

Article

Foundational Tools for Building a New Bioeconomy

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WHILE BIOTECHNOLOGY HAS been transforming the diagnosis and treatment of disease, it has also been altering everything from the production of crops to how we manufacture goods. Berkeley Lights, which sits at the nexus of biotechnology, microfluidics, and information technology, is playing a critical role in enabling the way living cells can be harnessed as microscopic factories to power the emerging bioeconomy.

Berkeley Lights emerged from the lab of Ming Wu, professor of electrical engineering and computer sciences at the University of California, Berkeley. It was founded in 2011 to commercialize so-called optoelectronic positioning, which uses light to move cells. The company, which bills itself as a digital cell biology company, has an automated technology platform to sort, clone, culture, and analyze tens of thousands of single cells at a time on microfluidic chips and capture their individual activity in great detail.

Using the workflows developed by Berkeley Lights, customers can capture a deep understanding of the behavior of individual cells by recording critical data such as relevant phenotypic characteristics and linking that to genetic information and doing so for thousands of cells in parallel. The workflows—automated processes that begin with the importation of cells into Berkeley Light’s Beacon system at one end and exporting data at the other—can allow a user to find the best cell for a desired product.

“It’s the most magical piece of technology I’ve ever seen,” said John Cumbers, founder of Synbiobeta, an organization that brings together biological engineers, investors, and entrepreneurs interested in synthetic biology. “It allows for predictable, robust, reproducible, biological systems. We haven’t had that ever in biology. That’s massive.”

Berkeley Lights’ approach has been to enable functional testing of single cells throughout its various customers’ operations by finding opportunities for them to exploit this ability earlier in their product development process. To do that, the company works closely with potential customers to identify challenges they face and find workflows and assays that can address

their problems. It also engages with customers through traditional sales of its equipment and consumables. To expand access to small customers, the company in June launched a subscription-based program known as TechAccess. The subscriptions are offered on a one-year, renewable basis and give customers the ability to benefit from the technology without the need for upfront capital expenditures.

At the heart of the Berkeley Lights platform is a postage-stamp sized consumable chip that contains anywhere from 2,000 to 20,000 individual compartments called “nanopens.” Through the use of light, the technology moves individual cells into each pen and then can conduct experiments and take measurements on the performance of each cell. The ability to test thousands of cells on a parallel basis reduces the time it takes to complete experiments from weeks or months to days.

“The challenge today is that these cells express genomic information in a bunch of ways that we just can’t accurately predict. And because we can’t accurately predict it, we need to do functional testing. And that functional testing is hard,” said Eric Hobbs, CEO of Berkeley Lights. “It takes a long time and costs a lot of money. We solve that problem by providing a high-throughput, high-resolution functional test to make sure that the cells are making that cell-based protein that our customers need to be made.”

FASTER, BETTER, CHEAPER

Consider the way the Berkeley Lights’ platform is transforming the process of antibody discovery. Traditionally, drug developers would use hybridoma technology to create a desired antibody. This involves a process in which a scientist would inject a mouse with an antigen, take the B cells from that mouse once an immune response was detected, and fuse the B cells with a myeloma cell—an immortal B cells—to produce a supply of the antibody.

When creating a hybridoma, it takes about eight to 12 weeks before the cells can be functionally characterized.

And, when the fusion process is performed, a large number of cells are lost, which can destroy the genetic diversity of these cells. It can take a few months before a drug developer can determine whether the process yielded any therapeutic candidates.

By contrast, with the Berkeley Lights technology, B cells from the animals can be placed directly into its system and characterized at an individual level. Within eight hours, the system can determine whether there are therapeutic candidates to pursue.

The biotechnology giant Amgen was an early adopter of the Berkeley Lights technology. It said instead of using thousands of cells to derive a single point of data, it can conduct experiments on single cells with thousands of cells on a single chip. “We can actually see how fast the cells are growing, how much antibody they produce, how effectively the antibodies bind to their target and modify the biology,” said Philip Tagari, vice president of research for Amgen in a video published by Amgen. “This technology has changed how Amgen develops cell lines and searches for antibodies. Research that used to take weeks or months can be done in hours or days.”¹

He said the technology will allow the company to solve complex problems that are too hard or too expensive to solve with traditional tools and it will allow the company to search for the one in a million cells that can make extraordinary medicines.

The antibody discovery company Genovac, a Berkeley Lights customer, did a comparative study of the Berkeley Lights technology against conventional hybridoma. Using Berkeley Lights’ technology, it was able to find ten times more unique antibody therapeutic candidates, did so in a fifth to a tenth of the time, and did so at one twentieth of the cost compared to the hybridoma process.

EXPANDING WORKFLOWS

Though much of Berkeley Lights early focus has been on the use of its technology in the development of antibody therapies and cell therapies, the growing demand for synthetic biology for industrial applications represents a significant area of potential growth. In 2019, Ginkgo Bioworks, which engineers organisms to replace industrial and pharmaceutical applications, entered into a \$150 million, multi-year, non-exclusive agreement with Berkeley Lights to incorporate the company’s optofluidic

platform into Ginkgo Bioworks’ automated genetic engineering foundries.

By incorporating the Berkeley Lights platform into core workflows of Ginkgo’s automated foundries, the company said scientists are able to observe and manipulate thousands of individual cells, providing unprecedented control over them. Ginkgo expects the collaboration will drive growth in output and efficiency of its foundries and enable new innovation in synthetic biology and its application across numerous industries from food to fragrances.

The company said it expects the technology to more than triple its capacity to measure the performance of cells, increasing the overall speed and efficiency of product delivery to its customers. The ability to measure and observe the performance of individual cells at a microscopic scale will significantly reduce the time needed for data collection. The company also noted that the Berkeley Lights platform provides data richness from single cell analysis that is currently unavailable in data from conventional bulk measurements.

“We’re exponentially improving our ability to engineer biology every year and new technologies like Berkeley Lights’ platform are essential to maintaining that pace of improvement,” he said. “The Berkeley Lights team has already had an incredible impact on pharma—including cell line development and antibody discovery—and we believe this partnership will bring about a step-change in the speed and scale at which we engineer biology for applications across a variety of industries.”²

Together, the two companies are also expanding the application of Berkeley Lights’ optofluidic platforms through the creation of new workflows available beyond those already released for the biopharmaceutical market. While the existing workflows on the Berkeley Lights platform had been primarily focused on mammalian cells for drug discovery and development, the collaboration with Ginkgo Bioworks will allow Berkeley Lights to generate a number of new workflows, leveraging its platform for several organisms including yeast, bacterial, and fungal cells that will enable the development of a broad range of synthetic biology products.

“We are in an era where cell-based products are changing everything from healthcare and biofuels to

1 The Digital Cell Biology Revolution, Amgen, June 13, 2019, <https://www.youtube.com/watch?v=98YeqTfjork>, accessed May 14, 2021.

2 Ginkgo Bioworks and Berkeley Lights Bring Unprecedented Speed and Scale to Synthetic Biology with \$150MM Collaboration, PR Newswire, October 1, 2019, <https://www.prnewswire.com/news-releases/ginkgo-bioworks-and-berkeley-lights-bring-unprecedented-speed-and-scale-to-synthetic-biology-with-150mm-collaboration-300928615.html>, accessed May 15, 2021.

agriculture and food,” said Keith Breinlinger, CTO of Berkeley Lights. “At the same time, using cells to make new, better, and more efficient products is in its nascency. We believe you will see a huge groundswell in this market in the coming years.”³

INVESTING IN GROWTH

Berkeley Lights went public in 2020 raising \$205 million in an upsized IPO that came above its expected range at \$22 a share. Though the company is down from its 52-week high of \$113.53 per share, it is trading at around twice its offering price and has a market cap in excess of \$2.6 billion.

For the year ending December 31, 2020, the company generated revenue of \$64.3 million, a 31 percent increase over the \$56.7 million generated for the same period the previous year. It posted a \$41.6 million loss for the year compared to a \$18.3 million loss in 2019. Despite the challenges posed by the COVID-19 pandemic, the company ended the year with an installed base of 75 platforms, a 56 percent increase over 2019. It has not made any forecast about when it expects to turn profitable, although it has provided guidance that it expects to generate revenue of \$90 million to \$100 million in 2021.

There should be plenty of room for growth. The three areas the company is initially targeting—antibody therapeutics, cell therapy, and synthetic biology—had products sales of \$148 billion in 2019 and are expected to grow to more than \$250 billion in the next four years. Together, they represent what Berkeley Lights estimates to be an addressable market opportunity of \$23 billion.

The expanding demand for cell-based products, the increasing complexity of these products, and the need for greater precision in the assays used to develop them is helping drive growth for the company. At the same time,

the emergence of new therapeutic modalities that require precise functional validation, including multi-specific antibodies, cell, and gene therapies using DNA or mRNA therapeutics, is also driving growth opportunities for the company.

The challenge of manufacturing these therapies is also creating an additional opportunity for Berkeley Lights. It is developing workflows that move the functional validation of manufacturing parameters early into the process, giving customers higher predictability of manufacturing yield and throughput. It is also enabling new manufacturing approaches with higher throughput. In 2020, the company released six new workflows, bringing the total number of commercial workflows to eight, one of which allowed it to move into the expanding markets for cell line development and contract development and manufacturing companies.

Though Berkeley Lights offerings are unique, it does compete against more conventional tools from providers who offer equipment and assays on different machines. Nevertheless, its automated workflows that provide integration into a single package for now provides it with a compelling offering that positions it to grow with the market.

“We know that cells are capable of producing the products and product classes that we need. We, in fact, know that cells are better than humans at manufacturing things like proteins that we just simply chemically and synthetically can’t produce yet. The fundamental unit alive—the cell—can make these proteins very efficiently,” said Hobbs. “We’re right on the cusp of creating that future that we desire. It’s right in front of us. And what we have to do and understand is how do we find those cells that produce the products we need? And, I do believe that that’s through functional tests and I believe Berkeley Lights provides the highest throughput functional tests available in the market today.”

3 *ibid*