-level programming language with the goal of enabling large-scale production of synthetically engineered organisms. On the manufacturing side, Gen9, a company founded by scientists from Harvard University, the Massachusetts Institute of Technology (MIT), and Stanford University, has developed a biological fabrication facility designed to produce synthetic DNA at scale.

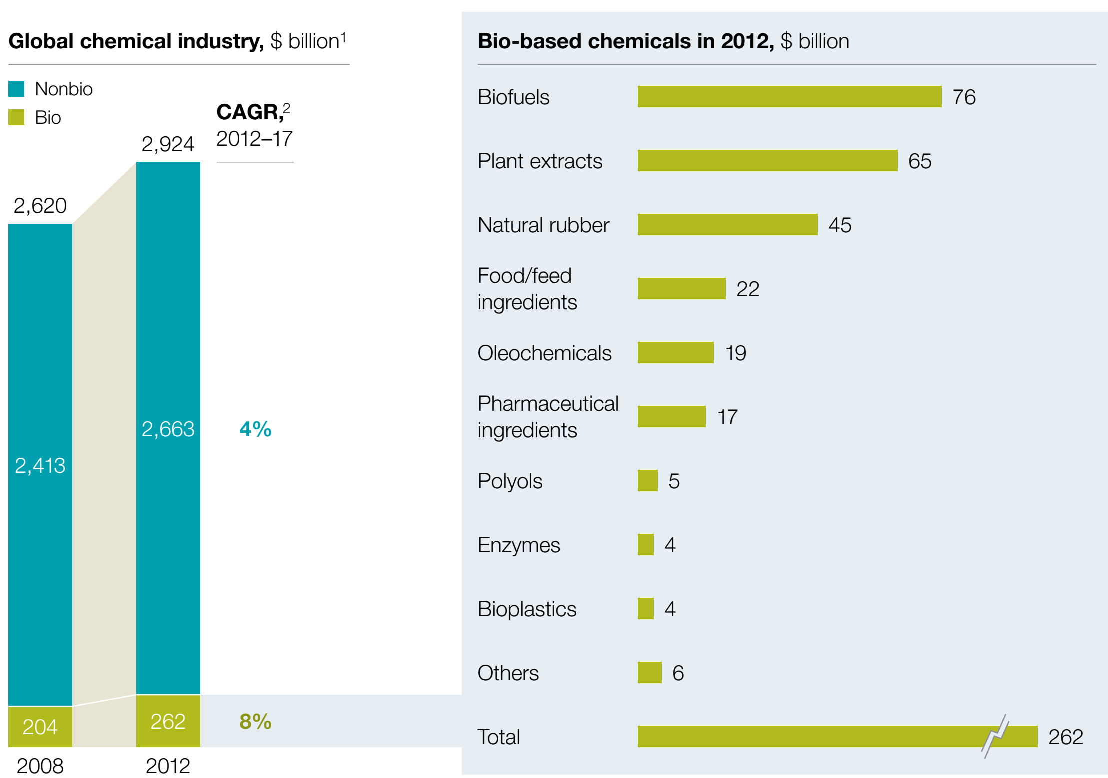
[1] *Disruptive Technologies: Advances That Will Transform Life, Business, and the Global Economy*, McKinsey Global Institute, mckinsey.com, May 2013.

Just as in the semiconductor industry, SynBio needs an ecosystem that includes process-development experts, designers (biologists), process designers, engineers skilled at scaling up processes, and intellectual-property designers (such as Ginkgo BioWorks). They also need tool developers to create the applications required to design and build cells—companies not unlike the electronic-design-automation players in the semiconductor industry.

Based on the growing involvement of leading SynBio players and the emergence of a critical mass of start-ups, this evolution is starting to gather steam. A number of companies are beginning to invest in synthetic-biology capabilities. Algenol Biofuels and Joule Unlimited, for example, have created demonstration plants that can produce high-value substances using synthetically engineered organisms—ethanol in the case of Algenol Biofuels and diesel fuel at Joule Unlimited.

Exhibit

Bio-based chemicals is a ~$260 billion market and growing rapidly.



[1]Figures may not sum, because of rounding.
[2]Compound annual growth rate.

Source: American Chemistry Council; IHS Global Insight; McKinsey analysis

Moving from the current vertical scale-up approach to a horizontal scale-out plan could alter the economics and structure of the industry in a positive way.

The impact of SynBio is already apparent in the chemical and health-care industries, where its first generation of processes now collectively supports roughly $360 billion in business. The next sections examine these two industries and identify parallels to the evolution of the semiconductor industry. It also explores opportunities for semiconductor players to apply their knowledge of the process and equipment technologies used in chip making to drive SynBio scale improvements.

Biologics in the chemical industry

The $2.9 trillion chemical industry depends heavily on petroleum-based feedstock as its primary input. This reliance, however, has subjected it to price increases and shocks as petroleum prices have risen and fallen. As a result, in the past ten years, the chemical industry has begun turning to synthetic biology to produce biological feedstocks in place of petroleum-based ones (exhibit).

Companies such as Amyris, DuPont, and Solazyme are employing SynBio to develop technically engineered biological organisms such as bacteria and algae to convert bio-based feedstocks into chemicals. A number of leading manufacturers are using these chemicals to develop products ranging from tires to fuels to fragrances. What's more, the chemical industry's use of synthetic biology is a good example of an application of cellular computing. Biologists are using organisms they have programmed to shift the chemical industry's input materials away from a petroleum base toward one that uses biologics. In fact, bio-based chemicals now make up roughly 9 percent of chemical-industry revenues, generating about $260 billion in annual sales.

Although significant progress has been made, most SynBio initiatives remain under scale. The critical processes to achieve the size required for cost-effective operations involve yield and process improvements, and the semiconductor industry's knowledge in these areas could help drive SynBio to its next growth level. Another factor contributing to the current lack of scale is the vertically integrated nature of the biochemical industry. Moving from the current vertical scale-up approach to a horizontal scale-out plan could alter the economics and structure of the industry in a positive way—eliminating the investment redundancies across players in areas such as plant and equipment, basic process engineering, and development talent. Here, too, the semiconductor industry's experience in enabling and navigating this shift could become a vital element of unlocking the value of synthetic biology in chemicals.

Biologics in the health-care industry

To develop new drugs, the health-care industry has historically relied mainly on artificial "small molecule" compounds. Recently, companies have begun to employ synthetic biology in their quest to develop increasingly complex drugs using organisms like yeast and bacteria for production. Known as biologics, this biotech field has already evolved into a $100 billion market. Leading industry players such as Amgen and Roche are vying with new entrants such as Samsung BioLogics that are trying to capture a piece of this pie, which is expected to experience strong future growth.

The opportunity to shift from the scale-up model to a horizontal scale-out approach is equally applicable and important here. A scale-out model could dramatically lower the cost of developing these medicines and reduce the timelines needed (see sidebar, "Adapting the scale-out model for the SynBio ecosystem"). Moving from today's vertically integrated model to a scale-out approach will create opportunities for new and existing players alike. And the semiconductor industry, with its experience in developing such models, is well situated to participate in this growth. In fact, several firms have already entered the arena. Companies like Autodesk are creating design tools for this industry, while Agilent recently invested about $21 million in Gen9.

Adapting the scale-out model for the SynBio ecosystem

The genomics-driven SynBio industry is primarily vertically integrated: the pharmaceutical players building biologics and the chemical companies developing bio-based products establish most of their value chains internally. That includes development tools, synthetic DNA, organism development, and testing procedures. Some in the SynBio community are attempting to convert this vertically integrated model of development to a scale-out model where companies develop best-of-breed components for each part of the value chain and in the process unleash new bio-application innovations.

The parallels between the semiconductor and SynBio industries are strong in certain cases. In fact, the scale-out attempt in SynBio is similar to the experience of the vertically integrated systems companies that once developed semiconductors largely in-house using the scale-up model. More recently, however, the model has evolved into a thriving scale-out semiconductor industry that develops specific chip sets for specific use cases. In this model, a tool-and-design industry provides the development tools and a fabrication industry manufactures the chips.

The big opportunity here is for semiconductor companies to make use of their experience with the scale-out model and bring their business expertise to the SynBio industry. To understand why this approach can work in SynBio, chip players need to examine the SynBio ecosystem and value chain and appreciate how they are beginning to look very similar to those of the semiconductor industry. The exhibit describes the parallels between the SynBio and semiconductor ecosystems.

Is computing the next SynBio frontier?

Computing as we generally know it—its fundamental logic and memory building blocks—is silicon based. SynBio challenges this fundamental computing assumption by making cell-based computing, or cellular computing, a reality. In the past 12 months, scientists at MIT and Stanford have successfully created computing's two fundamental building blocks—logic and memory—using synthetically engineered organisms.

SynBio can help the industry expand its fundamental view of computing from silicon to a cell base, dramatically changing expectations regarding what computing can do and which industries it can affect. It also poses an important question: what kind of ecosystem will the industry need to make biological computing a reality?

One vision of the future sees SynBio evolve into a thriving scale-out ecosystem of design, software, and manufacturing companies that create economic disruptions across multiple trillion-dollar industries. This ecosystem would play an important role in creating the models and tools to develop biological circuits and computing.

Exhibit

The ecosystem for synthetic biology is nascent, but emerging segments are parallel to the semiconductor industry.

	Synthetic-biology segment	Semiconductor equivalent
1	Players that create artificially or synthesized DNA and building blocks, or "BioBricks" (eg, Agilent, DARPA,[1] Gen9)	Integrated-circuit firms and foundries
2	Players creating design tools to help develop BioBricks and building systems (eg, Autodesk, BioJADE, DARPA)	Electronic-design automation/ computer-aided design
3	Players developing systems that use building blocks designed to do specific tasks (eg, Amyris, Solazyme)	Semiconductor end-use markets
4	Government bodies developing policies to provide incentives and regulate the industry (eg, DARPA's Living Foundries grants, Organisation for Economic Co-operation and Development, the United Kingdom's Synthetic Biology Roadmap Coordination Group, and several US federal departments under the National Bioeconomy Blueprint)	Semiconductor-specific government regulations

[1] Defense Advanced Research Projects Agency.

While the promise of commercial-scale bio-based computing may still be years if not decades away, the SynBio-driven cellular-computing industry will need the business expertise of the semiconductor industry to build these capabilities and support a large number of applications across multiple industries. What's more, computer-chip players could take the lead in building a SynBio ecosystem of process and tool designers and developers, based on the many similarities the two industries share.

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The advances in synthetic biology over the last decade have moved the industry from the basic manipulation of organisms to the design and manufacture of commercial-scale biological factories. Successful use cases and proven industry applications suggest that SynBio will play an increasingly significant role in consumers' lives and in the chemicals, food, fuels, and pharmaceuticals they use. Moreover, the technology offers the potential to create a new approach to building biological circuits and, ultimately, cellular computing.

However, SynBio must meet challenging process-engineering and development requirements, not to mention high capital thresholds, to achieve economical scale. For stalwarts of the semiconductor industry, these are familiar themes, and the sector's hard-won expertise in productively dealing with them could accelerate SynBio development. Furthermore, the growth of SynBio creates a number of exciting opportunities for the development of tools and processes, as well as the application of proven yield-acceleration approaches and services. Collectively, these openings could translate into real business opportunities for players in the semiconductor industry. As a consequence, we believe that semiconductor players with expertise in equipment and processes, as well as experience in manufacturing at scale, could play a disruptive role in the unfolding SynBio space. ○

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