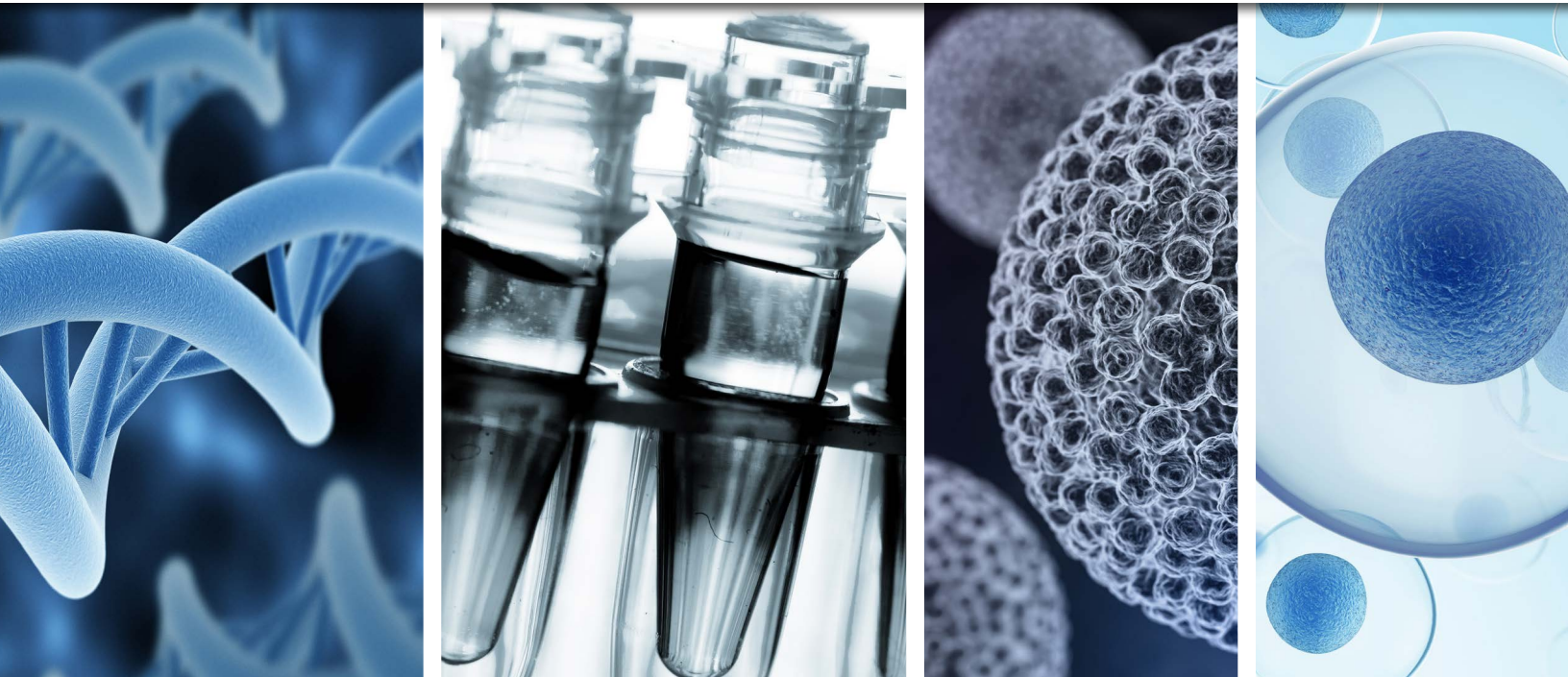


Echo Acoustic Liquid Handling *for* Genomics Research

EMPOWERING GENOMICS RESEARCH WITH ASSAY MINIATURIZATION



Genomics Research

APPLICATIONS

BROCHURE

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Echo Acoustic Liquid Handling Technology

Echo acoustic liquid handling technology revolutionizes scientific research by using sound energy to provide highly accurate, fully automated, non-contact dispensing of fluids. By utilizing the unique Dynamic Fluid Analysis™ technology by Labcyte, the Echo system determines fluid composition, fluid 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 (nL) droplets into an inverted microplate. Larger volume transfers are achieved by rapidly transferring several hundred droplets per second.

Transfers can be made from any well to any well, allowing for miniaturization and automation of complex assays to dramatically reduce reagent costs and save precious samples.

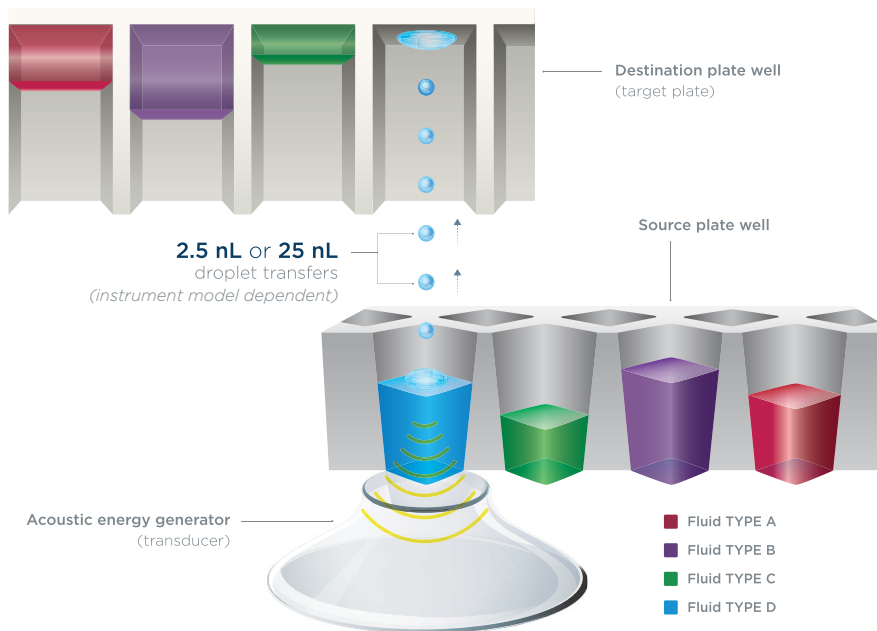


FIGURE 1: The Echo system transducer rapidly moves between wells on the source plate while the destination plate also moves, allowing rapid transfer from any well to any well for multiple fluid types.



Echo® 525 LIQUID HANDLER

“ The attractiveness of the instrument was its extreme flexibility. You can transfer from any well to any well, in any combination, extremely fast, and also with extremely low volumes.

- **Andy Watt**
Ionis Pharmaceuticals

Labcyte offers different models of the Echo® Liquid Handler to meet customer volume and throughput needs. For genomics applications, we recommend using the Echo® 525 Liquid Handler, the first rapid acoustic liquid handler designed specifically for biochemical and genomics reagent transfer. The Echo 525 Liquid Handler provides rapid transfers from 25 nL to 5 µL per well. With its versatile fluid range, transfer volume range, any well to any well transfer capability, and powerful applications software, the Echo 525 Liquid Handler supports a wide range of genomics workflows.

Impacts on Genomics Research

Up to 100x Reduction in Assay Volume

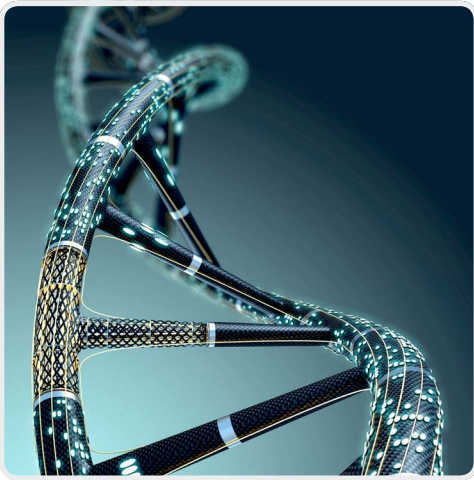


Since introducing the Echo Liquid Handler in 2004, we have continued to help our customers attain better scientific data while reducing costs and waste in a wide range of applications. In 2012, with the introduction of the Echo 525 Liquid Handler, we were able to quickly extend those benefits to genomics research. Echo Liquid Handlers overcome traditional barriers in genomics by dramatically reducing sample and reagent volume requirements. While miniaturization reduces research costs, the Echo system's non-contact transfer also eliminates cross-contamination to ensure reliable and reproducible data. From the basics of PCR setup to the complexities of synthetic biology, the Echo Liquid Handler saves time and money, improves decision making, and empowers research programs.

Impact of Miniaturization in Genomics Research Applications

Application	Cost per Reaction (as recommended)	Miniaturized Cost per Reaction	Volume Reduction (up to...)
Gibson / Golden Gate DNA Assembly	\$15.90	\$0.16	100x
NGS Library Prep	\$72.91	\$0.73	100x
Sanger Sequencing	\$0.26	\$0.06	4x
MDA Setup	\$17.64	\$4.41	4x
SmartSeq 4 Setup	\$112.00	\$22.00	5x
PCR / qPCR	\$0.27	\$0.05	6x

Echo Liquid Handlers *for* Synthetic Biology



For more information, visit www.labcyte.com/synbio

Miniaturize and Accelerate DNA Assembly and QC for Gene Synthesis

Traditional DNA assembly methods require reactions of 10–20 microliters per well. The Echo Liquid Handler can reduce the volume up to 100-fold, drastically cutting reagent costs. With the ability to reliably transfer volumes as low as 25 nanoliters, Echo systems can extend the useful life of a primer library and eliminate the need to dilute high-concentration primers, saving on storage and primer costs and preventing dilution errors. Market-leading synthetic biology companies use Echo Liquid Handlers to automate gene synthesis with higher throughput and lower cost than they could with tip-based liquid handlers.



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.¹

— Paulina Kanigowska, *et al.*
JALA 2015

Reduce Costs with Miniaturization of Gibson and Golden Gate Assembly Methods

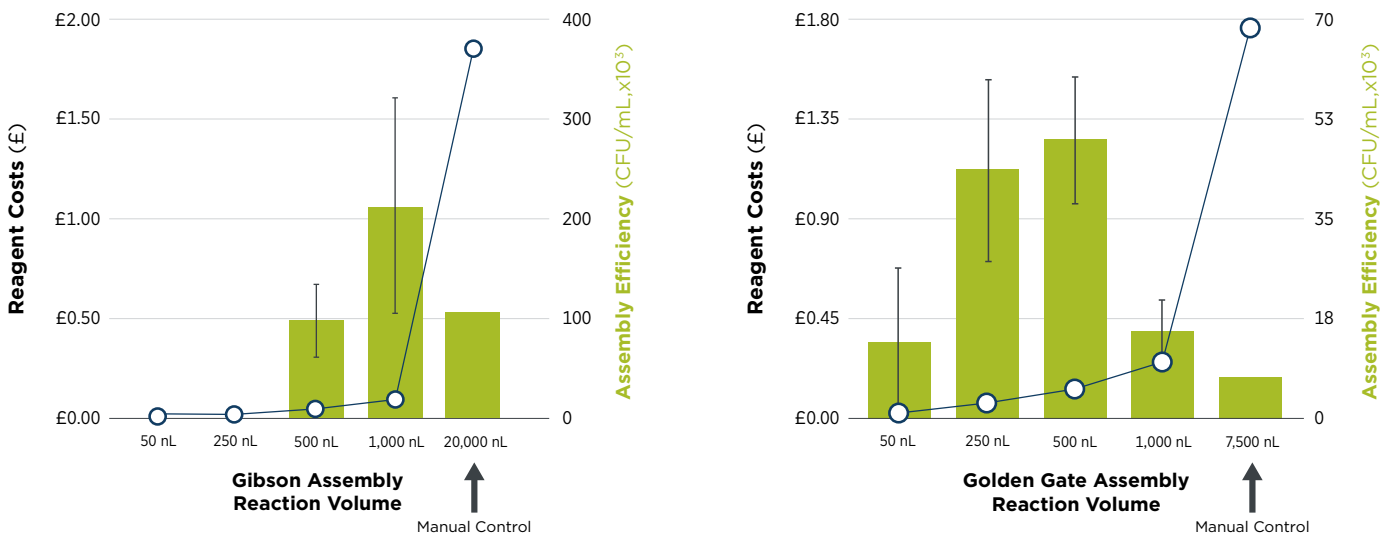
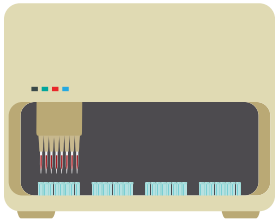


FIGURE 2: Cost-effectiveness and assembly efficiency comparison of different reaction volumes. Panel A: Gibson assembly. Panel B: Golden Gate assembly.¹

Save 15 Hours on Your Synthetic Biology Workflow

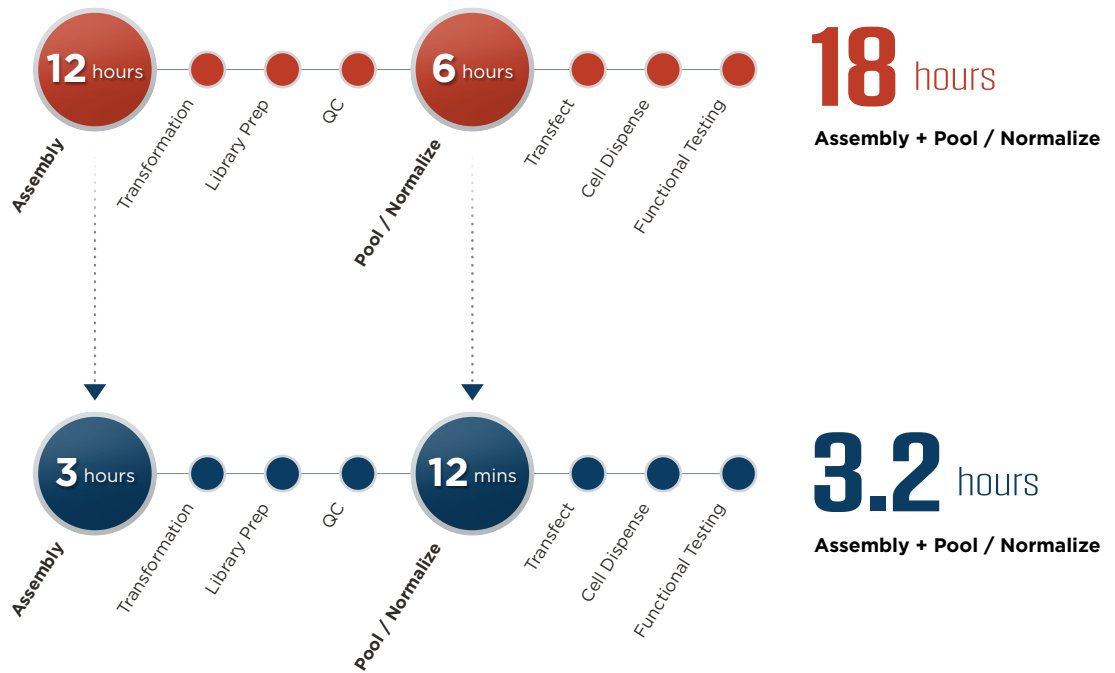
A Comparison to the Traditional Liquid Handling Approach



Traditional LIQUID HANDLER



Echo® 525 LIQUID HANDLER



The Echo system can rapidly pool oligos or DNA fragments from library plates. Since there is no contact with the fluid and no time spent changing or washing tips, the Echo system can transfer each oligo or fragment from any well of a microplate in less than a second. This can save 15 hours in a high-throughput setting. Furthermore, since the Echo 525 system has the ability to transfer volumes as low as 25 nanoliters, high-concentration libraries do not have to be diluted prior to transfer, resulting in simultaneous normalization while pooling. This enables equal distribution of reads to every sample and very even representation of all samples. This greatly reduces the time to normalize and pool libraries and improves the reliability of the entire library preparation process.

Echo Liquid Handlers integrated into an Access™ Workstation provide a high-throughput, fully automated system for pooling oligos, assembling constructs, and spotting colonies. Whether using the Gibson Assembly® or Golden Gate cloning method, tipless acoustic liquid handling reduces costs, waste, and saves time.



[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 Liquid Handlers *for* Sequencing



For more information, visit www.labcyte.com/sequencing

Low Cost, Highly Efficient Library Preparation

Echo Liquid Handlers enable library preparation in low microliter volumes for a range of sequencing methods. Echo systems dramatically reduce reagent costs, save samples, and eliminate steps, all while improving library quality and throughput.

With Sanger sequencing, BigDye® reagent costs can be a limiting factor. Sequencing volumes can be reduced from 10 µL to 2.5 µL using the Echo Liquid Handler for a 4-fold reduction in cost per reaction.

16S rRNA sequencing has long been the method of choice for microbiome researchers. The Echo Liquid Handler allows for miniaturized 16S rRNA sequencing, and NGS reagent cost reduction also enables researchers to shift to miniaturized shotgun sequencing.

Comparison of NGS Library Prep Costs

Description	Manual Pipetting	Echo® Liquid Handler
Amount of DNA	50 ng	0.06 – 2.0 ng
DNA volume (rxn)	25 µL	200 nL
Library prep volume (rxn)	25 µL	300 nL
Total volume	50 µL	0.5 µL
Reactions per kit	96	9600
Cost per reaction	\$72.91	\$0.73

When NGS sequencing programs scale, the cost of library preparation is a limiting factor. Using the Echo Liquid Handler for NGS library preparation versus conventional liquid handlers enables reaction volumes to be reduced by up to 100-fold, dramatically reducing study reagent costs.² With the Echo Liquid Handler’s low-volume acoustic transfer capability, researchers can significantly increase the number of libraries generated while maintaining current budgets.

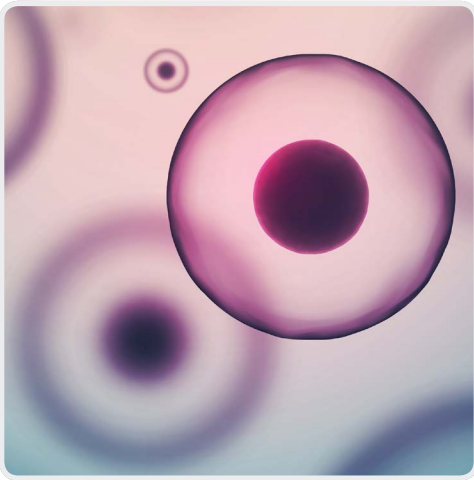
These benefits can be realized with sample preparation kits including Illumina Nextera®/Nextera® XT, KAPA HyperPlus, NEBNext® Ultra™ II, NuGEN Ovation®, and others. This low-volume transfer ability also means that high-concentration libraries do not have to be diluted prior to transfer, resulting in simultaneous normalization while pooling. This enables equal distribution of reads to every sample and even representation across all samples.



We use the [Echo system] because it allows us to perform complex assays in very high throughput, but also allows us to miniaturize those assays and keep costs down.

– **Dr. Chris Bakal**
The Institute of Cancer Research

Echo Liquid Handlers *for* Single-Cell Genomics



For more information, visit www.labcyte.com/single-cell-genomics



[The Echo 550] allows acoustic dispensing of minute volumes and rapid setup of low-volume MDA reactions, while limiting the opportunity for introduction of DNA contamination and reducing tip waste. Reducing the reaction volumes also decreases the costs of MDA reagents.³

- **Christian Rinke, et al.**
Nature Protocols 2014



Using the Echo 525, a scale-down by 50–100x can be achieved with minor modifications of the protocol, leading to significant cost reduction without sacrificing data quality. Furthermore, we demonstrate the superiority of contact-free liquid transfers in molecular biology applications with regard to reproducibility and contamination prevention.

- **Dr. Stephan Lorenz**
Wellcome Trust Sanger Institute

Low-Volume Sequencing Libraries from Single Cells

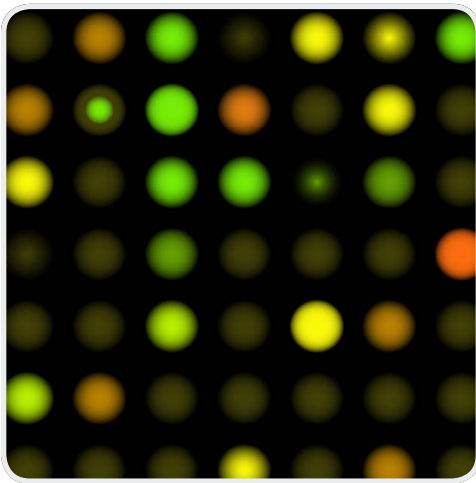
Amplification of DNA from a single cell is inherently susceptible to contamination. Exogenous DNA from tips or nozzles used during the transfer of samples or reagents into a PCR reaction cannot be resolved even with UV-radiation steps prior to transfer. The Echo Liquid Handler's non-contact acoustic transfer completely avoids contact with any DNA to substantially lower contamination risk. Furthermore, the precision and accuracy of the transfer at lower nanoliter volumes eliminates repeat experiments, further reducing reagent costs.

Echo Liquid Handlers miniaturize library preparation for whole genome and transcriptome analysis of genetic material from single cells. With precise, accurate, non-contact transfers, Echo systems can reduce multiple displacement amplification (MDA) and RNA-seq reactions by 75% or more. Libraries for sequencing RNA or DNA can be reduced to 10 μL or less.

Impact of Miniaturization on MDA Reaction Cost

Description	QIAGEN REPLI-g	Echo* Liquid Handler
Cell material	4.0 μL	1.0 μL
Denaturation buffer	3.0 μL	0.75 μL
Stop solution	3.0 μL	0.75 μL
Master mix	40 μL	10 μL
Total volume	50 μL	12.5 μL
Tip cost	\$0.60	-
Cost per reaction	\$17.64	\$4.41

Echo Liquid Handlers *for* qPCR



For more information, visit www.labcyte.com/qpcr



Our findings demonstrate that a single [Echo] system replaces 8–10 traditional liquid handling robots while increasing quality and reproducibility.⁴

— Carol Cain-Hom, *et al.*
J Lab Automation 2016

Cost Effective, High-Throughput RT-qPCR

To avoid the impacts of poor liquid handling performance, researchers traditionally use larger volumes of samples and reagents to prepare qPCR assays, keeping costs high and lowering throughput. Echo Liquid Handlers enable miniaturization with reaction volumes as low as 250 nL, which reduces costs, facilitates higher throughput, and eliminates cross-contamination.

Additionally, precise and accurate transfer of sub-microliter volumes enables the addition of concentrated reagents without prior dilution. With options for integrated plate handling automation and software tailored for genomic research, Echo systems can easily scale for production environments.

Comparison of Genotyping Data and Cross-Contamination Traditional vs. Acoustic Droplet Ejection Liquid Handling

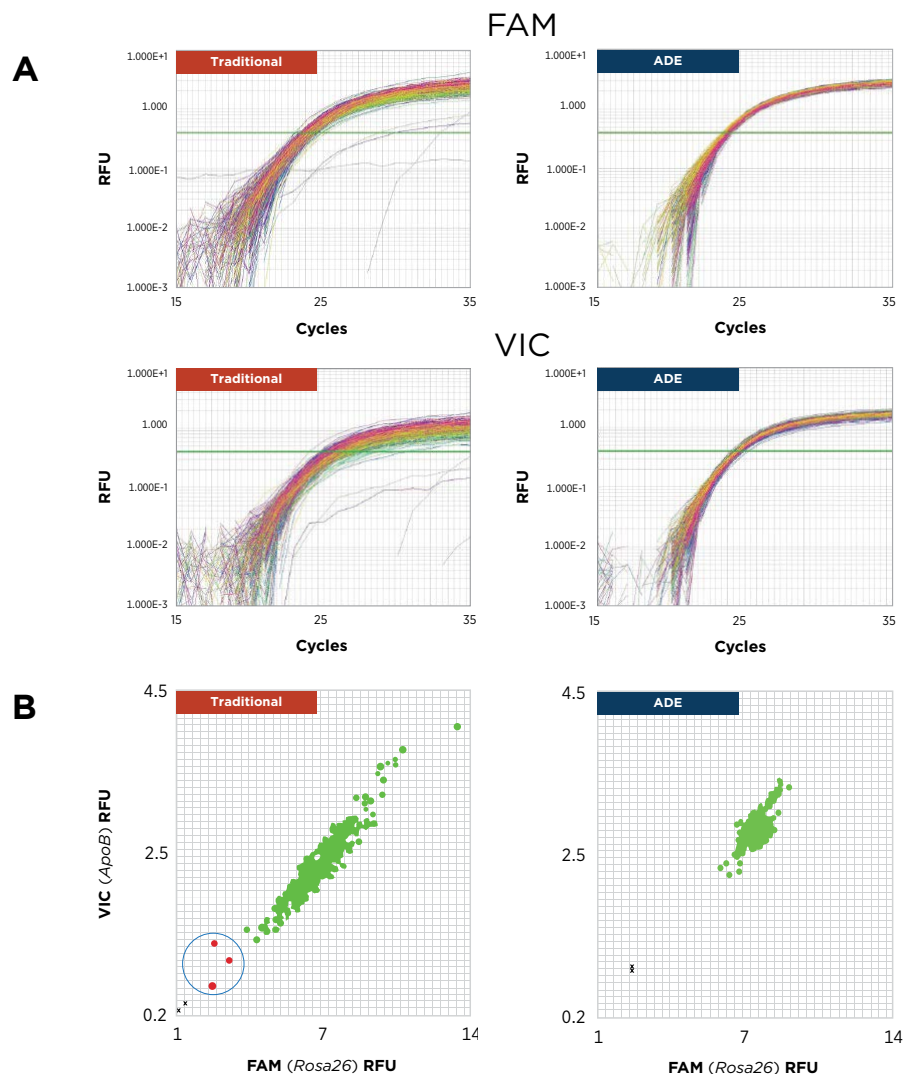


FIGURE 3: Comparison of quantitative PCR (qPCR)-based genotyping data quality by platform. Amplification curves (A) and cluster plots (B) are depicted for both traditional- and acoustic droplet ejection (ADE)-assembled reactions. (A) Curves are illustrated for FAM (top) and VIC (bottom) channels; the green line shows the C_q threshold (0.4). (B) The same data are interpreted as a cluster plot. Black Xs are no-template controls (NTCs), green dots represent experimental samples, and red dots (highlighted by a blue circle) denote ambiguous data samples that cannot be clearly assigned a genotype.⁴

Access™ Laboratory Workstation *for* Genomics Research

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 genomic applications. With the Access Workstation, Echo Liquid Handlers can be easily incorporated into an integrated system to automate genomic workflows including, but not limited to, qPCR, PCR, enzyme reactions, DNA/RNA quantification, sample pooling, and normalization.



For more information, visit
www.labcyte.com/access-workstation

Typical Devices Used in a Genomics Configuration

- Labcyte Echo 525 and/or 550/555 Liquid Handler
- BMG FLUOstar Multimode Reader
- Agilent Technologies PlateLoc Sealer
- Agilent Technologies Microplate Centrifuge
- Brooks Automation XPeel Peeler
- Roche LightCycler 480 or 1536
- Inheco ODTc 384 or 96 Thermal Cycler
- Mecour Thermal Tower

Echo® Software Applications *for* Genomics Research

Quick and Reliable Liquid Handling Task Management

Labcyte has a suite of Echo® Software Applications to assist researchers in creating liquid handling protocols for specific applications. Each application is designed around a specific liquid handling workflow and uses a combination of wizards and graphical interfaces to simplify the creation of plate formats, liquid transfer routines, and output files. Researchers can quickly create a variety of protocols off-line for the Echo Liquid Handler and use built-in simulators to validate every transfer before running live. The suite of Echo software applications enables the Echo Liquid Handler to quickly and efficiently accomplish any liquid handling task. For genomics workflows Echo® Cherry Pick guides file-driven transfers from any well to any well, and Echo® Plate Reformat enables the design of custom layouts used to assemble assays or reformat and replicate screening libraries.

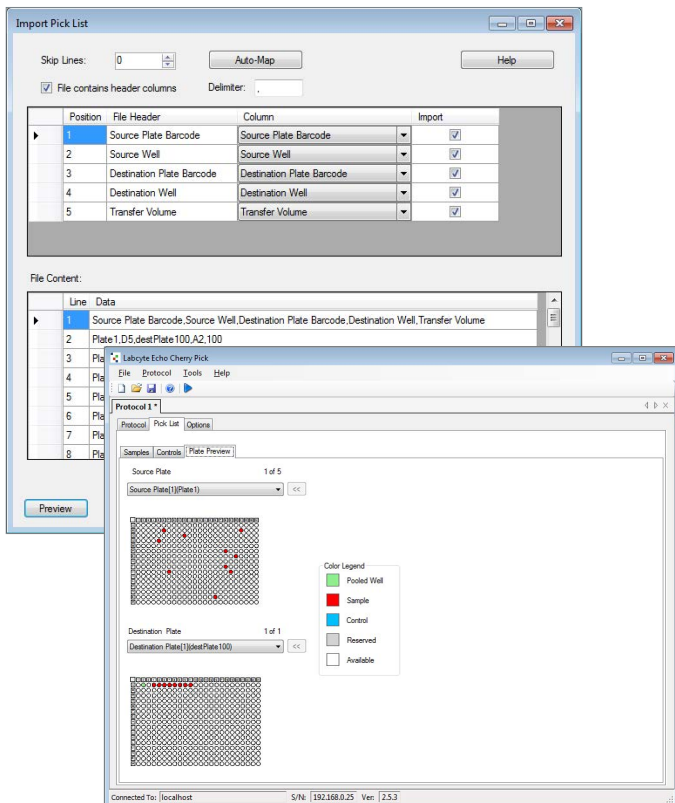


Echo® Cherry Pick

Echo Cherry Pick software uses information in pick lists to transfer from any source well to any destination well, for pooling oligos for gene synthesis or libraries for sequencing.

For more information, visit www.labcyte.com/echo-cherry-pick

File-driven transfers from any well to any well

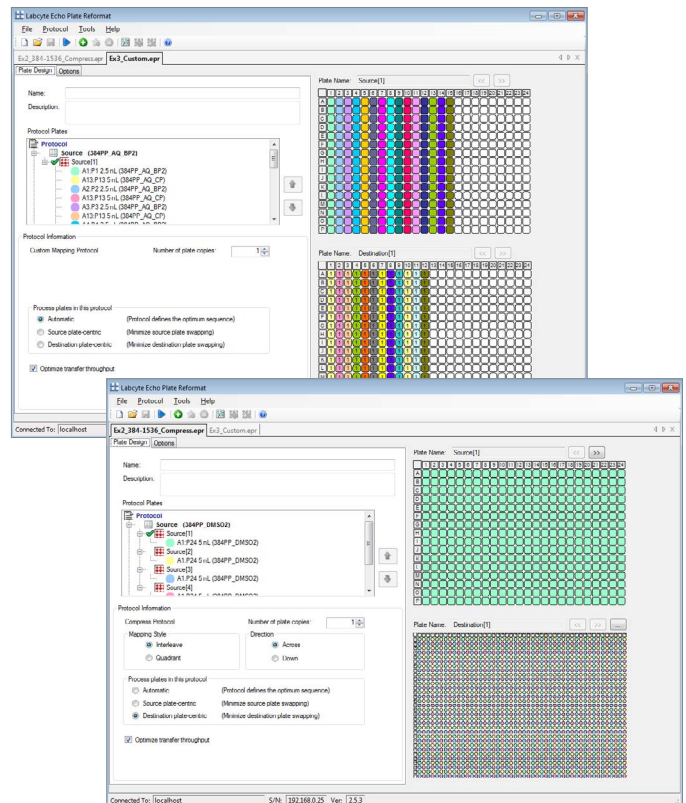


Echo® Plate Reformat

Echo Plate Reformat software offers a variety of transfer functions to design custom layouts. Resulting protocols can be used to assemble assays for NGS library prep, synthetic biology, gene expression, or genotyping.

For more information, visit www.labcyte.com/echo-plate-reformat

Design, develop, and assemble assays



Echo[®] Qualified Consumables *for* Genomics Research



Echo[®] Qualified Source Microplates

Echo[®] Qualified 384-well 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, tissue culture-treated, or sterile options.

For more information, visit www.labcyte.com/echo-qualified-source-plates



Echo[®] Qualified Reservoir

The Echo Qualified Reservoir microplate enables convenient assay assembly and efficient large reagent volume transfers, with the ability to dispense up to 2.55 mL per well.

For more information, visit www.labcyte.com/echo-qualified-reservoir

Labcyte Service and Support



Maximize Your Instrument Performance

Timely service and preventive maintenance are essential for optimal instrument performance and data quality. Labcyte offers a range of service contract options for the Echo Liquid Handler and Access Laboratory Workstation to fit every lab's needs and budget. Labcyte provides global field service and applications support with local personnel in the United States, United Kingdom, continental Europe, Australia, and Asia. Our application scientists have extensive experience with genomics workflows and provide support and training on all Labcyte products to help you maximize the utility of the Echo Liquid Handler and Access Laboratory Workstations.

For more information, visit www.labcyte.com/labcyte-support

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- 4 Mammalian Genotyping Using Acoustic Droplet Ejection for Enhanced Data Reproducibility, Superior Throughput, and Minimized Cross-Contamination. Cain-Hom *et al.*, *J Lab Automation*, 2016.



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