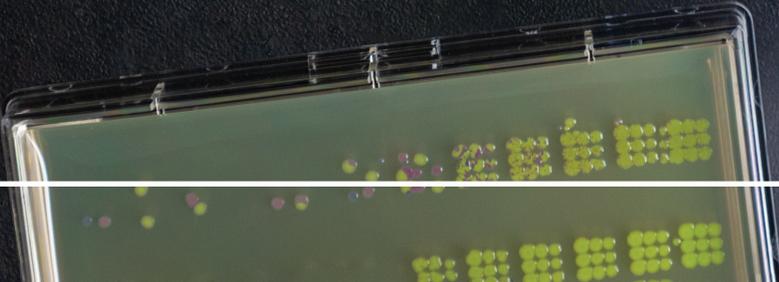




Building a Better DNA Assembly Line

Arzeda leverages technology from Labcyte, TeselaGen and Twist Bioscience to accelerate their synthetic biology workflow

SEPTEMBER 2019







CASE STUDY

Arzeda needed a better way to construct plasmids to produce their designer proteins. The process was too slow, too error-prone and used far too many resources. The company had two choices: it could hire several people and develop a new solution from scratch, or it could combine proven technologies from trusted vendors into a seamless, integrated platform for high-throughput DNA assembly. Their choice offers an example many biotech startups could follow.

PHOTOGRAPHS BY SPENCER WALLACE

CASE STUDY

Emily Leproust, CEO
and co-founder of
Twist Bioscience



In the software world, companies thrive because the industry shares ideas and resources. Code gets reused again and again, meaning companies don't have to invest their capital to reinvent existing processes.

That ethos doesn't always transfer to the life sciences. Startups are typically balancing the available cash and the need to move quickly. While few biotechnology processes approach code's modularity, there could still be off-the-shelf platforms that solve some of the industry's most challenging bottlenecks.

Here we present one such solution. Arzeda designs and creates proteins, delivering important molecules for the life sciences, food, chemical and other industries. They must test thousands of protein-producing plasmids, each of which must be assembled from linear DNA fragments, a process laden with potential bottlenecks and errors. Rather than opting for an expensive custom solution, Arzeda went to the experts, combining:

- Twist Bioscience's DNA fragments to create plasmids that encode Arzeda's designed proteins
- TeselaGen's DNA assembly design and laboratory automation software, DESIGN and BUILD, that orders sequences from Twist and generates worklists for the Echo Liquid Handler
- The Labcyte Echo Liquid Handler, which moves nanoliter volumes for fast, efficient DNA assembly

This collaboration provides a turnkey solution that increases productivity, reduces consumable use, generates more accurate plasmid designs and lowers costs. In fact, the integrated platform allowed Arzeda to increase the number of enzymes built and tested by about 10x as DNA construction had been the bottleneck — both in terms of cost and time. As soon as the end of 2019 Arzeda expects to increase the efficiency to a hundredfold. It's an approach that could be easily applied to many company's R&D pipelines.

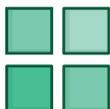
I keep seeing the wheel being reinvented. Every company, every lab is doing the same thing, over and over, to solve the same problems. What if there was a workflow solution that could be shared, benefit everyone and become an industry standard?

—ARZEDA

The Ingredients

Building Blocks

TWIST BIOSCIENCE



We make high-quality DNA and deliver it in Echo qualified 384-well plates so they can be used directly for plasmid construction without transferring plates. Using TeselaGen's software, Arzeda designs the fragments for modular assembly of the desired constructs, orders the DNA fragments and generates the work instruction for the Echo Liquid Handler to assemble the constructs. With those pieces, it's a turnkey solution. —TWIST BIOSCIENCE

Twist DNA fragments are the central component to this process. The company's silicon-based DNA synthesis platform quickly and affordably produces high-quality synthetic DNA that Arzeda can combine into plasmids using sophisticated DNA assembly methods.

Because Twist produces high-quality DNA, with few errors, Arzeda can reduce the amount of sequencing they must do to ensure quality lowering their overall costs.

Twist has also enabled its application programming interface to integrate with TeselaGen's software to enable seamless in-app DNA ordering. In addition, Twist provides DNA in 384-well plates that are fully compatible with the Labcyte Echo Liquid Handler, further streamlining the process.

Blueprints

TESELAGEN



You can imagine the gene fragments or pieces of DNA that you might want to assemble in various different ways. We can source those really easily from Twist, and then we can have our customers put them together in various ways using our software. —TESELAGEN BIOTECHNOLOGY

Arzeda needs to generate their plasmids as efficiently as possible, which often requires reusing fragments to assemble closely related DNA sequences. TeselaGen's software determines how to best put the plasmids together and which DNA fragments should be synthesized by Twist, automating the process of DNA assembly and nearly guaranteeing successful plasmid construction.

Once Twist has delivered the DNA fragments, Arzeda uses TeselaGen's secure, cloud-based software to write detailed instructions for the Echo Liquid Handler to transfer specific volumes of resuspended DNA fragments to the appropriate destination wells, setting up miniaturized DNA assembly reactions. TeselaGen's BUILD app knows exactly which Twist fragments it needs to add together to get the desired results. The process is incredibly fast and almost entirely automated. It takes about five minutes to generate the worklist instructions and import the resulting CSV file to the Echo Liquid Handler's control software.

This rational approach makes the process more predictable. Fewer mistakes means Arzeda spends less time circling back to rework plasmids, reducing wasted design and synthesis time. TeselaGen's software is the glue that binds these processes together.

Liquid Handling

LABCYTE



The Echo system Arzeda uses transfers in 25 nanoliter increments, streaming hundreds of drops per second. That allows them to miniaturize every part of their scientific experiment, driving costs down and speeding their workflow up. If they were using a conventional technology, running a similar process, it would take around 18 hours or more. The Echo system can typically do it in 3 hours. —LABCYTE

The Echo Liquid Handler uses sound waves to move nanoliter-sized liquid droplets. The instrument sends focused energy pulses through the bottoms of microwell plates to vertically transfer droplets from source plates to inverted destination plates. Surface tension holds the liquid in place. The instrument easily handles complex operations, going from any well in one plate to any well in another without errors.

This technology is much more efficient than manual pipetting or even robotic dispensing systems. The Echo system works faster and uses smaller amounts, reducing costs. Moving tiny volumes saves on reagents, like the enzymes Arzeda uses to stitch Twist's DNA fragments together. The Echo system saves on disposables, such as plastic tips, reducing waste, and tipless transfer eliminates the risk of cross-contamination.



The Combined Solution

With this partnership now in place, Arzeda purchases high-quality DNA fragments from Twist that have been generated by TeselaGen's software. The software automatically translates the assembly designs to instructions for the Labcyte Echo Liquid Handler for efficient plasmid construction.

This integrated solution speeds up the workflow and reduces errors, waste and overall costs. Equally important, it's a plug-and-play solution. Rather than hiring a large team to design and implement this platform, which would have likely taken years to accomplish, Arzeda got the system up and running in around two weeks. This makes it an excellent option for synthetic biology startups that want to spend their seed money on other priorities.



The Labcyte Echo Liquid Handler



The Partners

Arzeda has harnessed computational protein design to build novel enzymes and develop new pathways that enable cost-effective, sustainable production of value-added specialty chemicals and ingredients. Pathway design software unlocks new opportunities for specialty chemicals, advanced materials and health and nutrition products that would otherwise be impossible to exploit.

Labcyte is revolutionizing liquid handling. The company's Echo Liquid Handlers use sound to precisely transfer liquids without contact, eliminating pipettes. Labcyte instruments are used worldwide by pharmaceutical and biotechnology companies, hospitals, service laboratories, contract research organizations and academic institutions.

TeselaGen has developed a deep learning solution to support rapid, precise and accurate DNA-assembly and modification. TeselaGen's cloud-based platform bridges the gap between good ideas and valuable products like vaccines, biologic medicines and sustainably sourced chemicals.

Twist Bioscience has developed a DNA synthesis platform that industrializes biological engineering, manufacturing synthetic DNA by "writing" the genetic code on a silicon chip. This technology can manufacture many synthetic DNA-based products, including genes, tools for next generation sample preparation and antibody libraries for drug discovery and development.



WHAT CAN TWIST DO FOR YOU?

sales@twistbioscience.com

twistbioscience.com

[#WeMakeDNA](https://twitter.com/WeMakeDNA)