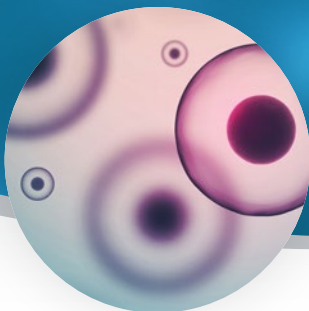
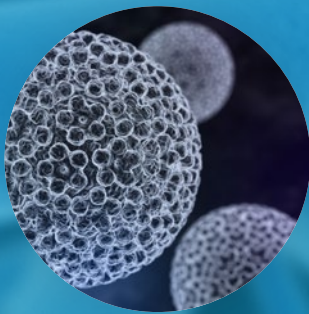




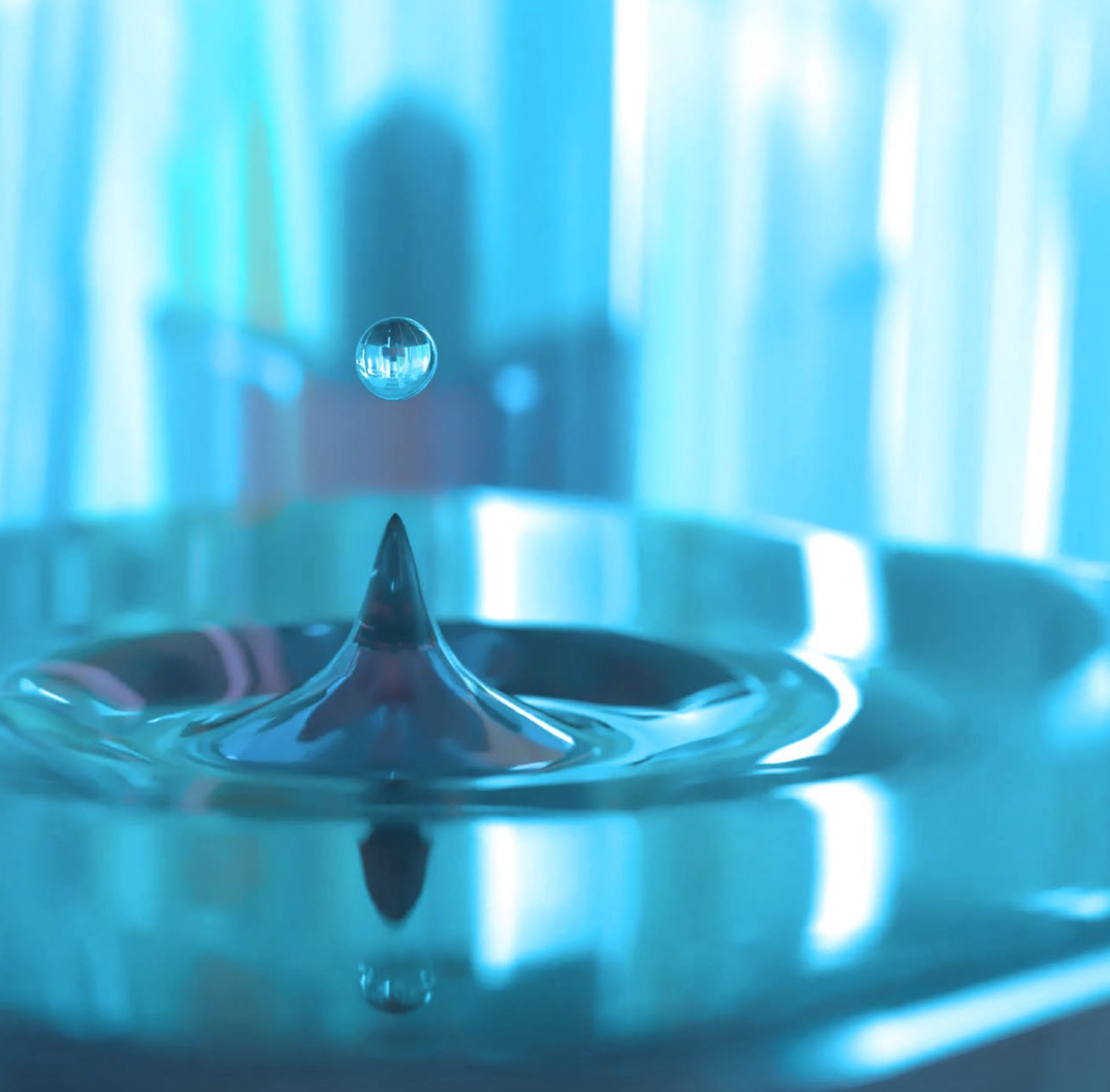
# ECHO ACOUSTIC LIQUID HANDLING FOR SYNTHETIC BIOLOGY

EMPOWERING BETTER SCIENCE WITH ADVANCED DNA ASSEMBLY



**DISCOVERY**  
*in motion.*





IMPACTING  
SYNTHETIC BIOLOGY  
WITH SOUND

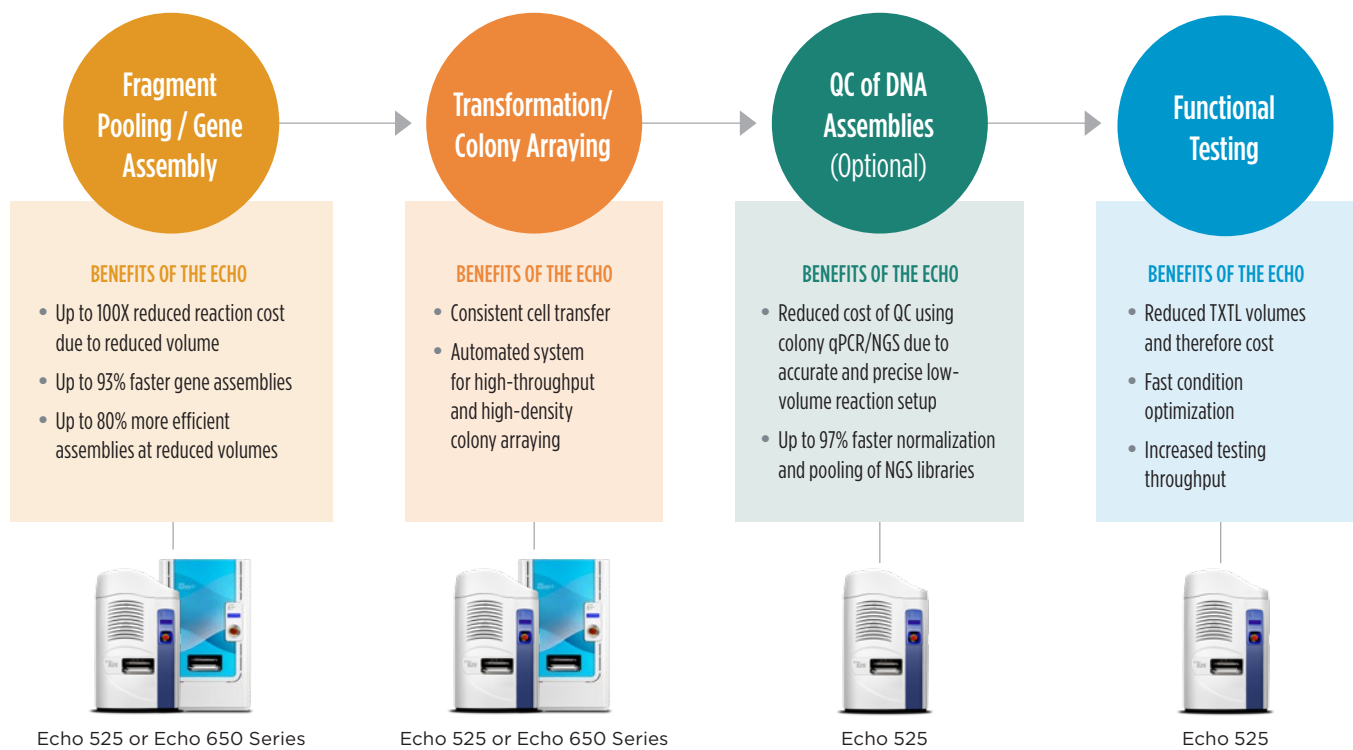
# Advantages of the Echo Liquid Handler in Synthetic Biology

## Compared to Tip-based Liquid Handlers

- Fast, tip-less and contact-free transfers from any well in the source plate to any well in the destination plate, enabling 10X faster assemblies
- Reducing gene assembly reaction volumes up to 100X, enabling significant cost-savings, while improving assembly efficiency
- Decreasing reaction volumes for up to 100X cost-savings in next-gen sequencing (NGS) or colony qPCR validation steps
- Enabling complex optimization involved in TXTL or cell-free protein expression
- Setting up high-throughput colony arraying of transformed or transfected cells, up to 1536 colonies per plate



## Gene Synthesis Workflow



**The Echo Liquid Handler is an essential part of critical steps of any gene assembly workflow.**



# Echo Liquid Handler for Synthetic Biology

Echo acoustic liquid handling technology revolutionizes synthetic biology applications by using sound energy to enable highly accurate, fully automated, non-contact dispensing of fluids in nL to  $\mu$ L volumes. By reducing reaction volumes the Echo offers significant reagent cost- and time-savings while improving reaction efficiency.

*"(The Echo) is an extremely fast instrument...a significant savings in terms of time. We've been able to compress pipelines that take about 12 hours to about 3 hours."*

Dr. Sunil Chandran, Amyris Biotechnologies

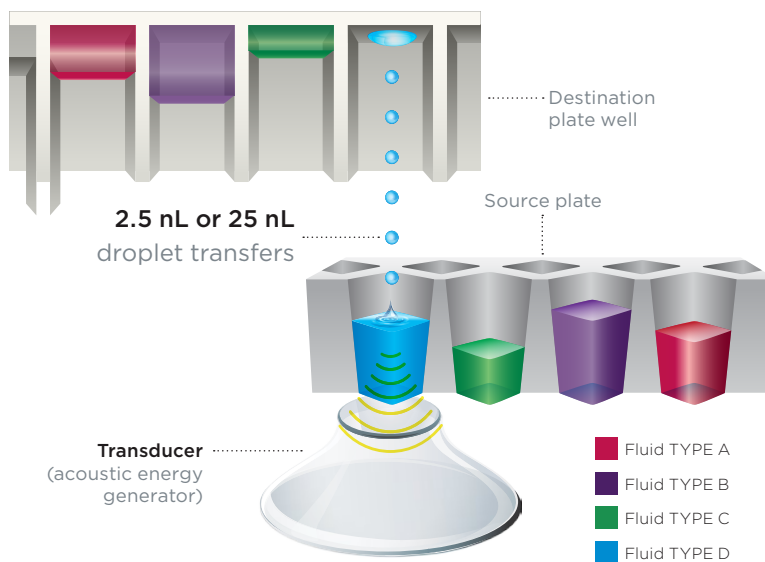


Echo 525 LIQUID HANDLER

## How Does the Echo Move Liquids with Sound?

Using the proprietary Dynamic Fluid Analysis technology, the Echo determines fluid composition and height, and the power needed to eject a precise volume of fluid into the destination well. This analysis happens in milliseconds, enabling precise and accurate transfer of nanoliter droplets into an inverted destination microplate. The desired transfer volumes are achieved by rapidly transferring multiple droplets per second.

Transfers can be made from any well in the source to any well in the destination. The tip-less and contact-free technology of the Echo allows for miniaturization and automation of complex assays to dramatically reduce reagent cost and assembly time while improving data quality.



**Acoustic droplet ejection** - The transducer is positioned below the source microplate well and emits focused sound energy repeatedly to the meniscus of the fluid to be transferred. A stream of 2.5 or 25 nL droplets (model dependent) is reliably ejected into a well of an inverted destination microplate



## Miniaturization and Acceleration of DNA Assembly and Validation QC for Gene Synthesis

Since introduction of Echo Liquid Handlers in 2004 they have been an essential part of synthetic biology labs to enable better and faster workflows while reducing costs and waste in a wide range of applications. Some of these applications, such as complex and high-throughput gene assembly and cell-free protein expression, would not have been possible without the use of Echo Liquid Handlers.

DNA assembly using traditional tip-based liquid handlers requires reaction volumes of ~10–20  $\mu\text{L}$ . The Echo Liquid Handler can reduce these volumes up to 100-fold for gene assembly and/or validation steps, while maintaining or even improving data quality and drastically reducing reagent costs. Moreover, the Echo offers up to 10X time-savings in different labs. The Echo 525, introduced in 2012, has enabled even faster throughput with its 25 nL dispense volume.

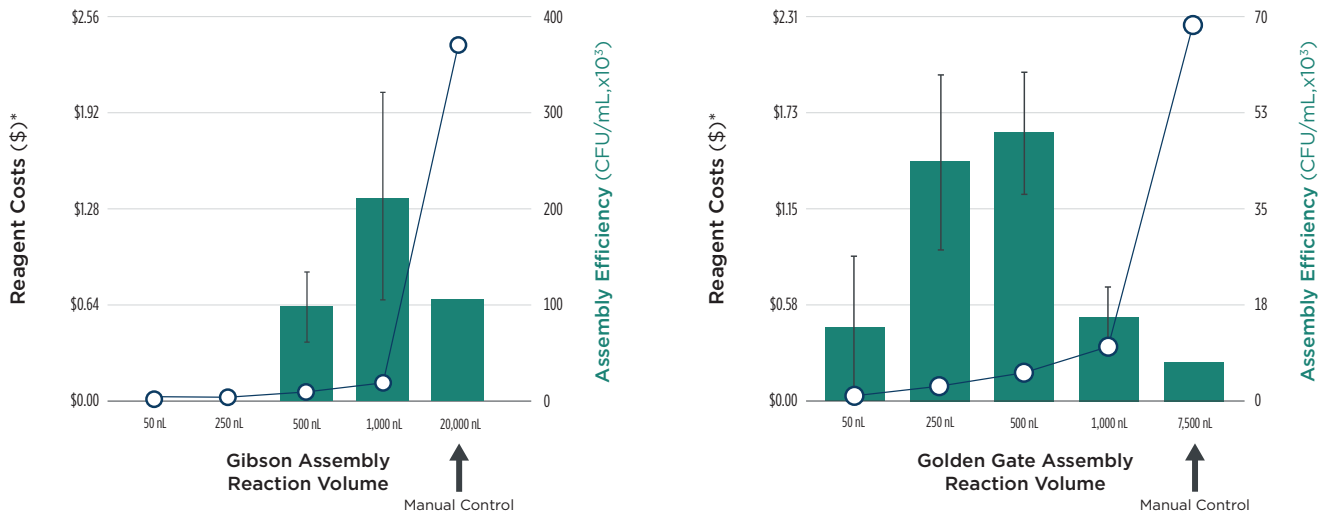


*“We were able to successfully downscale PCRs and the popular one-pot DNA assembly methods, Golden Gate® and Gibson® assemblies, from the microliter to the nanoliter scale with high assembly efficiency, which effectively cut the reagent cost by 20- to 100-fold.*

*We envision that acoustic dispensing will become an instrumental technology in synthetic biology, in particular in the era of DNA foundries.”<sup>1</sup>*

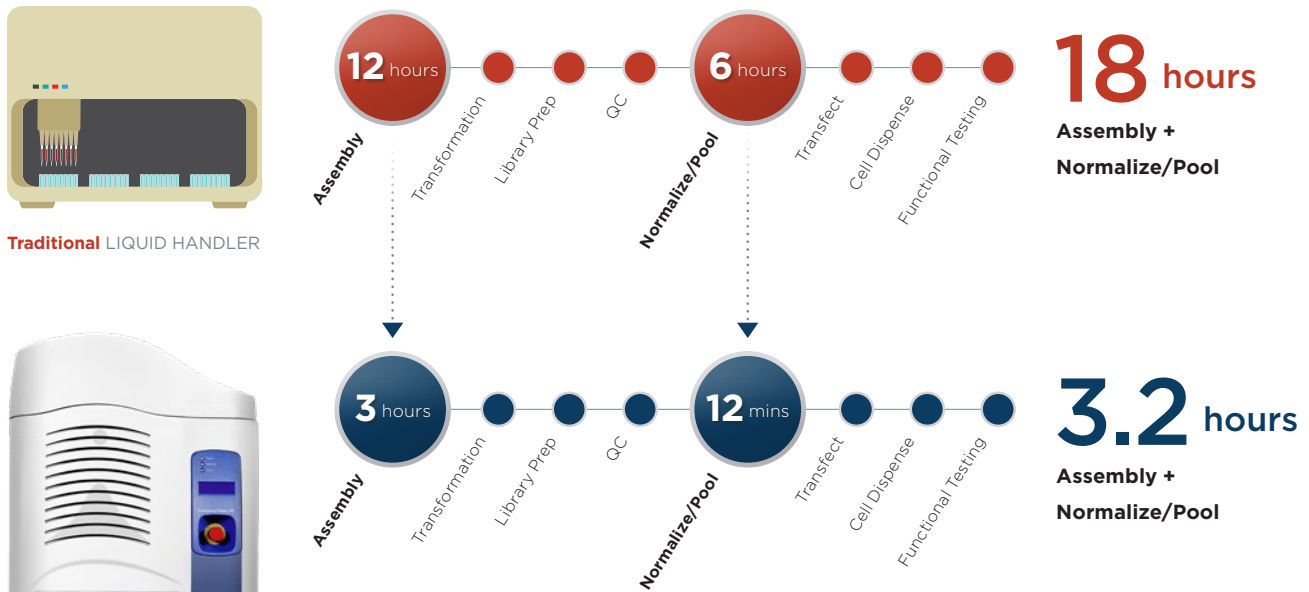
Paulina Kanigowska, *et al.*, JALA 2015

# Reducing Reaction Costs while Improving Assembly Efficiency with Miniaturization



Gibson and Golden Gate Assembly: Cost-effectiveness and assembly efficiency comparison of different reaction volumes.<sup>1</sup>

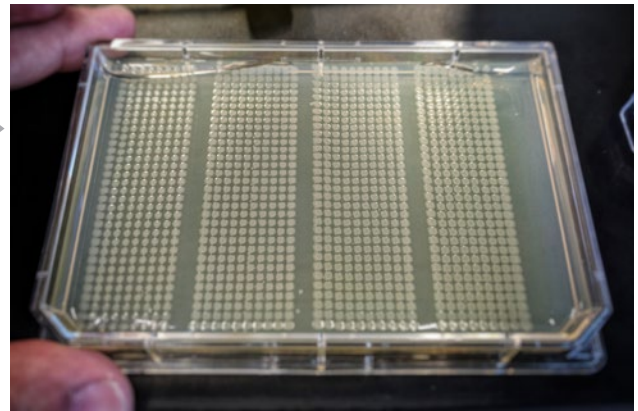
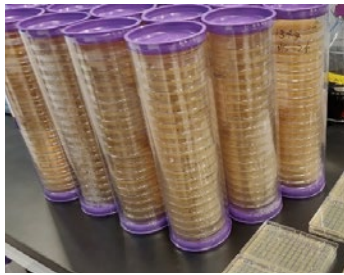
# Up to 82% Increase in Speed of Gene Assemblies and NGS Validation Steps



The Echo can rapidly pool DNA fragments for gene assembly and normalization and pooling of NGS libraries for sequencing, with each transfer taking less than a second. This provides time savings of up to 82% in a gene assembly and validation process, while providing superior %CV of the pooled libraries through accurate and precise transfers.

# Colony Arraying Using the Echo Acoustic Liquid Handler

The Echo Liquid Handler has become the instrument of choice for high-density and high-throughput fully automated colony arraying onto media/agar plates. Hundreds of Petri dishes can be replaced with one densely spotted (up to 1536 spots) SBS standard plate filled with media and agar.



Images courtesy of George McArthur, Ansa Bio

## Optimization and Rapid Processing of Cell-free Protein Expression Reactions with Miniaturization

Cell-free transcription-translation (TXTL) or cell-free protein expression systems are versatile platforms for production of recombinant proteins within synthetic biology. Because *in vitro* protein synthesis is decoupled from cellular functions, the experimental cycle time can be greatly reduced, while the application range is expanded. Using the Echo Liquid Handler in combination with the cell-free protein expression master mixes enables rapid gene and protein expression projects that require high-throughput processing, flexibility and reproducibility, in a low-cost manner.

The fast and any-well-to-any-well transfers of reagents and DNA pieces by the Echo allows for up to 10X faster reaction optimizations while lowering the reagent consumption and cost by at least 3-fold, compared to tip-based liquid handlers.

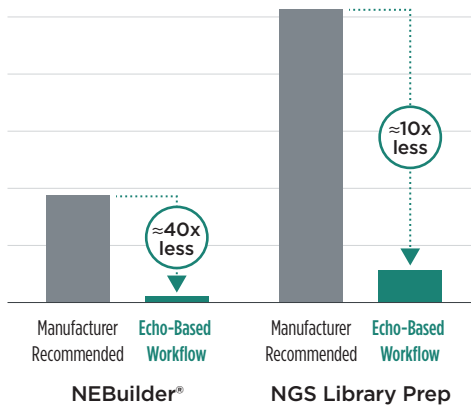


*“The Echo 525 automates complex liquid aliquot rarray at high speeds and at miniaturized scales, saving significant time and money. It has proven to be extremely versatile and robust; my teams have used it to set up PCRs, cell-free protein synthesis reactions and biochemical assays, and even to array colonies of transformed bacteria on solid media. At Ansa, the Echo 525 is the workhorse for our automated DNA assembly platform.”*

**George McArthur, PhD, Head of Product, Ansa Biotechnologies**



# Low-Cost, Highly Efficient NGS Library Preparation

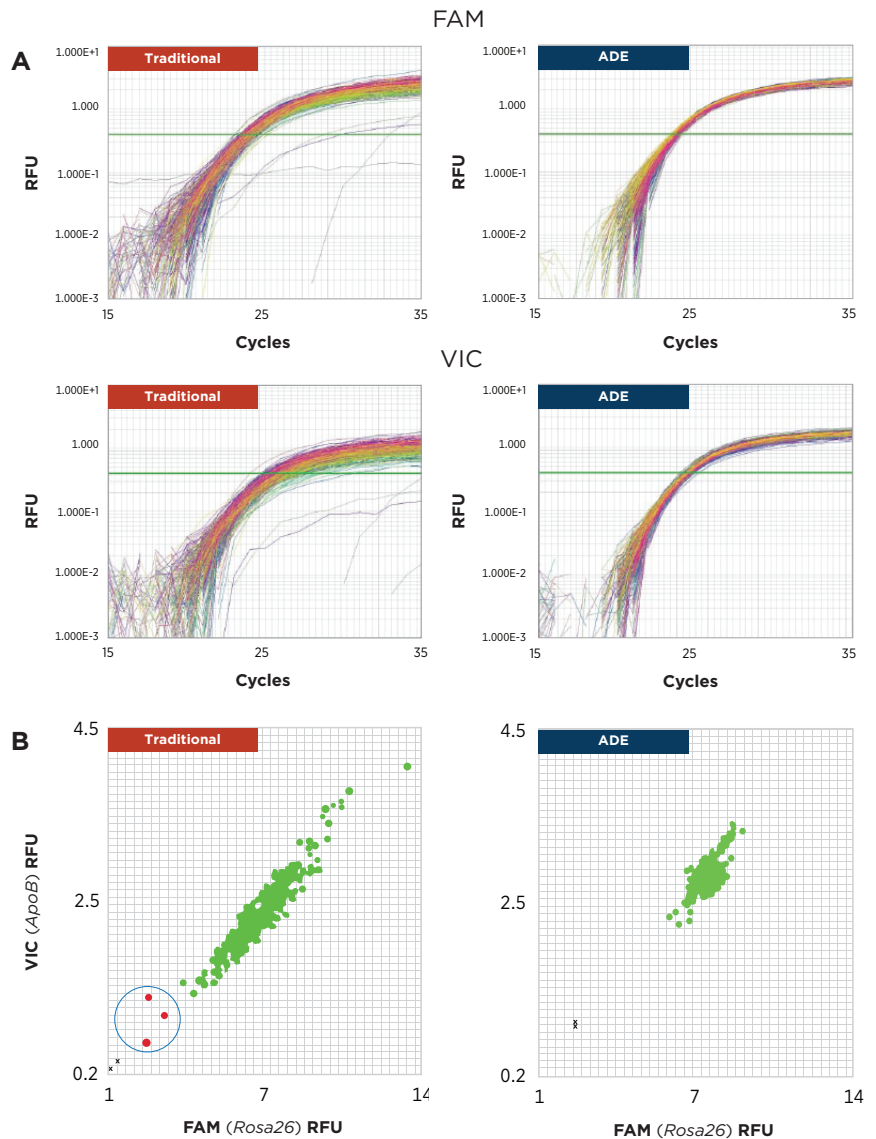


As the cost of sequencing has gone down, the cost of library prep is becoming the bottleneck in many high-throughput NGS applications, including NGS methods used for validation of assembled genes. One way to reduce library prep cost is to reduce reaction volumes. Echo Liquid Handlers enable NGS library preparation in low microliter volumes for a range of sequencing applications. Echo systems dramatically reduce hands-on and turnaround times, offer up to 100-fold less reagent costs through miniaturization, and eliminate steps to optimize the workflow, all while ensuring high library quality and throughput.<sup>2</sup>

## Cost-Effective and High-Throughput Colony qPCR

To avoid the impact of poor liquid handling performance, researchers traditionally use larger volumes of samples and reagents to prepare qPCR reactions. Echo Liquid Handlers enable miniaturization of these reaction volumes down to at least 2  $\mu$ L, reducing costs and facilitating higher throughput. Furthermore, the tip-less and contact-free technology of the Echo reduces the chances of cross-contamination, as shown in the data to the right.

The data show that acoustic drop ejection technology reduces the chances of cross-contamination while generating tighter data, in terms of consistent Cq values.





# Access Laboratory Workstation and Access Systems for Synthetic Biology Applications

## Out-of-the-Box Automation for Echo Liquid Handlers

Combine the revolutionary performance of the Echo Liquid Handler with automated plate handling and integrated devices to create walk-away systems tailored for a range of synthetic biology applications. With the Access Workstation and Systems you can automate several steps of your synthetic biology workflow, including but not limited to: gene assembly, colony arraying, validation steps using colony qPCR or NGS methods, as well as any TXTL or cell-free protein expression techniques used for functional testing.



*“At Codex DNA, the Echo 525 Liquid Handler and Access Workstation from Beckman Coulter Life Sciences has become an integral part of our BioXp™ system gene synthesis workflows. Processes that would take 8 hours with traditional liquid handlers now take less than 30 minutes with the Echo, enabling the construction of DNA variant libraries at an unprecedented scale. Moreover, the high accuracy and precision of non-contact acoustic transfers ensure that we’re delivering every oligonucleotide with the utmost confidence.”*

**John E. Gill, Senior Director of R&D, Codex DNA**

# Echo and Biomek: Better Together with a Large Dynamic Range from nL to mL

## Echo Liquid Handlers



- 2.5 or 25 nL and above
- Gene assemblies
- Colony arraying
- Colony qPCR or NGS
- Simultaneous normalization and pooling
- Cell-free protein expression or TXTL

## Biomek i-Series



- 0.5  $\mu$ L – 5 mL
- Sample handling from tubes or plates
- Transformation or transfection
- Mini-preps
- Colony picking
- Functional assays

## Walk-away and High-throughput Applications

Faster, low-cost and high-throughput sample processing are achieved by combining the speed and low-volume accuracy and precision of Echo acoustic technology with the flexibility of Biomek i-Series workstations.



Echo integrated  
directly with Biomek to  
enable more seamless  
sample processing



# Echo Software Applications

## for Synthetic Biology Workflows

Echo Software Applications assist researchers in creating liquid handling protocols for specific applications. You can quickly create a variety of protocols off-line and use the built-in simulators to validate every transfer before running them live.



### Echo Cherry Pick

- Worklist-driven transfers
- Gene assembly
- Normalization and pooling
- TXTL reaction setup



### Echo Plate Reformat

- Simple, drag-and-design interface
- Setting up colony qPCR reactions
- Setting up NGS reactions
- Colony arraying

# Echo Qualified Consumables

## for Synthetic Biology Workflows

**Echo Qualified Source Microplates** ensure precise, accurate liquid transfers, delivering the best possible results in miniaturized assays. Echo Qualified Source Microplates are deionized and are packaged in anti-static bags to ensure precise drop placement. Microplates are available with low dead volume, custom barcode, DNase and RNase free or sterile options.



**The MicroClimate Environmental Lid** minimizes edge effects and preserves the concentrations of solutions in microplate wells. The novel fluid-absorbing matrix inside the lid creates a vapor barrier, protecting the sample from evaporation and greatly reducing edge effects, and therefore increasing the microplate efficiency by 37%.



**The Brooks Life Sciences FluidX AcoustiX Sample Tubes** transform workflows by enabling acoustic dispensing directly from tubes, on Echo 650 series. The tubes can be accessed individually – ideal for applications that require subsets of large reagent or sample libraries to be accessed frequently.



# Beckman Coulter Life Sciences Service and Support

## Maximize Your Instrument Performance

Timely service and preventive maintenance are essential for optimal instrument performance and data quality. Beckman Coulter Life Sciences offers a wide range of service contract options for the Echo Liquid Handler and Access Laboratory Workstation and Systems to fit every lab's needs and budget.

Our application scientists have extensive experience with genomic workflows and provide support and training on all our product offerings to help you maximize the use of your systems.

[beckman.com](http://beckman.com)

### REFERENCES

1. Kanigowska P, Shen Y, Zheng Y, Rosser S, Cai Y. Smart DNA Fabrication Using Sound Waves: Applying Acoustic Dispensing Technologies to Synthetic Biology. *J Lab Autom.* 2016;21(1):49-56. doi:10.1177/2211068215593754
2. Shapland EB, Holmes V, Reeves CD, et al. Low-Cost, High-throughput Sequencing of DNA Assemblies Using a Highly Multiplexed Nextera Process. Shapland et al., *ACS Synth. Biol.*, 2015. doi.org/10.1021/sb500362n
3. Cain-Hom C, Pabalate R, Pham A, Patel HN, Wiler R, Cox JC. Mammalian Genotyping Using Acoustic Droplet Ejection for Enhanced Data Reproducibility, Superior Throughput, and Minimized Cross-Contamination. *J Lab Autom.* 2016;21(1):37-48. doi:10.1177/2211068215601637
4. Bailey J, Eggenstein E, Lesnick J. Application Note: Miniaturization and Rapid Processing of TXTL Reactions Using Acoustic Liquid Handling. [beckman.com/resources/reading-material/application-notes/miniaturization-rapid-processing-txtl-reactions-acoustic-liquid-handling](http://beckman.com/resources/reading-material/application-notes/miniaturization-rapid-processing-txtl-reactions-acoustic-liquid-handling)

**FOR RESEARCH USE ONLY.** Not for use in diagnostic procedures.

\* Reaction costs converted from British pound sterling to US dollars based on the September 2020 exchange rate (1.28).

© 2020 Beckman Coulter, Inc. All rights reserved. Beckman Coulter, the stylized logo, and the Beckman Coulter product and service marks mentioned herein are trademarks or registered trademarks of Beckman Coulter, Inc. in the United States and other countries. ECHO is a trademark or registered trademark of Labcyte Inc. in the United States and other countries.

All other product names and brands are properties of their respective owners.

For Beckman Coulter's worldwide office locations and phone numbers, please visit Contact Us at [beckman.com](http://beckman.com)

AAG-7891SB09.20

